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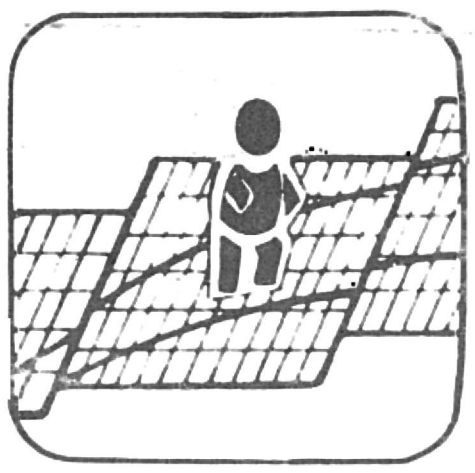

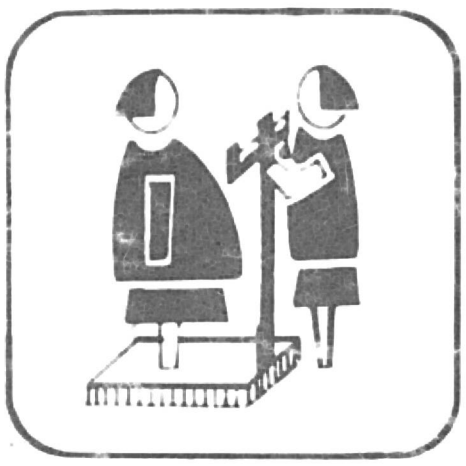

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PUBLICACIONES INCAP RELACIONADAS CON DESNUTRICION PROTEINICO-ENERGETICA

Noviembre, 1989

Instituto de Nutrición de Centro América y Panamá
Apartado Postal 1188 □ Guatemala, Guatemala, C.A.

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Esta bibliografía especializada compila las publicaciones sobre malnutrición proteínico-energética en general, realizadas por profesionales del INCAP de 1966 a 1987.

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No. 3 Diagnóstico e indicadores de desnutrición

No. 4 Nutrición e infección

No. 5 Tratamiento de la desnutrición proteínico-energética

No. 6 Desnutrición, planificación y desarrollo

El propósito de esta serie de cinco documentos es proporcionar información básica a docentes, investigadores y planificadores sobre las investigaciones realizadas por el INCAP en el campo de la desnutrición.

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FACTORES FAMILIARES DE LA DESNUTRICION PROTEICO CALORICA EN EL PRE-ESCOLAR, EN APOPA, EL SALVADOR

Dr. José María Ticas.**
Dr. Werner Ascoli ***
Dr. Miguel A. Guzmán****
Srita. Olga Tatiana Osegueda*****

ANTECEDENTES

En la epidemiología de la malnutrición se han descrito un gran número de factores contribuyentes, entre ellos se pueden mencionar: pobreza, ignorancia, infecciones frecuentes, abandono por la madre, creencias o hábitos alimentarios malos, baja disponibilidad de alimentos, etc. Existen muchos trabajos en que se mencionan estos factores (1,2, 3,4,5), pero raras veces han sido cuantificados.
En 1959, Welbourn (6) en Uganda, Africa, estudió un grupo de niños africanos que habían asistido con regularidad a un Centro de Salud. Comparando aquellos niños que desarrollaron malnutrición severa con aquellos que se desarrollaron normalmente encontró que los malnutri-

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* Trabajo presentado en el I Congreso Latinoamericano de Nutrición-Caracas 1968.

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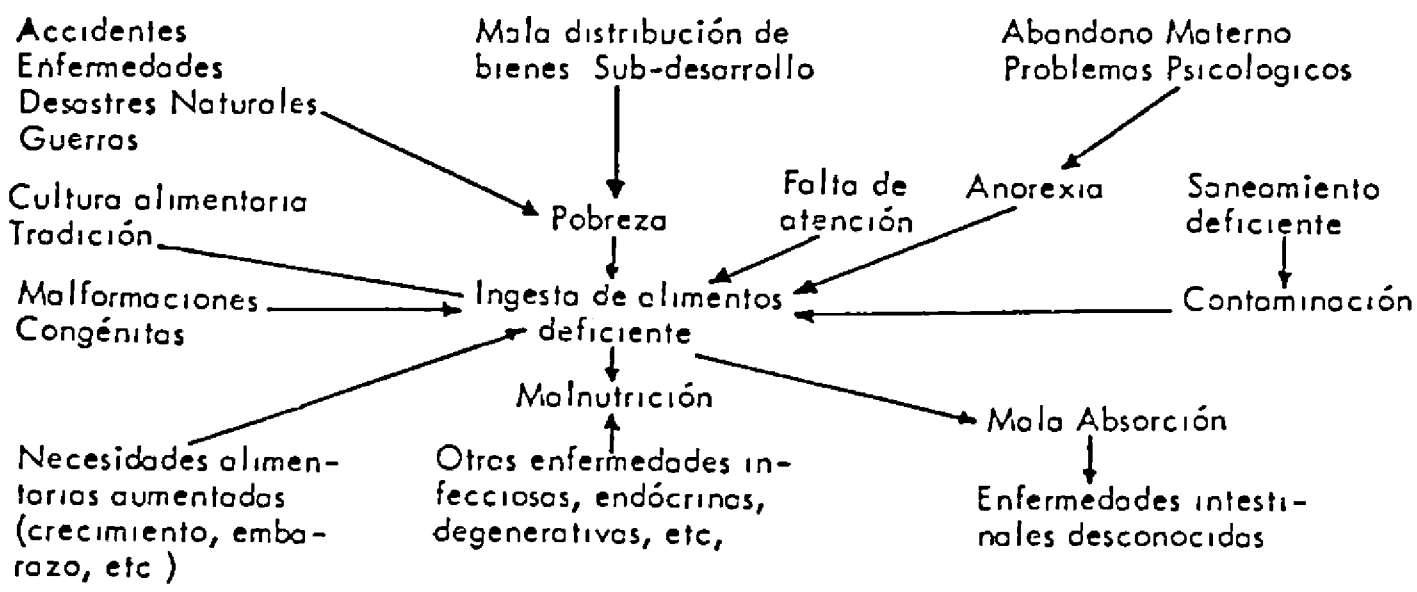
dos venían con mayor frecuencia del área rural y de familias con mortalidad alta. El siguiente cuadro muestra otras diferencias·

	Malnutridos %	Normales %
Abandono por la madre	46	9
Lactancia por un año o más	9	52
Lactancia por menos de 6 meses	64	13
Destete antes de un año de edad	73	41

En Durban, también en Africa, Scragg y Rubidge (7) estudiaron las causas contribuyentes en 1565· casos de malnutrición severa hospitalizados. Aunque no cuantifican sus resultados, entre las causas mencionan pobreza, viviendos malas, falta de atención materna, alta tasa de ilegitimidad, ignorancia e infecciones
Mundel y Fischl (8), en Israel, también sin cuantificar sus datos, compararon a 87 niños malnutridos con un grupo de niños normales, encontrando los siguientes factores familias más numerosas, familias más inestables en su lugar de residencia, enfermedades y hospitalizaciones.
Williams (4) en Ghana, en un estudio de 28 niños con Kwashiorkor , encontró 48 causas básicas divididas en la siguiente forma

4 falta de alimentos
19 causas sociales y psicológicas
17 infecciones
8 destete prematuro.

En el mismo artículo, la autoia presenta un esquema sobre algunas causas de malnutrición que parece interesante.



En vista de que existen muy pocos trabajos que dan una idea cuantitiva del problema nutricional, y que aún existen menos datos que permitan al trabajador de Salud Pública atacar el problema nutricional al nivel de la familia, se considera de sumo interés realizar un trabajo que permita llenar estos dos vacíos.
En muchas ocasiones hemos observado la "frustración" del trabajador de Salud Pública ante una situación la cual no puede atacar por falta de conocimientos adecuados.
Conociendo en detalle el peso que cada factor desencadenante ejerce sobre la situación nutricional de la familia, pone en mano de estos trabajadores un arma para atacarlo eficientemente.
Considerando el problema nutricional a nivel regional o nacional, este tipo de datos permite trazar planes a largo plazo mucho más realistas y factibles.

MATERIAL Y METODOS

1.- Muestra.

Se seleccionaron 80 familias de Apopa una comunidad en la parte Central de El Salvador que contaba con pre-escolares que recibían atención rutinaria en el Servicio de Salud. El estado Nutricional del niño menor de cada familia se clasificó según Gómez (9) en Normales y Desnutridos de 1o., 2o., y 3o., grados.
El criterio para su selección fue conforme al orden de llegada a la Unidad de Salud, cuando alguno de sus miembros buscaba atención médica.

2.- Recolección de Datos.

Se elaboró una ficha para poder registrar los datos de la encuesta, recurriéndose a la entrevista en el hogar para interrogar a la madre y también realizar la encuesta dietética respectiva.
A nivel comunal se verificó un estudio para determinar que clase de alimentos existían en el mercado, sus precios y sus unidades de medida para poderlas convertir a medidas de peso.

a) DATOS DIETETICOS.

Se realizaron encuestas dietéticas, siguiendo el método del registro diario (Observación Directa) en 32 de las 80 familias del estudio.

b) DATOS ECONOMICOS.

Para poder valorar el poder adquisitivo de las familias se procedio al interrogatorio de las madres de todas las 80 familias sobre los

ingresos mensuales procedentes de salarios, ventas de productos agrícolas, pecuarios, manufacturados etc.,

c) DATOS SOCIALES Y CULTURALES.

Estos datos fueron obtenidos por interrogatorio de las madres.

d) DATOS PATOLOGICOS.

Estos datos se obtuvieron por la revisión de los expedientes clínicos del servicio más el interrogatorio de las madres La información fue limitada a los 3 meses previos a la encuesta.

RESULTADOS.

Las características demográficas de la muestra se indican en la tabla No.1. El número de niños para cada uno de los grupos nutricionales es de 13 para los normales, 44 para los desnutridos de primer grado y 23 para los de segundo y tercer grado.
El número de miembros por familia para cada grupo aumenta con los diferentes grados, lo que indica que los grados más avanzados ocurren en familias con mayor número de niños pre-escolares Sin embargo, el número de niños escolares disminuye, lo cual pudiera indicar una mayor mortalidad en las familias con los grados más avanzados de desnutrición o un egreso de los niños más temprano del hogar.
En la tabla No. 2 se observan los gastos de las familias para la alimentación. Mientras más avanzado es el grado de desnutricion, menos es el gasto mensual para alimentación por familia y por individuo
Igualmente es menor el ingreso mensual, mientras que la proporción de egresos para la alimentación no difiere en mucho.
Por último se muestra el costo mensual de una dieta mínima adecuada, que en el caso de las familias con niños de 2o y 3o grado de desnutrición sobrepasa los ingresos mensuales en un 16.5 %.
A continuación, la tabla No. 3 muestra la adecuación de calorías y proteínas de las familias y de los niños Estos datos indican que solamente en la adecuación de calorías los niños en la familia con desnutrición de segundo y tercer grado están en desventaja en relación a la familia. Con respecto a proteínas totales y proteínas de origen animal la distribución intrafamiliar es equitativa en los tres grupos, aunque proporcionalmente menor conforme aumenta el grado de desnutrición.
El ausentismo de la madre durante las comidas del niño se observa en la tabla No 4. Tanto el porcentaje de madres que se ausentan como en el porcentaje de comidas sin la madre, los niños con los mayores grados de desnutrición son los más afectados. Este hecho parece indicar que estas madres se ausentan del hogar por razones económicas.
El abandono del hogar por el padre también se investigó, no encontrandose diferencias entre los tres grupos nutricionales

La investigación de las razones para no dar alimentos de alto valor nutritivo a los niños, por interrogatorio de las madres dió los resultados que se muestran en la tabla No. 5.
La gran mayoría de las madres manifestaron que al niño no le gustan estos alimentos. Una tercera parte· dieron razones económicas, y una quinta parte razones de enfermedad. Los factores ignorancia y no disponibilidad fueron menores. En vista de los datos económicos presentados anteriormente pudiera pensarse que la mayoría de las madres trata de encubrir su pobreza dando la razón de que los alimentos no le gustan al niño o bien expresan sus propios gustos.
El factor enfermedades infecciosas se encuentra en la tabla No. 6. Entre éstas se incluyen diarreas, infecciones respiratorias, sarampión y tosferina. La incidencia en los tres grupos no varía mientras que la duración promedio de las enfermedades y por consiguiente el número de días de enfermedad por niño por año aumentan apresuradamente conforme aumenta la desnutrición. Este hecho indica que la susceptibilidad a las enfermedades infecciosas es igual, pero su duración y probablemente su severidad aumentan con la desnutrición. Estas enfermedades también influyen a empeorar el grado de desnutrición, tanto por su efecto directo sobre el organismo como por la anorexia y menor absorción que las acompañe.

DISCUSION.

El presente estudio podría constituir un método para establecer el diagnóstico referente al consumo de alimentos en la familia y, en cierta medida, a la utilización de nutrientes puesto que analiza la incidencia de infecciones en los niños.
Su utilidad es válida para cualquier familia que se estudie, ya que trata de identificar aquellos factores que son responsables de un bajo consumo de alimentos en los menores de 5 años, llegando así a tener una concepción más ajustada de la realidad socio-económico y cultural de la familia, lo cual significaría una enorme ventaja para el trabajador de campo que trata de recuperar a niños desnutridos, porque sólo entendiendo la problemática familiar se puede esperar posibilidad de obtener éxito en la rehabilitación nutricional.
También es útil para medir estos factores a un nivel comunal, tal como se ha detallado en el estudio, permitiendo el establecimiento de normas más racionales en la determinación de programas nutricionales, así por ejemplo, en la comunidad estudiada se hace evidente el grave problema económico familiar, seguido por el de las enfermedades infecciosas y terminando con los de orden social y cultural, de tal manera que cualquier programa de nutrición aplicada en este tipo de comunidades debe incluir una suplementación alimentaria a la mayoría de las familias mientras no existan disponibles en el mercado productos de alto valor biológico y bajo costo lo cual permitiría rescatar un buen número de familias de la indigencia alimentaria en que viven.

Otra actividad a desarrollar, por su trascendencia para la solvencia económica de muchas familias, sería el de una planificación familiar, sanamente orientada

Dado el impacto que significan las infecciones para el estado nutricional, nunca será de más insistir sobre el saneamiento ambiental apareado a un programa educativo tendiente a disminuir la alta contaminación fecal del ambiente y, finalmente, aumentar a niveles óptimos la cobertura de individuos vacunados.

Obviamente, estos resultados no incluyen una serie de factores a nivel nacional tales como producción, distribución, almacenamiento y mercadeo de alimentos que atacados por una política nacional de alimentación al más alto nivel, de por sí, pueden reducir su costo y aumentar la disponibilidad a nivel de la familia en comunidades como la aquí estudiada.

TABLA No. 1
CARACTERISTICAS DEMOGRAFICAS DE LA MUESTRA
APOPA 1966 - 67.

ESTADO NUTFICIONAL	No. de Niños Menores de 5 años	Miembro/ familia	Promedio de Niños de 0-4 años por familia.	Promedio de Niños de 5-14 años por familia.
Normal	13	5 8	1 7	1 9
Desnutrición de 1er grado	44	6.2	1 8	1 7
Desnutrición de 2o y 3er. grado.	23	6 6	2 0	1 4

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TABLA No. 2
GASTOS PARA LA ALIMENTACION FAMILIAR
APOPA 1966 - 67

ESTADO NUTRICIONAL	Promedio de Gastos para Alimentacion ₡/mes.		Promedio de ingreso ₡/mes	% de Egresos para alimentación	Costo de Dieta Minima adecuada ₡/mes	% costo de Dieta Mínima/ingreso
	Familia	Persona				
Normal	130 84	22 4	214 37	61 0	150 30	70 1
Desnutricion de 1er gdo.	102 93	16 6	198 01	52 0	160 40	81 0
Desnutrición de 2o y 3o grado	81 24	12 3	146 04	55 6	170 20	116 5

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TABLA No. 3
POR CIENTO ADECUACION DE CALORIAS Y PROTEINAS EN 32 FAMILIAS Y NIÑOS MENORES DE 5 AÑOS.
(METODO DE REGISTRO)
APOPA 1966-67.

ESTADO NUTRICIONAL	CALORIAS		PROTEINAS TOTALES		PROTEINAS ANIMALES	
	Familia	Niño	Familia	Niño	Familia	Niño
Normal	89 5	106 1	116 7	157 0	50 4	46 7
Desnutrido de 1er gdo	109 7	101 1	109 7	135 1	32 5	49 7
Desnutrido de 2o y 3er grado	90 0	67 4	101 3	94 1	23 2	29 0

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TABLA No. 4
AUSENTISMO DE LOS PADRES - APOPA 1966-67.

ESTADO NUTRICIONAL	MADRE		PADRE
	% que se ausentan	% de comidas que se Ausentan	% de Ausentes
Normal	7 7	15 3	7 7
Desnutrición de 1er gdo	6 3	20 5	31 8
Desnutrición de 2do y 3er grado	11 9	26 4	17 4

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TABLA No. 5
RAZONES PARA NO DAR ALIMENTOS DE ALTO VALOR NUTRITIVO
APOPA 1966- 67.

R A Z O N E S	% DE FAMILIAS
No gusta al niño	86.4
Ecorórticas	30.9
Producen enfermedades al niño	19.8
Falta de conocimiento	13.6
No existen en el mercado	2.5

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TABLA No. 6
ENFERMEDADES INFECCIOSAS POR TASA DE ATAQUE, DURACION
Y DIAS DE ENFERMEDADES POR NIÑO.
APOPA 1966-67.

ESTADO NUTRICIONAL	Tasa de ataque/ 100	Duracion Promedio (Días)	Días Enfermedad/ Niño/año.
Normal	470	6.1	45 9
Desnutrición de 1er. gdo.	460	7.1	52.1
Desnutrición de 2do. y 3er grado	480	9 7	70 7

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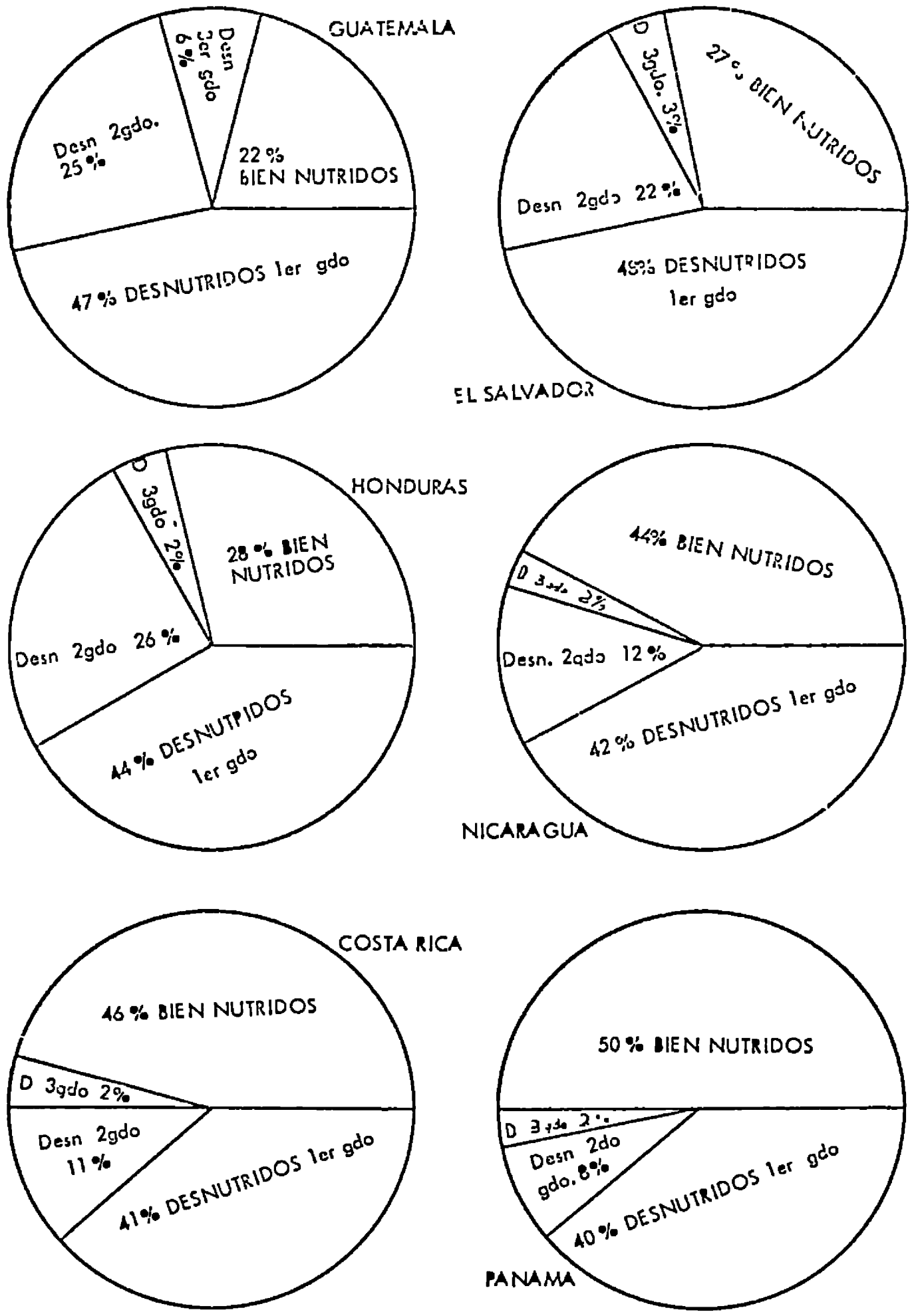

FUENTE Graficos elaborados según datos notificados en "Hechos que revelan Progreso en Salud" 1971. Publicación de OPS.

I-385 Béhar, M. "Disturbances of nutrition (Chapter 7). (1) Protein-calorie malnutrition. (5) Miscellaneous deficiencies. In: Diseases of Children in the Subtropics and Tropics. D.B. Jelliffe (Ed.) 2nd. ed. London, Edward Arnold (Publishers) Ltd., 1970, pp. 161-184, 204-214.

Chapter 7
Disturbances of Nutrition

(*1*) *Protein–Calorie Malnutrition*

M. BÉHAR
Guatamala, C.A.

Health or disease are the resultants of the interaction between man and his environment. The tropical and subtropical areas of the world have, at the present time, ecological conditions favouring the greater frequency and severity of certain pathological conditions, among which are the nutritional deficiencies. This is not primarily related to the physical characteristics of the environment, but more to the biological and particularly to the socio-economic characteristics of these areas, which include most of the nations which are behind in technological, social and economic development. The disease pattern in the tropics, particularly in nutrition, is at the present time very like that of the more developed nations, 50 to 100 yr ago when they were in a similar stage of development. Kwashiorkor is fundamentally the same syndrome described as 'Mehlnarshaden' or 'Starch dystrophy' in Europe at the beginning of the present century. Rickets, a nutritional deficiency particularly influenced by the physical environment and, for this reason, more likely to occur in the temperate zones of the world, has been practically eliminated from these areas for the last 30 to 40 yr. The disease is, however, still seen in tropical and subtropical countries in spite of the abundance of sunlight in these areas and as a consequence of the living conditions determined by socioeconomic factors.

Children, as organisms in the process of growth and development, less prepared to confront the adverse forces of the environment, are particularly prone to suffer the unfavourable ecological conditions more than the adult population. In the particular case of nutritional deficiencies, they also have proportionately greater nutritional requirements than adults for the most essential nutrients.

All these factors explain why nutritional deficiencies are at the present time one of the major health problems in the tropical and subtropical regions, and why the problem is particularly serious in children. For the maintenance of good nutritional status, the diet should be adequate, both in quantitative and qualitative terms. Nutritional deficiency syndromes may result from an overall, quantitative deficiency of all-essential nutrients, with an adequately

Disturbances of Nutrition (Capítulo 7). (1) Protein-Calorie Malnutrition. (5) Miscellaneous Deficiencies. En: Diseases of Children in the Subtropics and Tropics. Ed. D. B. Jelliffe. 2a. ed. London, Edward Arnold (Publishers) Ltd., 1970 pp. 161-184, 204-214.
I-385

balanced diet; with calories in this case, representing the main limiting factor. This situation cannot be corrected, however, by providing more calories, as this would result in a deficit of the other nutrients. An increase of the whole balanced diet is therefore necessary, in this case, for its correction.

Other nutritional deficiency syndromes are the result of insufficient availability of one or more specific essential nutrients for the organism. However, due to the fact that diets deficient in one essential nutrient are also likely to be deficient in others which are usually provided by the same food items, as well as to the frequent interactions between nutrients, it is rare to observe, under natural conditions, a pure deficiency of one specific essential nutrient. In pellagra, for instance, where nicotinic acid deficiency is primarily responsible, deficiencies of B complex vitamins are also usually present. Nevertheless, it is important in the classification of nutritional deficiency syndromes, for deciding as to both prevention and treatment, to identify the nutrient or nutrients primarily responsible.

In this chapter, the overall deficiency of the total diet which, as has been indicated, results primarily in an insufficiency of calories, is discussed together with protein deficiency to which it is closely interrelated in the group of syndromes known collectively as protein–calorie malnutrition. The vitamin and mineral deficiencies of greater importance, as public health problems for children in the tropical and subtropical areas, are covered in other sections.

Greater attention is given to the nutritional deficiencies of primary or dietary origin resulting from an inadequate intake of nutrients. Even with an adequate diet, nutritional deficiencies may also result from pathological conditions of the host determining greater than normal requirements, or interfering with the proper absorption or utilization of the ingested nutrients. These nutritional deficiencies of secondary origin are relatively less important as public health problems than the primary ones, and in general, are not different in the tropics than in the temperate zones, they are therefore not given special attention in this chapter The effect of the common infectious diseases highly prevalent in the tropical areas on the nutritional status of the host, is however, briefly discussed when pertinent, because of its public health significance and because these infectious processes are also influenced by nutritional deficiencies

The term protein–calorie malnutrition (PCM) comprises a variety of very closely interrelated clinical syndromes. These various syndromes are the result of differences in the severity and duration of the deficiencies, the age of the child, and the relative importance of the protein deficiency in regard to that of calories Intermediate or combined forms in different stages of development are frequently observed The presence of infectious processes and/or of other superimposed or concomitant nutritional deficiencies, further complicates the picture. This explains why no complete agreement exists among different clinicians, working in different areas, and even within the same area, in regard to the classification and terminology of the PCM syndromes. The more typical conditions in the advanced or severe stages of development are, however, easy to identify There are the syndromes known as marasmus and kwashiorkor which are described first. The intermediate or

combined forms are then discussed, and finally, the less advanced stages (described as mild to moderate forms) in which the differentiation in types is even more difficult and frequently impossible.

Protein–caloric malnutrition in any of the forms indicated is frequently observed in most of the tropical and subtropical countries, and in many of them constitutes one of the most serious health problems (Scrimshaw and Béhar, 1959; Trowell, Davies and Dean, 1954).

Marasmus

Aetiology. Marasmus, of primary or dietary origin, which is the most commonly observed in the tropics, is the result of starvation in small children. The children are fed a diet which may be adequate in qualitative terms in regard to the concentration of nutrients in the foods given, but very insufficient in total amount to satisfy the minimum requirements of the rapidly growing child. Under these circumstances, calories become the most limiting factor and in the adaptation mechanism the child survives utilizing its own tissues to maintain minimum metabolic functions. In such cases, even if the diet is grossly deficient in most of the essential nutrients, the clinical, physiological, biochemical and pathological alterations characteristic of these deficiencies are not apparent. The results are therefore the same if the child is fed with diluted cow's milk or with thin starchy gruels, as long as the severe calorie restriction is similar.

The picture may develop in infants fed exclusively on mother's milk when the amount of breast milk is markedly reduced. This may happen in malnourished mothers, but only if malnutrition is extreme. It also can occur with prolonged breast feeding with inadequate other foods (late marasmus or breast starvation). More frequently, marasmus is seen in young infants fed artificially. For the large majority of low socioeconomic status populations living in tropical and subtropical areas, substitutes to the mother's milk are unavailable or even unknown. If small infants have to be fed artificially, they may be given over-diluted cow's milk, very thin gruels made out of cereals or other starchy products. The fear of diarrhoea is one of the major factors determining this practice. Even mothers of higher socioeconomic status, or of a better educational level who may start feeding their infants, after weaning, with adequate amounts of cow's milk, may reduce the child's diet very drastically and for long periods of time if the child develops diarrhoea, and this unfortunately occurs very frequently because of the poor sanitary conditions of the environment. Since in most tropical areas acute diarrhoea is the main cause of death of small children, the fear of this condition is such that mothers will let their children cry from hunger and rapidly lose weight rather than give them foods which they believe will aggravate the diarrhoea. Unfortunately, this erroneous concept of severe dietary restriction for the treatment of diarrhoeas, which was encouraged by paediatricians, has persisted and has been exaggerated in many populations.

Social changes also induce or force the mothers to early weaning when they are not yet educationally prepared or do not have adequate resources for safe artificial feeding. This situation is continuously increasing in areas of rapid

industrialization and/or urbanization. Other conditions of the child, such as prematurity, local diseases or malformations of the mouth and nose which interfere with adequate feeding, and particularly with breast feeding, may also be responsible for a limited food intake causing marasmus. In the tropics, where medical services are less available and adequate, and where there is less consciousness of what is proper nutrition and its importance, all the causes of secondary malnutrition such as chronic debilitating and serious organic diseases or metabolic and endocrine disorders, are more likely to result in severe malnutrition. These cases of secondary marasmus are, however, much less important as public health problems than the primary or dietary cases, but should be kept in mind by physicians working in tropical areas, particularly with patients who do not respond well to adequate dietary treatment. In the large majority of cases, however, and for orientation of the necessary preventive measures, a severely restricted food intake should be considered as the primary and most important cause of marasmus in the tropics.

Marasmus is more frequent in infants than in older children. This is due to two main factors. First, the rapidly growing infant, with very high calorie requirements, can develop the extreme wasting that constitutes marasmus in a relatively short period of time, usually in a matter of a few weeks, when the dietary restriction is severe. In older children, with lower calorie requirements, it takes longer and there is a greater risk for these children to develop serious complications during the process. In such cases, either a serious infectious disease or the development of kwashiorkor is superimposed to their weight loss and then they are either treated or die before reaching the stage of marasmus. The other factor is that for cultural reasons, infants are more likely to be subject to the marasmus-producing type of diet. The effects of this diet and early weaning also increase the incidence of diarrhoea in infants. Marasmus is not, however, the only form in which protein–calorie malnutrition develops in infants, as has been considered by some authors: infants, as well as older children—and even adults—may develop any of the syndromes of PCM if the proper causative factors operate (Jelliffe, 1960; Venkatachalam, Srikantia and Gopalan, 1954; Stanier and Holmes, 1954).

Clinical picture

When the infant is severely restricted in his food intake, growth stops; and he then utilizes his own reserves starting with the subcutaneous fat and then the muscles. During this time, he is usually very hungry, cries continuously, making anxious movements with the head and lips, takes his fingers to the mouth as if trying to find some sort of oral satisfaction and sleeps very poorly. The infant may be either constipated or present the frequent small dark green mucous stools of 'hunger diarrhoea'.

Children not properly cared for during this stage develop the full-blown picture of marasmus. Although their hunger is evident, these cases usually continue to be poorly fed, mainly because of ignorance of the mothers as to how to feed them properly, or due to lack of resources or, as previously indicated, to fear of diarrhoea. Vomiting is also frequent at this stage when

the child is fed improper amounts or quality of food. If a child in this condition is seen by empirical healers (witch doctors, quacks, druggists) or by inexperienced physicians, emphasis is given to treatment with drugs or other measures, some of them self-defeating or dangerous, such as the administration of purgatives, and proper and necessary dietary corrective measures are not instituted. Infectious diseases or acute diarrhoea act frequently at this stage as the precipitating and aggravating factors.

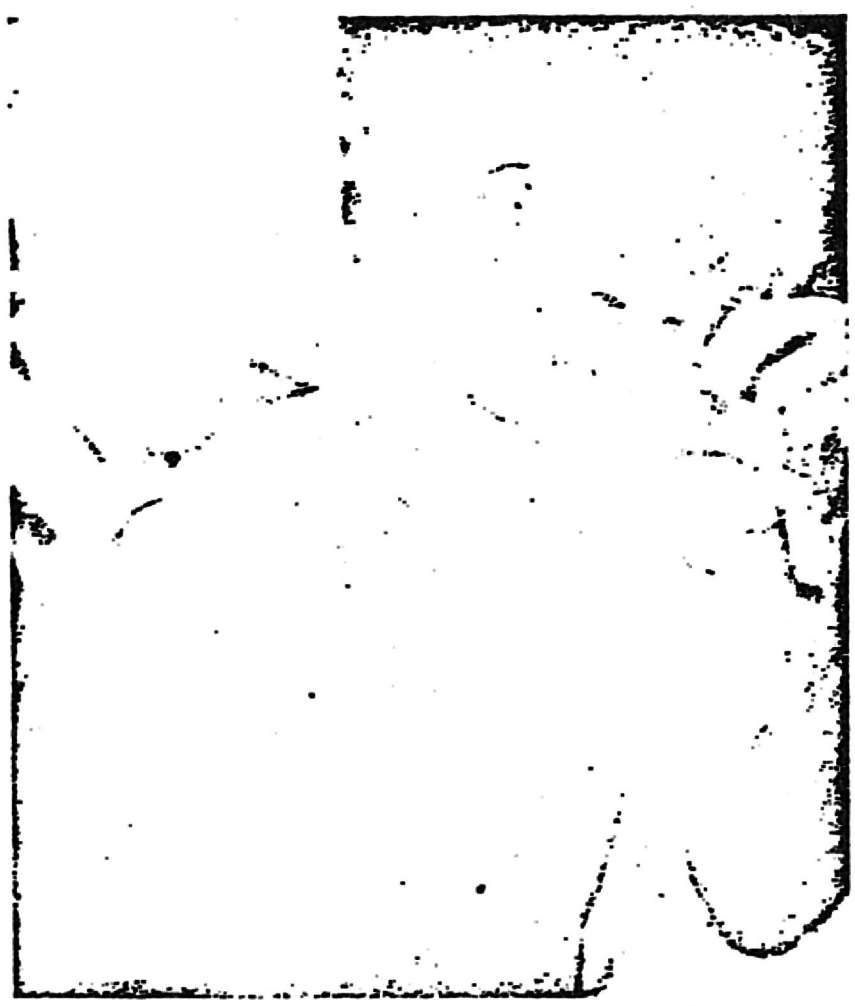

Fig. 7.1. Nutritional marasmus, with terminal diarrhoea. Note extreme loss of both subcutaneous fat and muscle. (Western Nigeria)

The child seen with the full developed picture of marasmus (Fig. 7.1) is usually brought by the mother because of one of the complications mentioned and is an extremely emaciated small child, with practically no subcutaneous fat with the possible exception of the Bichat pouch (sucking pad) which seems to be the last to disappear. The muscles are also extremely atrophic, their shape can, however, be seen under the flaccid skin when contracted, particularly in the face, and may be palpated. The skin is thin, flaccid, wrinkled, seeming larger than the body it covers, particularly when the wasting has been rapid. The mucous membranes are usually reddish, contrasting with a pale and cold skin, particularly at the face and extremities. The bony prominences are marked. The hair is usually not markedly altered, although it may be very thin and dry. The child, although miserable in his general puny appearance, is usually alert, following with his eyes the move-

ments made in his environment, and gestures with anxiety as if asking for care. All these features make up the typical face of the marasmic child which has been compared with that of a very little old man, or a little monkey.

Dehydration frequently complicates the picture when severe diarrhoea and/or vomiting have preceded the admission of the child to the hospital. In these cases, the eyes and fontanelle are sunken, the mucous membranes dry, and the skin even more wrinkled and maintaining the wrinkles produced when it is pinched. These children with dehydration and electrolyte imbalance may also present neurological signs and alterations in muscle tone characteristic of this complication.

The child is usually hungry but does not tolerate large amounts of food and vomits easily. The complications of dehydration and infectious processes, particularly of the respiratory tract, which are difficult to detect owing to the feeble reaction of the defence mechanisms, are usually the terminal episodes. Sepsis of the skin or mucous membranes such as severe moniliasis or cancrum oris are also frequent complications in some regions (Jelliffe, 1952).

PATHOLOGICAL, PHYSIOLOGICAL AND BIOCHEMICAL ALTERATIONS

The clinical criteria for classifying a case as marasmus are not standardized. Indeed, this is not easy, since there is a continuous spectrum from underweight children to marasmus, as well as intermediate cases between this syndrome and kwashiorkor.

It is probable that some similar fundamental alterations are present in both conditions, but in general, we can say that the histological, functional and metabolic alterations are less marked in marasmus than in kwashiorkor We believe that this is due to the fact that the child developing marasmus is forced, in view of his very limited calorie intake, to consume his own tissues. In catabolizing muscles as a source of calories, enough amino acids and other essential nutrients become available to satisfy the minimal needs for maintenance of vital structures and functions. The utilization of fat and muscles to satisfy the basic calorie needs, also requires the maintenance of the fat transport mechanisms and the complex enzyme systems needed for gluconeogenesis. These possibilities may explain why the alterations found in cases in which strict criteria are used for defining marasmus, are minimal, when compared with serious alterations found in kwashiorkor (Viteri *et al*, 1964).

Pathologically, although there is marked atrophy of practically all the organs and tissues the histological alterations are minimal. The haematocrit and haemoglobin concentration values are only slightly reduced except when anaemia of a superimposed cause is present. Vitamin A absorption is normal in marasmus in contrast with very reduced absorption in kwashiorkor (Arroyave *et al*, 1959), and it seems to be the case for other intestinal absorptive mechanisms (Thompson and Trowell, 1952). Although these may not be the primary responsible factors for this difference, the duodenal enzymes have been found in normal concentration in marasmus and extremely reduced, frequently absent, in kwashiorkor (Veghelyi, 1948) The urinary excretion of 17-hydroxycorticosteroids is higher in marasmus than in kwashiorkor, suggesting a failure of the adrenocortical system in kwashiorkor which does not exist in marasmus (Arroyave and Castellanos, 1961).

The basic metabolic rate has been found to be subnormal when expressed in terms of body surface but normal, or even higher than normal, when expressed in terms of body weight in severely marasmic children (Montgomery, 1962).

This has been explained on the basis of the relative preponderance in these children, of tissues such as the central nervous system, heart and kidney which under basal conditions account for a large proportion of oxygen consumption

Overhydration in terms of total body water per unit of weight is found in marasmus

and involves both the intracellular and extracellular fluids (Gomez *et al*, 1957). Total serum proteins and their fractions, although usually reduced, are not nearly as markedly affected as in kwashiorkor (Scrimshaw *et al.*, 1956). The value of total serum protein is usually between 5 and 6 g.% with values of around 3% of albumin and they may even be between normal values. Serum enzymes like amylase and pseudocholinesterase which are very reduced in kwashiorkor, are much less affected in marasmus, frequently between normal values (Waterlow, 1959).

Prognosis and treatment

The prognosis with regard to the life of the child is, in general, good in marasmus, unless severe complications such as dehydration, electrolyte imbalances and infections are also present. If the child does not present these complications or if they can be properly controlled, practically all the cases will recover with an adequate dietary treatment. This consists primarily in providing for the child a complete and balanced diet adequate for his apparent or 'biological' age, but much higher in calories than would be required for a normal child. Levels of 200 cal kg. of body weight and frequently even more, are needed. The progress in weight will indicate if the caloric intake is adequate. The recovery may be slow in extremely marasmic children during the initial stages of treatment, when their food intake cannot be forced to the desired levels, but they usually make adequate and progressively more rapid improvement unless the marasmus is 'secondary' and the initial cause is not discovered and corrected.

The prognosis in terms of complete return to normality is less certain. Not enough and adequately controlled long-term follow-up studies have been made with children recovered from marasmus, but the information available suggests that the smaller the child and the longer the period of serious dietary restriction, the fewer are the possibilities of complete recovery. This has been based on observation of anthropometric measures, particularly height and weight for age, but it would be far more important to know if the situation is similar in the important areas of functional development, especially intellectual capacity, and this has not yet been definitely established.

Kwashiorkor

Aetiology. Kwashiorkor is the result of a diet very low in proteins but providing enough calories to satisfy the needs of the child. The main characteristic of a kwashiorkor-producing diet is its low protein concentration. The proteins are usually also of low biological value and therefore reduce the utilizable protein even further. Cereal grains, starchy fruits and roots are the basic constituents of this type of diet It is obvious therefore, that kwashiorkor is a disease of artificially fed or weaned children Although kwashiorkor may occasionally be seen in breast-fed infants (Davies, 1955), these are probably children receiving small amounts of breast milk and additional sugar or starches. As a rule kwashiorkor occurs only some weeks or months after weaning In most tropical areas, infants are breast-fed at least during their first year of life, and kwashiorkor occurs more frequently during the second and third yr of life although it may also occur in older children (Behar and Scrimshaw, 1960). When in these cultural groups which are not accustomed

to the use of proper substitutes for mother's milk, the children are weaned earlier as a result of social changes, the age of higher incidence of kwashiorkor decreases accordingly. A typical example of this situation was observed in Trinidad where mothers living in the cities started to wean their children at about three months of age and the peak of the incidence of kwashiorkor was then at about 6 mnth of age (Jelliffe and Symonds, 1960).

Kwashiorkor seldom occurs as a consequence of an improper diet alone; in most cases, an infectious disease acts as the precipitating factor; this may be an acute diarrhoea, a respiratory infection or one of the common diseases of childhood, such as measles. A further deterioration of the diet, poorer utilization, and higher requirements are the main mechanisms by which the infectious processes precipitate the development of kwashiorkor (Scrimshaw, 1964). Other stresses, such as the psychological impact of separation of the child from the mother, may also have similar effects (Thompson and Trowell, 1952),

Clinical picture

Apathy and anorexia are early manifestations of kwashiorkor. The child being fed an imbalanced diet very low in proteins, becomes less lively and refuses to eat, but it is usually after an acute episode of diarrhoea or of another infectious disease or other stress from which he never recovers completely, that the full-blown picture of kwashiorkor ensues.

Fig 7 2 Kwashiorkor showing marked oedema, mental changes and sparse, light-coloured hair (compare last with mother). (Indonesia)

Pitting oedema is the main clinical characteristic of kwashiorkor, on which the diagnosis is based (Fig. 7.2). It is soft, painless and of a varied degree. It may be observed only in the feet and ankles or generalized to the whole body with the eyelids swollen shut, limiting the movements of the extremities and with fluid in the peritoneal cavity. The oedema usually starts in the lower extremities often spreading to the upper extremities and to the face. The trunk is the less frequently affected part of the body. *Psychological changes* are almost constant and very characteristic in kwashiorkor. Most children are apathetic, indifferent to their environment and have an expression of misery. They resent being disturbed and protest with a monotonous and weak cry to any stimulus, even when food is given them. In some cases, the children are completely lethargic. At admission to the hospital, all the psychometric tests show considerable impairment when applied in these cases (Barrera Moncada, 1963). This is, however, a transitory stage which is usually corrected in a few days when adequately treated. Any evaluation of psychological or mental damage due to the severe protein deficiency, should therefore be done after initial recovery.

Skin lesions, although not always present, are very characteristic of kwashiorkor (Figs. 7.3 and 7.4). The skin always shows some degree of atrophy, but the typical dermatosis is seen with variable frequency and severity. This dermatosis starts, in some cases, in the form of large areas of erythema simulating second-degree burns, which become progressively dry,

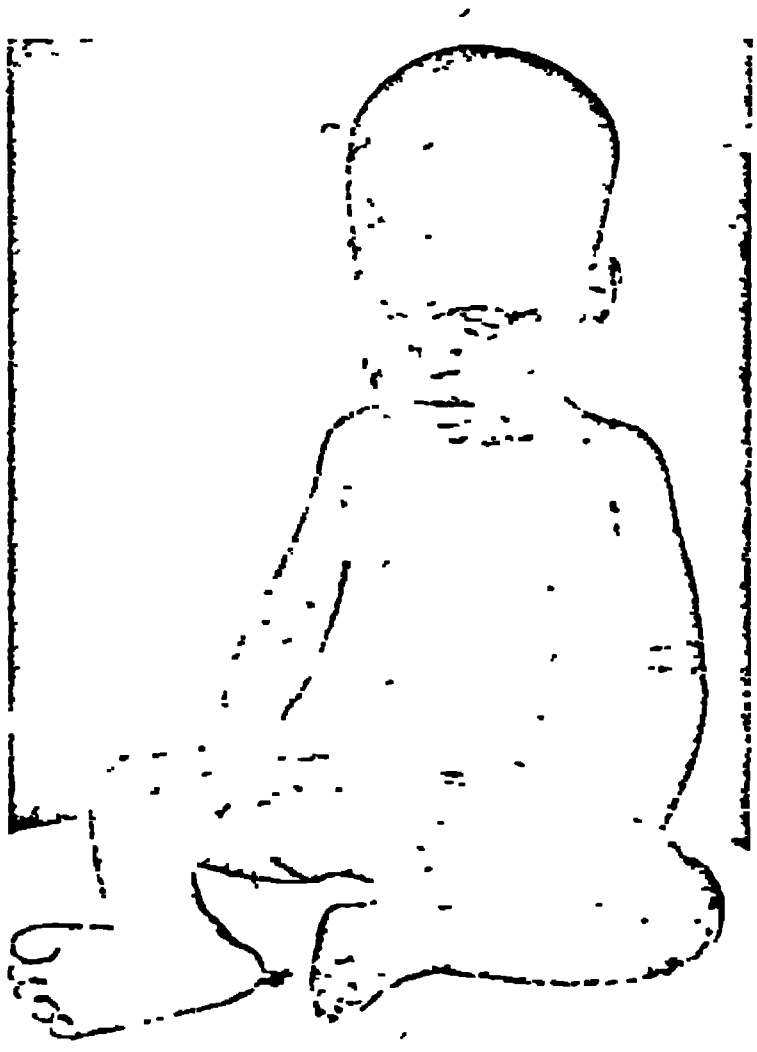

Fig. 7.3 Classical kwashiorkor in Bengali boy, aged 23 mnth, showing misery, oedema, hair changes and 'flaky-paint' dermatosis (Calcutta, India)

hyperkeratotic and hyperpigmented. In other cases, or in other areas, in the same children, the lesions start as small, frequently punctiform areas of hyperpigmentation and hyperkeratosis which grow progressively and become confluent and similar to the previous ones. In areas of dermatosis, the epidermis peels off in large scales, leaving a tender skin which in the areas of gross oedema or of pressure, are wet and can easily be infected sometimes becoming areas of indolent ulceration. The areas of continuous pressure or irritation where marked oedema exists, are more frequently affected by the

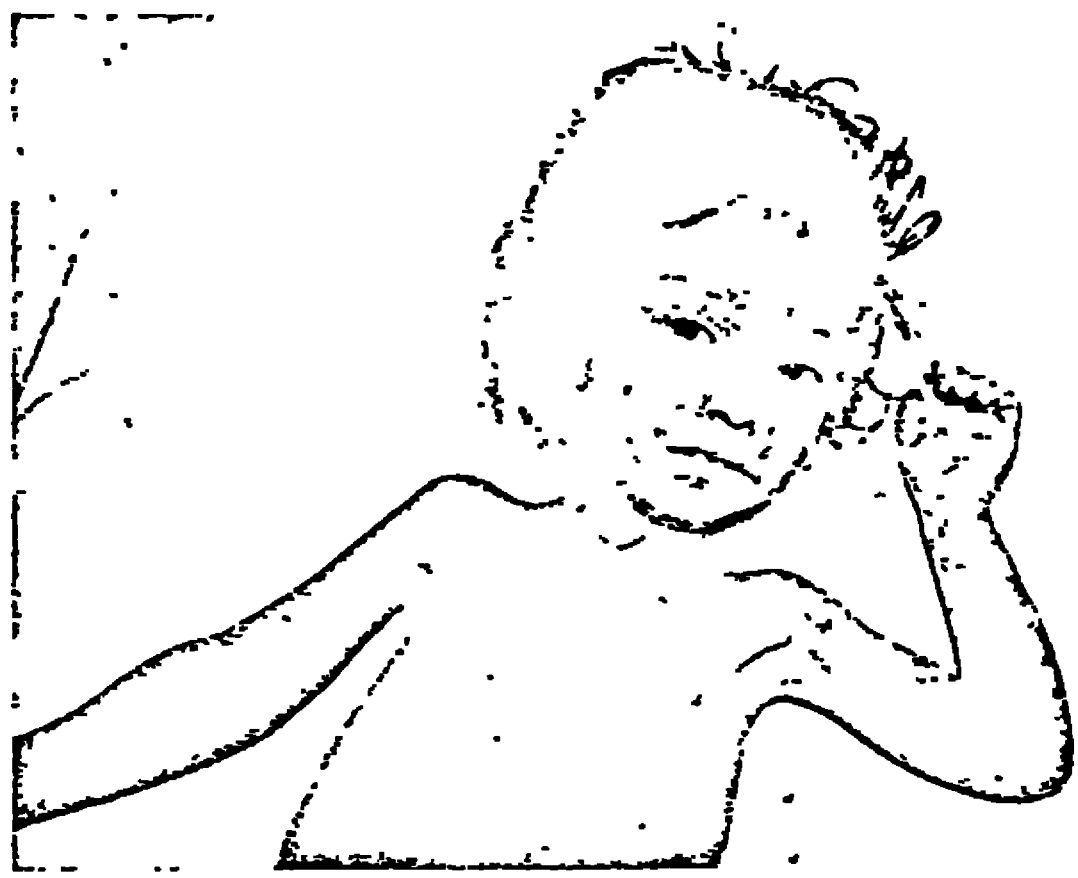

Fig. 7.4. Kwashiorkor showing 'flaky-paint' rash, misery and cheilosis. (Guatemala)

dermatosis. They are not like the dermatosis of pellagra, limited to areas exposed to sunlight. Petechiae and/or areas of echymosis may also be seen. This usually occurs in very severe cases and should be considered a sign of bad prognosis.

The hair usually becomes dry, thin, loses its normal sheen and can be pulled out easily and without pain. When it is normally curly, it becomes straight. It may present characteristic changes in pigmentation, although these are not as constant as the changes in texture. Black hair becomes brown or reddish yellow and sometimes, even white (Figs. 7.5 and 7.6). These colour changes may be observed through all the length of the hair, or in stripes of different intensity of depigmentation. Periods in which the hair growth depigmented alternating with periods of more pigmented hair, produce what has been described as the 'flag sign' (Peña Chavarria *et al*., 1948) (Fig. 7.7).

Knowing that the hair grows at about 8 mm. per month, the observation of these changes is a good record of the nutritional history of the case. Frequently, however, even severe cases show perfectly black hair and gross pigmentary alterations may be observed in mild cases. Similar changes to those observed

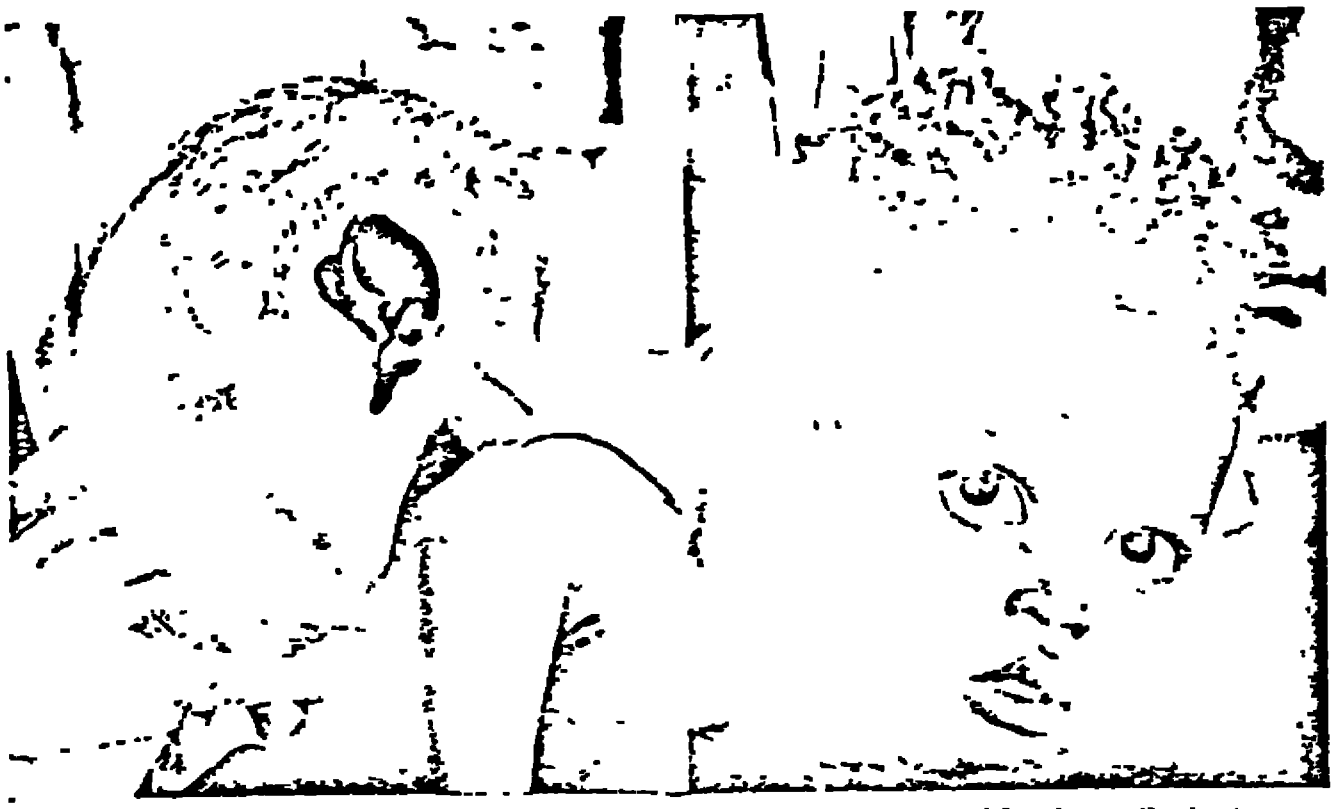

Fig. 7.5. Kwashiorkor, showing hair changes and apathy. (Northern Sudan)
Fig. 7.6. Kwashiorkor, showing marked hypochromotrichia. (Uganda)

in the hair may be seen in the eyelashes and even in the nails, although less frequently and less clearly, probably because of their slower rate of growth.

Diarrhoea is almost always present in the recent history of the children with kwashiorkor and most of them have it when admitted to the hospital. Frequently, the diarrhoea started some weeks or months before, as an acute episode with the characteristics of an infectious process. Since then, the

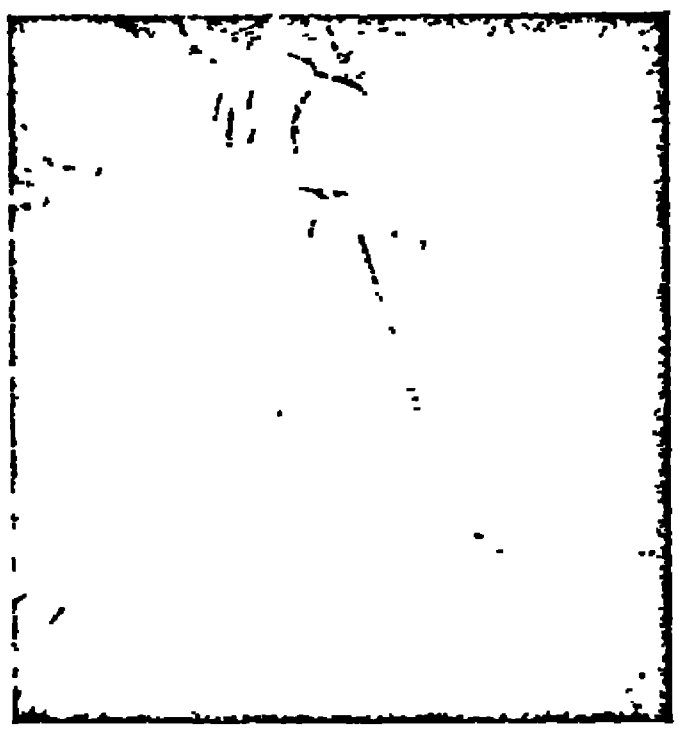

Fig. 7.7. Recovered case of kwashiorkor, showing 'flag sign' in hair (Guatemala)

children have not recovered completely, the diarrhoea becoming chronic or remittent. When the child is admitted to the hospital, the diarrhoea is usually non-specific in character, with indigested foods frequently present in the

faeces. This is usually promptly corrected by the dietary treatment without any specific measure. Diarrhoea is much less frequent in areas where the staple food for the children is cooked banana. The stool volume is very large, even when diarrhoea is not present, a manifestation of the intestinal malabsorption characteristic of the syndrome. Vomiting is also frequent, particularly if the children are forced to eat more than the very small amounts of food they usually accept during the first days of hospitalization.

The extremities are frequently cold and cyanotic. The *muscles are wasted and their tone is diminished.* The abdomen may be distended as a result of intestinal flatulence and flaccid abdominal muscles, and the liver may be enlarged. *Retardation in growth and development* has been described as a constant feature of kwashiorkor. This is, however, minimal in the cases which develop in previously well-nourished children, when they are suddenly changed to a kwashiorkor-producing diet; and when these children recover they are very close to the normal height, weight and other parameters of growth and development. As will be discussed later, however, these cases are very seldom seen; in most instances, the kwashiorkor syndrome develops in children already chronically malnourished, with variable degrees of retardation in growth and development and of wasting. This condition of the child is, therefore, determined by its previous situation before he develops the kwashiorkor syndrome, and not a characteristic of the syndrome. The 'sugar baby' type of child (Jelliffe, Bras and Stuart, 1954) which conserves his subcutaneous fat, may even be obese and recovers very rapidly on a high-protein diet, is the typical example of kwashiorkor without previous chronic malnutrition.

Many other signs and symptoms of other nutritional deficiencies, particularly of vitamins, are also frequently seen in children with kwashiorkor; they are not constant and vary from one region to another according to the nature of the usual diet. Although all of the kwashiorkor-producing diets, in addition to proteins, are also deficient in other essential nutrients and these deficiencies are frequently manifested in the children with kwashiorkor, we prefer to consider them as superimposed or concomitant deficiencies and not as characteristic of the syndrome. Some of these deficiencies are, however, favoured by the metabolic disturbances resulting from protein deficiency. This seems to be the case, for instance with vitamin A where its absorption and probably also its transport and utilization, are impaired in kwashiorkor (Arroyave *et al*, 1959). This may explain the high frequency and severity of ocular lesions due to vitamin A deficiency observed in children with protein malnutrition (p. 184), in areas where the deficiency of this vitamin is endemic (Oomen, 1954).

Other frequent complications of kwashiorkor are dehydration and electrolyte imbalances as a result of severe diarrhoea and or vomiting. The simultaneous coexistence in the same child of dehydration and oedema is not rare. Infectious processes, particularly of the respiratory system, are also frequent and not easy to detect because even a severe bronchopneumonia may be present without the characteristically dramatic manifestations of this condition in well nourished children.

A kwashiorkor case may die suddenly, or only a few hours after respiratory failure due to bronchopneumonia, without having had fever, hyperpnoea or diarrhoea, or other clinical manifestations of the severe lung infection.

Intermediate or combined forms

Cases of kwashiorkor without some degree of preceding or accompanying calorie deficiency are very seldom seen. These cases only develop when small children, after having been well fed, are suddenly put on a starchy diet very low in protein and are forced to consume large amounts of this diet. Usually, this type of diet will very soon produce anorexia and the total food intake and therefore calorie intake will be markedly reduced. However, it may happen that mothers and grandmothers, very concerned over the feeding of the children, but without adequate knowledge of what is a proper diet and its need and importance, will put a child after a sudden weaning or after an attack of diarrhoea, on a diet based on starches and force him to consume it. The kwashiorkor syndrome of the type previously described, then develops in a few weeks; the more typical example is the 'sugar baby' syndrome described by Jelliffe, Bras and Stuart (1954).

Much more frequently, however, the signs and symptoms of kwashiorkor develop in a child who already has a more or less advanced degree of calorie deficiency. It is usually a child that has not been growing well for weeks or months and is more or less underweight. This may be because the diet he is receiving, although sufficiently balanced, is insufficient in total amount or, more frequently, because the low protein diet he is being fed produces anorexia and is consumed in amounts which are insufficient to satisfy minimum calorie needs. In both cases, frequent, recurrent or chronic infections, particularly diarrhoeal processes act as aggravating factors. It is at this time that another more serious attack of diarrhoea, a severe respiratory infection or measles, may precipitate the child into acute protein deficiency. Another precipitating factor may be a serious deterioration of the diet for socio-economic or cultural reasons, such as loss of employment of the father, breakdown of the family or the withdrawal for unsound 'therapeutic' reasons of the small amount of adequate protein sources the child might have been receiving. All of these factors result in kwashiorkor in which the manifestations of severe protein deficiencies are superimposed to a variable degree of emaciation and/or growth and development retardation.

When these children are properly treated, in a few weeks the signs and symptoms and the biochemical and pathological characteristics of kwashiorkor disappear, but they are still grossly emaciated and/or markedly retarded in growth and development (Brock *et al.*, 1955).

These cases have been described as marasmic-kwashiorkor or more frequently simply as kwashiorkor. Since cases of this type are the rule in many areas where PCM is prevalent, clinical, metabolic and pathological manifestations of calorie deficit have been considered as constant and characteristic components of the kwashiorkor syndrome. Furthermore, this situation has led some workers to believe that there is no reason to make any distinction between marasmus and kwashiorkor and that the different syndromes of

protein–calorie malnutrition are only circumstantial manifestations of the same condition which is described only as severe malnutrition (Gómez *et al.*, 1957).

We consider it important, not only for academic reasons but also from the practical point of view, to have a more definite idea of the relative role of the various nutrients in the pathogenesis of the different syndromes. This will provide a more solid basis toward the understanding of the epidemiology and a better orientation on the measures to be taken for treatment and prevention.

It is important, for instance, to emphasize the fundamental role of dietary proteins both in quantity and in quality in the pathogenesis of the different syndromes.

Haematological alterations

Some degree of anaemia is always found in children with kwashiorkor. In most cases, this is only mild to moderate, and when severe there are other aetiological factors involved. The type of anaemia varies from region to region and even within the same region; practically every type of anaemia has been described in kwashiorkor. It is probable that the metabolic disturbances of severe protein deficiency contribute to the appearance of defects related to deficiencies of the haemopoietic factors. For instance, when the anaemia is of the microcytic hypochromic type associated with iron deficiency, an incomplete and inadequate response to iron is obtained until the protein deficiency is corrected.

A macrocytic type of anaemia, with megaloblastosis is also frequently found and has been considered to be associated to folate deficiency (Trowell and Simpkiss, 1957), and more recently to vitamin E deficiency (Majaj *et al.*, 1963).

The exact mechanism of interaction of these deficient nutrients and protein deficiency is not yet clear. Anaemias of normocytic normochromic type are also observed and have been interpreted either simply as the result of hemodilution (Soto Allande *et al*, 1956), or to be the type more directly associated with protein deficiency. Finally, it is not rare to observe anaemias in which the Price–Jones curve or more simply a careful study of the smear reveals a dimorphic type of anaemia with simultaneous presence of microcytes and macrocytes. In these cases, it seems that there are two different red cell populations; the mean corpuscular volume is of less help in these cases than the study of the smear which is recommended in all cases to have a better understanding of the anaemia under study.

The type of anaemia may rapidly change during the initial stages of treatment when the provision of proteins stimulates an increased overall metabolism with a rapid haemopoiesis during which some factor may become limiting. This is the case, for instance, when a normocytic or macrocytic anaemia is converted to microcytic once the iron stores are exhausted, as occurs if no adequate supplementation of this mineral is administered. A similar situation has also been described for folate (Ghitis *et al*, 1963).

Very low serum levels of iron and copper have been found in children with kwashiorkor even when the anaemia is not microcytic (Lahey *et al*, 1958), these children however, often show iron deposits in the reticuloendothelial cells of the bone marrow and liver. Their low serum iron and copper levels have been interpreted as being related to the reduced levels of their protein carriers (transferin and ceruloplasmin).

The bone marrow of children with kwashiorkor is frequently extremely hypoplastic and contains young and abnormal elements. A rapid transformation into a hyperplastic

bone marrow accompanied by peripheral reticulocytosis is observed when an adequate treatment is administered.

Other haemotological alterations which have been found in kwashiorkor include a diminished response to leucocytosis during infections and various inconstant and not yet clearly defined alterations in the coagulation mechanism.

Pathology

Practically all the information available from necropsy studies has been obtained from cases in which a variable degree of calorie deficit has been present in addition to the severe protein deficiency. These are the cases already described as intermediate or combined forms. It is, therefore, difficult to be certain about the pathological alterations which are directly related to the kwashiorkor syndrome The atrophy of the muscles and of other organs which is usually described, is, for instance, more probably related to the degree of calorie deficit By comparison of the lesions observed in these combined cases with those observed in pure marasmus, it can be concluded that the following are the most characteristic pathological alterations in kwashiorkor:

Liver. Marked fatty change is always found in the acute stage. The fat generally appears first as small droplets in the cells of the periportal area of the hepatic lobule and spreads progressively to the central vein The small droplets then coalesce to form large fat globules filling practically all the cell and displacing the nuclei and other cell structures toward the cell membrane Even large cysts by fusion of several fatty cells may be seen in severe cases With adequate treatment the fat disappears in the reverse order. During recovery, there is also evidence of hepatic cell regeneration, such as an increase in nuclear size and chromatin content, the presence of polyploids and numerous mitotic figures. An increase in the number of lymphocytes and plasmacytes in the sinusoids is then also observed.

Although there is an increase in the reticulin fibres radiating from the portal tract which may be interpreted as an incipient cirrhosis, the evidence now available indicates that the fatty change of kwashiorkor is totally reversible and does not lead to cirrhosis (Umaña and Tejada Valenzuela, 1961)

Gastrointestinal tract. The atrophy of the mucosa, particularly at the level of the fundus of the stomach and in the intestine is the most striking lesion. There is a marked atrophy of the intestinal villi and a decrease in the number and size of the chief columnar cells. The picture is very similar to the one observed in patients with primary malabsorption syndromes Although a rapid improvement is observed after treatment, some degree of atrophy of the villi may be seen even months after treatment and when the child can be considered otherwise recovered

Pancreas. Atrophy of the acini and hypofunction indicated by loss of the zymogen granules, are the most conspicuous lesions The islets of Langerhans appear histologically normal. Although fibrosis of the pancreas has been described as a constant finding (Trowell, Davies and Dean, 1954), it is possible that the collapse of the reticulum secondary to the atrophy of the acini has been interpreted as fibrosis. In our experience, this alteration is very seldom seen and when present, it is possibly due to fibrocystic disease of the pancreas with secondary malnutrition. The pancreatic alterations seem to respond very rapidly to an adequate dietary treatment and even frank hyperplasia may be seen when the child dies for other reasons during recovery. This is similar to what has been observed clinically for the salivary glands

The histological lesions in other organs are less conspicuous and constant Fatty degeneration of the cells of the convoluted tubules and hyalinization of the glomeruli have been observed in the kidneys In the lungs, a terminal bronchopneumonia, intra-alveolar haemorrhages and areas of atelectasis are frequently found at autopsy The thymus is very atrophic with fat replacing the lymphoid tissue Histologically, the atrophy and hyperkeratosis observed in the skin lesions are similar to the dermatosis of pellagra

Physiological and biochemical alterations The same general remarks made in relation to the confusion in regard to the alterations which can be considered characteristic of kwashiorkor or due to other accompanying or complicating factors of nutritional or infectious origin, are also pertinent in this section

Water, electrolytes and circulatory changes. Oedema is a constant characteristic of kwashiorkor. Although hypoalbuminaemia is also a constant finding, it cannot be considered as the only cause of oedema. Many other factors, including hydrodynamic changes, disturbed water and electrolyte balance and hormonal abnormalities seem to be involved. There is no evidence of right heart failure; at admission, the heart size as judged by X-rays is reduced rather than enlarged. Cardiac dilatation is however, observed during recovery, suggesting a meagre cardiac reserve. Decreased cardiac output has been found, which together with the distribution of the oedema, predominantly in the distal parts, suggests tissue anoxia as a result of peripheral circulation as a factor in the development of oedema. Only minor electrocardiographic changes including decreased voltage, T-wave abnormalities and in sporadic instances, arrhythmia have been found in kwashiorkor (Belli Cortes *et al.*, 1961).

Overhydration in terms of total body water per unit of body weight or body surface is constant and involves all fluid spaces (Frenk *et al*, 1957; Smith, 1960).

The osmolarity of the three major water compartments (intravascular, extracellular and intracellular) is reduced (Gordillo *et al*, 1957). Decreased glomerular filtration rate, lowered renal plasma flow, decreased osmolar clearance, increased free water clearance and impaired renal response to a water load, are the most important alterations found in renal function (Gordillo Paniagua, López Montaño and Soto Allande, 1959).

A marked potassium depletion, primarily at the intracellular level is a constant and important alteration (Hansen and Jenkinson, 1956; Metcoff *et al*, 1957; Smith and Waterlow, 1960).

Magnesium and phosphorus depletion have also been described (Metcoff *et al*, 1960; Montgomery, 1961). The reports on the alterations in antidiuretic hormone activity, in aldosterone excretion, and on the possible role of these alterations in kwashiorkor, are not conclusive.

Carbohydrate and energy metabolism. Hypoglycemia has been frequently found in kwashiorkor and has been incriminated as a cause of death. Glucose absorption and the handling of intravenous glucose and galactose loads have been found abnormal (Viteri, Arroyave and Behar, 1966) Enzymatic abnormalities of the glucose oxidation system and of the tricarboxylic acid cycle, probably related to intracellular ionic concentration, have also been described (Metcoff *et al*, 1960)

Lipid metabolism. Marked reduction in the intestinal absorption of different fat fractions is observed (Viteri, Arroyave and Behar, 1966) The data indicate an intestinal mucosa defect as the main responsible factor. The reduced fat absorption persists for many weeks and is still present, although not as marked as before treatment, when the child seems completely recovered from the clinical point of view and most other biochemical alterations have also been corrected. A particular intolerance to milk fats and better tolerance of vegetable fats has been described (Dean and Swanne, 1963). Abnormalities in lipid transport are also found and are probably related to a deficiency of plasma protein carriers. It may be one of the contributing factors of fatty change in the liver. All the lipid fractions of the plasma, which are generally reduced during the acute stage, rose promptly with adequate dietary treatment, even in the absence of dietary fat (Dean, 1960).

The importance of these alterations in vitamin A metabolism and probably also in relation to essential fatty acids, need to be particular emphasized.

Protein and amino acid metabolism. The total serum protein concentration is always reduced; this is mainly due to hypoalbuminaemia which is a basic change in kwashiorkor. The α_1 and α_2 globulins have been found relatively increased and the β-globulin frequently decreased The γ-globulins serum concentration is variable but always high, when expressed per unit of total serum proteins Since the concentration of total globulins is less altered than that of albumin, the A G ratio is frequently inverted. These serum protein alterations and impaired hepatic circulation are believed to be responsible for abnormal flocculation and turbidity liver function tests and high bromosulfalein retention occasionally found in kwashiorkor. Studies with ^{131}I labelled serum albumin have shown that the catabolism of albumin is lower in the acute stage than after recovery (Picou and Waterlow, 1962), the low albumin concentration being due to a decreased albumin synthesis.

Nitrogen balance studies have conclusively shown that the children with kwashiorkor are able to retain a larger proportion of dietary protein than normal children. The plasma total free amino acid concentration is low in kwashiorkor with a greater reduction in the essential than in the non-essential amino acids. Evidence of increased recycling of body amino acids has been provided by studies with ^{35}S labelled methionine (Picou and Waterlow, 1961). Low values are found for blood concentration and urinary excretion of urea. The urinary creatinine is also constantly reduced. The urinary excretion of amino acid nitrogen, purine derivatives and some abnormal protein and amino acid metabolites tend to be high. The absolute nitrogen content of the liver has been found normal when expressed as percent of body weight. The decreased liver protein concentration can be explained by an increase in fat content. Although low nitrogen concentrations have also been reported in the liver when expressed per unit of DNA, this may be explained by an increased concentration of DNA recently found (Umaña, 1966).

The activity in the serum of various enzymes including amylase, pseudocholinesterase and alkaline phosphatase is found constantly reduced in kwashiorkor. Other enzymes which have been found elevated in destructive processes of parenchymatous organs have also been reported as increased in kwashiorkor The study of the activity of different enzymes, in liver biopsies or in other tissues, have not provided a clear indication of the metabolic disturbances of kwashiorkor; a more systematic and dynamic study of the main metabolic pathways rather than the *in vitro* determination of the activity of a certain number of enzymes is needed for this purpose. The evidence available suggests that important adaptive mechanisms are operating in children with severe protein deficiency. The failure of these mechanisms will result in death.

Prognosis. Even under the best conditions, the mortality of children admitted to hospitals with kwashiorkor is still relatively high in the order of 10 to 20%. Neither the degree of oedema nor of cutaneous lesions or any other specific sign or symptom, can be used for prognostic purposes. A clinical evaluation of the general conditions of the child is needed for this purpose. The most important causes of death are severe dehydration with electrolyte imbalance and infectious processes, particularly bronchopneumonia. The danger of death from dehydration when present at admission, is particularly high during the first 48 hr of treatment; if the child survives this period, the alterations are usually well on the way to being corrected and the danger diminishes rapidly. For bronchopneumonia or other acute infections, special attention should be given during the first 8 to 10 days after admission. The death of children who have been properly treated during the first 10 days occurs very rarely and generally only due to other superimposed complications. A limited number of children die probably from metabolic disturbances not responding properly to the recommended dietary treatment. These children may have some irreversible lesions or alterations that are not as yet understood and it is not possible to correct. Severe hypoglycaemia preceding death has been reported in some of these cases.

In children who do not respond properly to an adequate dietary treatment after correcting the acute complication that they might have, the possibility of a chronic infection such as tuberculosis or an endocrine or metabolic defect, should be investigated.

The prognosis in regard to complete return to normal conditions varies with the age at which the child is affected and the duration and severity of the deficiencies. Older children who suffer acute deficiencies of short duration seem to recover more rapidly and completely, but in small children, particu-

larly infants who have had long periods of severe deficiencies, a permanent irreversible retardation in physical growth has been observed. It is probable that similar retardation in other areas of development also occurs, especially mental performance (p. 295); intensive research is going on in this field.

Treatment

The first efforts should be devoted to a careful evaluation of the child, particularly in regard to complications like dehydration and acute infectious processes which may threaten the life of the child before it can benefit from the basic dietary treatment.

The correction of dehydration and electrolyte imbalances in children with kwashiorkor, should follow the same general principles that apply to well nourished children, with the necessary adaptations in view of the following main considerations: that dehydration is generally hypotonic; that there is a severe potassium depletion; that some renal functional alterations are usually present; that there is a large amount of fluid abnormally accumulated, and that the cardiac reserve being diminished may be insufficient to manage a large and sudden mobilization of fluids into the intravascular space. Intravenous administration of fluids is imperative when the child is clinically dehydrated, but should be given cautiously. The solutions should be moderately hypotonic in regard to normal plasma ionic concentration; and should provide larger amounts of potassium than those recommended for well nourished children. Amounts of 5 to 6 mEq. per kg. of body weight are perfectly tolerated and needed. The administration of potassium should be instituted preferably after an adequate diuresis is obtained, but in cases in which the child is oliguric, after enough fluids have been given, the administration of potassium may be required to help correct the oliguria.

Any acute infection present at admission or appearing during hospitalization, should be promptly treated by the most effective means. In very severe cases, even if acute infections are not apparent, the administration of penicillin and/or sulphonamides during the first 8 to 10 days of hospitalization is recommended since many of these children die with severe bronchopneumonia which is frequently difficult to diagnose clinically.

The fundamental treatment is the administration of a diet high in proteins of good biological value and containing sufficient calories and all other essential nutrients. During the first days, small and frequent feeds will be necessary to ensure an adequate total food consumption in a child who is usually anorexic and prone to vomiting. Intra-gastric feeds, by drip or intermittently are given via a polythene tube in some units. During this period, special care by well-trained and devoted nurses is of fundamental importance. Often in only a few days, the anorexia is overcome and the children are then able and eager to eat the recommended diet.

Cow's milk is the most convenient and practical food as the basis of the dietary treatment; the substitution of cow's milk fats by vegetable fats has proven to be advantageous in the hands of some investigators (Dean and Swanne, 1963), particularly since fats are useful components of the therapeutic diet and the use of skim milk alone is not very convenient. In our

experience, however, whole cow's milk can also be used since the beginning of the treatment, if given in the proper dilution and amounts. Large amounts of sugar should be avoided during the initial stages and if calorie supplements are needed, either vegetable fats or sources of better tolerated carbohydrates should be used. Bananas, for instance, have proved to be particularly useful.

After the first few days of progressive adaptation of the child to the diet, a total intake of 3 to 5 g. of protein of high biological value per kg. body weight per day, should be obtained and maintained. The total calorie intake should then be of about 120 to 140 cal. kg. body weight per day, but this amount should be increased if adequate progress in weight is not observed. Cases with marked loss of weight usually require higher calorie intake. The diet should be varied as soon as possible and should provide ample amounts of all other essential nutrients.

With such a therapeutic regime, no specific dietary supplements are usually needed, although they are employed in some units, especially if a particular vitamin deficiency is known to be common locally. Therapeutic doses of vitamin A should be given intramuscularly only when ocular signs of this vitamin deficiency are present, because the lesions can progress very rapidly to irreparable damage. The administration of iron supplements is frequently required to correct iron deficiencies present at admission or developing during recovery. Similarly, folic acid administration might be required in cases with megaloblastic types of anaemia. The administration of potassium salts, as supplement to the diet—about 1 g. of potassium chloride—is also recommended to accelerate the repletion of this mineral, and administration of magnesium may be indicated (p. 340). The administration of blood or plasma transfusions may be indicated as life-saving measures when specially indicated in cases with severe anaemia or shock, but should not be routinely used as a means to correct the protein depletion.

With this treatment, recovery takes place in two stages (Brock *et al.*, 1955). During the 'initial recovery', the oedema disappears, as well as most of the other clinical manifestations of kwashiorkor and the major biochemical and physiological alterations return to near normal values. This takes place in 2 to 3 weeks. During the second stage, 'consolidation of cure', the child recovers the weight lost and a complete correction of all other reversible alterations takes place. In 2 to 3 mnth after admission, the child has reached normal weight for his height, and he can be considered as clinically recovered. Hospital attention is recommended for the first stage of recovery; the second stage can be carried out more economically and conveniently in other institutions with less medical resources or on a semiambulatory or even completely ambulatory basis if the socioeconomic conditions of the family are considered adequate. All efforts should be made during hospitalization to educate the mothers. Before the child is completely discharged, he should be eating a diet utilizing to best purpose the foods available and familiar to his family.

Mild-moderate PCM

These forms of PCM are mainly manifested by inadequate physical growth. The children are small for their age, and they do not present signs or symptoms

of grave malnutrition. They may be much less active and lively than normal children of their age, but this is usually unrecognized under the cultural patterns of the communities in which they live. Bone maturation, as indicated by X-ray studies of the wrist is also similarly retarded. It has also been found that they are equally retarded in mental development (Cravioto, 1963) but no conclusive evidence is as yet available to prove if this is due to malnutrition or more directly related to the social environment in which these children grow, nor is there evidence of the irreversibility of this developmental retardation. The physical growth retardation does seem to be irreversible when the nutritional deprivations are prolonged, as is generally the case. Even if a normal rate of growth is achieved later under a more-or-less adequate diet, the closing of the epiphysis takes place at the same chronological age as in normal subjects—when these individuals have not developed their full growth potential—and smaller adults are the final result. There is now enough evidence indicating that the anthropometric differences in children and adults found between populations of low socioeconomic conditions of the tropical areas and those of the more advanced nations are due much more to environmental factors, mainly nutritional deficiencies, than to genetic differences.

This condition can be considered as an adaptation mechanism to the dietary restrictions and other unfavourable environmental conditions. These mild to moderate forms are in our concept, a much more serious public health problem than the relatively small prevalence of the advanced and serious cases of protein–calorie malnutrition. They affect the large majority of children in the areas where the problem exists and are limiting the human resources of these areas by interfering with the development of the full potentiality of these individuals. They are also an important contributory cause to the high rates of child mortality, as these children are more susceptible to death from diarrhoeal diseases, measles or other common infections highly prevalent in the same areas.

Prevention

The prevention of protein–calorie malnutrition at the individual level only requires the administration of a proper diet to satisfy the child's nutritional requirements. The situation, however, has to be focused at the community and national level as a public health problem and implies a clear understanding of the epidemiology of the condition with its multidisciplinary aspects. The prevalence of protein–calorie malnutrition in a given area is more a social than a medical problem. The economical–agricultural aspects of food production and availability should be considered. Also of fundamental importance are the cultural factors determining food consumption for the various groups of population and for the different members within the families, particularly for the infant and preschool child. Of no less significance are the sanitary conditions of the environment, the health knowledge and practices of the population, and the availability and quality of medical services.

Protein–calorie malnutrition is the result of the synergistic effect of low food availability, particularly of foods which are adequate sources of protein

of high biological value for small children; poverty; lack of adequate recognition of the relationship between nutrition and health; erroneous cultural beliefs and practices in feeding, particularly in the case of small children; and a high prevalence of diarrhoeal disease and other infectious processes.

A detailed discussion of the epidemiology of protein–calorie malnutrition is not within the scope of this chapter as is an ample consideration of all the measures needed for its effective prevention. This requires intensive and coordinated programmes in which all the available resources of the communities should be mobilized to control each of the epidemiological factors mentioned. The increase in food availability includes augmented agricultural production, the establishment of sound agricultural policies to channel the production in relation to the needs of the population, more rational use of the land, improved methods for preservation, transportation and processing of foods, and the provision of adequate markets for the products by creating a high demand. This last implies improving the economic and cultural status of large sectors of the population, more effective utilization of the locally available products by improving their nutritional value, and the introduction of new adequate foods of possible local production like vegetable mixtures. The scientific and technological knowledge is available for all these purposes and the limitations for their application are mainly of a social, cultural and economical nature.

The prevalent cultural practices and beliefs in regard to nutrition and dietary habits, require extensive and fundamental education. Not only the general population but frequently governmental officials and leaders too, must often acquire greater awareness and understanding of the importance of good nutrition, its relation to health and how this can be achieved. Educational programmes, although directed toward the correction of inadequate practices, must respect, as far as possible, the cultural values of the population. This requires sufficient knowledge of the culture of the area.

The simple transmission of information which is frequently referred to as 'education' and does not fit within the culture of the population, is in most cases ineffective and may even be deleterious.

Educational programmes should also consider the available and potential resources of the population, as the recommending of impractical measures is deceptive both for the educator and the intended beneficiaries.

Both the content and the channels of communication should be carefully considered for the different population groups.

Most programmes conducted so far, have not been properly evaluated. Special efforts are therefore needed in regard to this important aspect of the prevention of conditions like PCM in which the final effect depends largely on the action taken by the individuals themselves. More research and experience is needed in this area of education.

Among the topics which should receive special attention in nutrition education programmes directed to the general population, are the following:

Encouraging women to prolong breast feeding for as long as possible, and stressing its importance during at least the first yr of life. This is particularly significant in areas or population groups where adequate substitutes for

mother's milk are unavailable or not readily accepted under present cultural patterns.

Introducing the infant as early as possible to readily available foods, such as those usually consumed by the adults of the family, which may be adequate sources of protein and other essential nutrients. To attain this purpose, new ways of preparing these foods for better adaptation to infants and young children may be needed.

An adequate diet for children during acute diseases, particularly diarrhoeal processes, with special emphasis on avoiding prolonged drastic dietary restrictions under these circumstances.

Of fundamental importance is the creating of consciousness of the relationship between nutrition and health and the value of good nutrition. Here again, it is necessary to proceed with a clear understanding of the cultural basis for the present situation. Cultures are not static, they change continuously and intelligent measures can be of great help in orienting these changes toward a better adaptation of man in his changing environment.

Environmental sanitation, adequate water supply, health education, particularly in relation to personal hygiene; hygiene in regard to preparation and storage of food and any other activities oriented toward the prevention of the common infectious diseases, especially diarrhoeal processes, are also needed for the prevention of protein–calorie malnutrition.

The programmes outlined in general terms give an idea of the magnitude and complexity of the task. Fortunately, however, since the different epidemiological factors act, as has been said, synergistically, the amendment of any one will favourably affect the others and will facilitate their correction. The definition of priorities based on the magnitude of each factor in any given area and of the resources available for their correction, is of great importance, but all factors should be considered. Help from the more developed nations can also be useful and for countries with severe problems, may be necessary. It should however, be primarily oriented towards the development of local resources and training of personnel for their better utilization. The use of surplus food from the more developed nations by those less privileged, can be very useful for emergency purposes or as an incentive to initiate the long-term plan based on the principles indicated. It must be stressed, however, that no nation should depend on help from such surplus material permanently, unless this is done on the basis of an economically sound interchange.

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(5) *Miscellaneous Deficiencies*

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Pellagra

Although many diets in childhood are often moderately deficient in nicotinic acid, yet pellagra is a rare disease in childhood. Other factors, such as the intake of protein, other elements in the vitamin B complex, and the continuation of these deficiencies over a period of many years, are concerned in the production of pellagra in adults, but tend to prevent the emergence of this disease in childhood (Chick, 1951). Pellagra has only occurred commonly among adults who derive a large proportion of their calories from corn (maize) although it may occur occasionally among those who take none of this cereal. Corn contains rather a small amount of nicotinic acid, but not much less than that in other white cereal flours or rice. Corn does contain, however, less tryptophan than other cereals and this amino acid when available in enough amounts, is a precursor of nicotinic acid. An excessive intake of alcohol is an important factor inducing pellagra in adults, but is almost unknown in children. Although pellagra, mainly in adults, still occurs in some parts of Africa where corn is the main staple, it is not seen in central

America and Mexico where corn provides up to 80% of the calories in the diet of large population groups. The treatment of corn with lime for the preparation of tortillas which makes more tryptophan and niacin available (Bressani *et al.*, 1961; Bressani *et al.*, 1958) as well as the supply of niacin by coffee, explain this situation.

The only foods which are rich in nicotinic acid are flesh foods; fish and leguminous seeds contain moderate amounts, but milk, vegetables and fruit contain only small amounts of this vitamin. Coffee can be an important source; the concentration of niacin in coffee varies, however, with the method of preparation (Bressani *et al.*, 1961; Bressani *et al.*, 1962). Since tryptophan is a source of niacin, 60 mg. of dietary tryptophan being equivalent to 1 mg. of niacin, all the proteins of high tryptophan content, mainly animal proteins, can also be considered adequate sources of the vitamin.

The recommended allowances (National Research Council, 1964) are expressed as niacin equivalents which take into consideration the niacin that may be obtained from tryptophan. Taking as a basis 6 6 mg. of niacin equivalent to 1000 cal., 6 mg. are recommended for infants as daily intake; this amount is increased to 9 to 11 mg. for small children and to 13 for adult women who should receive an extra amount of 3 mg. during pregnancy and 7 during lactation.

If pellagra appears in a child, the manifestations (Dodd, 1941) are largely the same as in adults, of which only the skin lesions can be regarded as almost specific to the disease. These occur on the exposed surface of the body; face, neck, back of the arms and hands, lower legs and feet, and are provoked by exposure to sunlight and wind, even mechanical irritation may play a part. Attacks of dermatosis are apt to occur at certain seasons of the year; in temperate regions, they recur every spring when the return of the sun provokes an attack among persons who have eaten poorly during the winter months. Even before this episode, and subsequent to its disappearance, the person remains in a state of chronic ill health. Sunlight provokes an attack of erythema on the exposed surfaces, these areas darken to become purple in colour, and then pigment accumulates so that areas of dark, rough crackled dermatosis occur. These have sharply defined margins; they persist for a long time, and while a little desquamation of the horny scales may occur, widespread and spontaneous desquamation is never seen, a point of distinction from the natural evolution of the dermatosis of kwashiorkor. Increased pigmentation of the whole of the exposed skin of the face, hands and feet may occur, but may not be recognized save in those having a naturally pale skin. Areas of hyperkeratosis may occur over the pressure sites such as the knuckles, elbows and knees; areas of dermatosis may effect the scrotum or perineum and the vagina may, like the mouth, be inflamed.

The mouth and intestinal tract are affected in a characteristic manner, although none of the changes are specific to the disease and are simulated closely by other causes of stomatitis, such as that present in mercury poisoning and pink disease; the diarrhoea tends to be chronic.

Cheilosis of the lips and sodden, cracked corners of the mouth are usually ascribed to an associated deficiency of riboflavin (p. 207); the stomatitis may

be due to a deficiency of either or both of these vitamins. The whole of the mouth is raw and red, much of the tongue may be bare, and the painful condition of the mouth and the excessive formation of the saliva present a miserable picture. A rather similar superficial inflammation occurs to a variable degree in the pharynx, oesophagus, stomach, small and large intestines, causing a variety of signs, including dysphagia, nausea and vomiting; while attacks of loose, watery stools are one of the most constant features of pellagra. The mental signs of pellagra are seldom marked in childhood, some apathy and irritability may occur; these seldom develop into the psychosis which is a feature of the more chronic phases of the disease in adults. Some anaemia, which may be macrocytic, may be present.

In children, the course of the untreated disease is variable, spontaneous remissions and relapses tend to occur; the latter appear often with the return of the sun in spring. Although acute and even fatal attacks of pellagra may occur, these are most uncommon and pellagra is seldom a fatal disease in childhood. Relapses recur over a period of many years.

The diagnosis is made by finding a combination of suggestive signs in a child whose diet has been poor; it is almost impossible to establish the diagnosis until the characteristic dermatosis occurs in the areas exposed to sunlight. The diarrhoea is seldom in itself suggestive and may arouse fears of ascariasis (p. 445), intestinal tuberculosis (p. 259) and other intestinal diseases, although coeliac disease and fibrocystic disease are very rare in all tropical countries. The skin lesions may be confused with those of pink disease (also rare in tropical countries) but in the latter the face is seldom involved, the fingers and hands are cyanotic and sodden, there are signs of excessive sweating, tachycardia and great irritability. Infantile eczema (p. 620) starts in infancy; the face is usually severely attacked with crusted papules, and scaly areas may affect the limbs and trunk, but the characteristic hyperpigmented areas of dermatosis, as in pellagra, are not seen. There are certain resemblances between the classical dermatosis of pellagra and the typical skin manifestations of kwashiorkor and both diseases may be present in the same person. The dermatosis of kwashiorkor occurs most typically on the moistened pressure sites around the groin and over the trunk; although it can be seen also on the face, hands and feet; it is not limited to the exposed areas; it goes through definite stages of development until it spontaneously desquamates at the centre to reveal pale, raw areas of skin, which heal quickly after treatment by milk protein, but the response to nicotinic acid is unsatisfactory. The oedema and rapidly fatal course of all untreated cases of kwashiorkor are other points of clear distinction. The histological changes in the two diseases are very similar (Gillman and Gillman, 1951); this may be due to the fact that the metabolism of nicotinic acid (the major deficiency in pellagra) is related to that of tryptophan (an essential amino acid and one presumably lacking in kwashiorkor).

The treatment of pellagra in a child is similar to that of the disease in an adult. Nicotinic acid causes a prompt alleviation of the sore mouth and soon improves the dermatosis and the diarrhoea. From 10 to 25 mg. may be given thrice daily as tablets; nicotinamide is preferable as it produces less burning

sensation in the skin. Pellagra is, however, a complex nutritional defect and cases are not cured by the administration of nicotinic acid alone; the whole vitamin B complex should be given and the consumption of protein of high biological value increased. The diet should be as varied as possible. Pellagra is usually an expression at the dietary level of poverty and ignorance, it reflects a social or family problem; unless these aspects can be assessed and corrected, the disease tends to recur.

The prevention of pellagra in children is seldom a problem sufficiently large to attract the attention of the public health authorities. If the diet of the family contains too large a proportion of corn, pellagra is apt to appear in the adults, the children being less commonly affected. All measures designed to raise the social and economic status of the affected families or classes will prevent pellagra in childhood. The diet should be more varied and special attention should be directed towards increasing the leguminous foods; animal protein should also be taken more freely and thus the vitamin B complex and tryptophan content of the diets are high and pellagra is prevented.

Riboflavin deficiency

Like other members of the vitamin B complex, riboflavin is an essential part of complex enzyme systems concerned in oxidation reactions within the cells of the body. The enzyme consists of a molecule of the vitamin coupled with a protein carrier; it is possible on theoretical grounds that protein deficiency states might also result in a deficiency of the complex enzyme and that similar clinical signs might occur in both a deficiency of riboflavin or a deficiency of protein. In actual practice, this is unimportant for riboflavin is found in foods rich in protein, such as meat, fish, milk, eggs, groundnuts and beans; so that a true combination of riboflavin deficiency and protein malnutrition is common. Minor degrees of riboflavin deficiency, with or without protein malnutrition, are common among poorly fed children.

The recommended allowances of riboflavin (National Research Council, 1964) were approximately assessed at 0·6 mg./1000 cal. On this basis, 0·6 mg. are recommended for infants. Small children will need from 0·8 to 1·0 mg.; the amounts recommended for women are about 1·2 mg. to which 0·3 mg. and 0·6 mg. should be added during pregnancy and lactation, respectively.

A large variety of manifestations have been described in riboflavin deficiency; few of these are indeed specific and may be closely stimulated by other diseases. If these signs are observed to be stationary on a diet which appears low in this vitamin and the addition of riboflavin causes rapid improvement, it is reasonable to regard this as constituting a clinical proof of the nature of these signs. In many nutritional surveys, this elementary observation has not been made and all sorts of slightly red eyes and mouths have been regarded as sure signs of deficiency.

Breast milk and cow's milk contain adequate amounts of riboflavin so deficiency signs do not appear in infants who are fed these foods. After weaning, the intake of riboflavin is often low in poorly fed children who receive little animal protein; clinical signs seldom appear except in those who develop kwashiorkor. In older children, the signs may appear unassociated

with those of protein malnutrition, although even at this stage riboflavin deficiency seldom occurs alone, the intake of protein, nicotinic acid and other factors in the vitamin B complex have usually all been low.

Sore red lips (cheilosis), a sodden fissured condition at the angles of the mouth (angular stomatitis), and a purplish raw tongue, covered with granular enlarged papillae, are three of the most constant signs (Bicknell and Prescott, 1953). Sodden corners at the palpebral fissures may occur, but the commonest change in the eyes is circumcorneal injection—minute vessels can be seen invading the cornea from the corneo-scleral junction. The latter change is, however, by no means specific, being also produced by exposure to heat, bright light and dust, as well as in all variations of conjunctivitis, trachoma and in vitamin A deficiency. Just as in the eye where it is important to distinguish between the signs of other diseases and those of ariboflavinosis, so in the mouth other conditions may simulate the appearances produced in this vitamin deficiency syndrome. The differential diagnosis is from the oral signs of anaemia, the changes which accompany chronic diarrhoea and stomatitis from other causes. Often the only clear point of distinction is the response to treatment. Ariboflavinosis is quickly cured by administering as tablets 2–5 mg. daily of the pure vitamin to a child, but other diseases of the mouth, lips and eye are not affected.

Ariboflavinosis may also occur as an associated deficiency in chronic intestinal disorders such as those frequently observed in kwashiorkor. Sore lips and tongue may considerably interfere with the infant's capacity to feed. These signs soon subside after instituting treatment of kwashiorkor with milk, which contains all the B vitamins; in addition, protein appears to act in a beneficial manner.

The prevention of riboflavin deficiency depends on increasing the intake of those articles rich in this vitamin—legumes, nuts and animal protein. Measures designed to improve the diet even in a general manner by adding variety and by increasing protein, almost always increase the content of riboflavin and thus prevent any deficiency.

Scurvy

Ascorbic acid (vitamin C) is present in all living tissues, but fresh fruits and plants are the best source. The intake of vitamin C depends on what fresh vegetables are taken. Cereals and cooked foods, such as meat and fish, as well as all fats contain little vitamin C. The extent of the destruction of vitamin C by heat has probably been exaggerated; prolonged cooking of vegetables, especially in the presence of alkalies, reduces the vitamin content, as much has passed into the surrounding water and may be thrown away. Foods which are steamed and cooked rapidly (e.g. sweet potatoes and plantains) retain much of their ascorbic acid (Bicknell and Prescott, 1953).

Fresh cow's milk and human milk contain fair amounts of ascorbic acid, and scurvy is only commonly seen in bottle fed babies who are given boiled milk but no supplement of fruit or vegetable juice. The spray-drying of milk causes little destruction of ascorbic acid; evaporated milks contain less, while pasteurized or boiled milk may contain very little. Prolonged storage causes

a reduction of the ascorbic acid, so that tinned preparations of cow's milk, especially if undue heat was used in their preparation, may contain little vitamin C.

There is less agreement in regard to the recommended allowances for vitamin C than for most other nutrients. The most recent (National Research Council, 1964) are 30 mg. daily for infants, 40 to 50 mg. for preschool children and 70 mg. for adults with extra amounts of 30 mg. daily during pregnancy and lactation. These figures are higher than most other recommendations and definitely much higher than the amounts needed to prevent the appearance of clinical manifestations of the deficiency.

Rich sources of ascorbic acid are abundant in the tropical and subtropical areas. Since the consumption of even a small amount prevents scurvy, this deficiency disease is not seen as a public health problem in any of these areas; sporadic cases can occur when infants are fed for long periods of time with boiled milk and cereal products and other cooked vegetables and fruit preparations. With the greater use, even in underdeveloped areas, of canned vegetables and fruit preparations produced industrially, attention should be given to their proper vitamin C enrichment.

Ascorbic acid has many functions within the body, an important one is the part played in the formation of intracellular substance—reticulum and collagen—without which many tissues fail to maintain normal structure and growth. One of the first structures to exhibit abnormality are the capillaries. Infants react in a different manner to the disease than do older children, so that two varieties are described: infantile scurvy and that of older children and adults.

Infantile scurvy. This occurs almost exclusively between the ages of 6–16 mnth, as the infant is born with large stores of ascorbic acid and several months of feeding on a diet composed exclusively of boiled cow's milk must elapse before clinical manifestations of the disease appear (Graham, 1953). Indeed, in all tropical and subtropical countries, infantile scurvy is a very rare disease in spite of an apparently low intake of ascorbic acid. This has been the subject of comment by many paediatricians, no reason has been found to explain this. It might well be that since these children are not growing properly because of calorie–protein malnutrition, the requirements of vitamin C are lower and its deficiency is not manifested even under very low ascorbic acid intake. Skeletal lesions suggestive of scurvy are frequently found in children with kwashiorkor in some areas.

In temperate regions, infantile scurvy was at one time a common problem in bottle fed babies. The frequency and severity of subperiosteal haemorrhages is the outstanding feature of the disease in infancy. Tenderness is noted first at the lower end of the femora, which are frequently grasped by the mother while changing the napkins. Soon exquisitely painful swellings surround the lower ends of both thighs. Subsequently the lower legs and upper part of the arms are affected in a variable manner. The child lies in the 'frog' posture, unwilling to move the affected limbs, which appear paralysed (*pseudo-paresis*) and is apprehensive lest they are touched. Bleeding gums and occasionally haemorrhage from one of the internal tracts or petechial haemorrhages into

the skin, complete the clinical picture. The radiological signs are distinctive—a dense line of increased calcification occurs along the diaphyseal line of the metaphysis with a zone of rarefaction behind this in the shaft of the bone. Subperiosteal haemorrhages are seen as large dense shadows surrounding the shaft of the bones above the diaphyseal line.

Scurvy in older children. This is also very rare in all tropical countries. Large subperiosteal haemorrhages are not a feature of the disease at a later age, and the disease resembles that seen in adults. After many months of severe deprivation of almost all fresh foods, the first manifestations are the enlarged and prominent hair follicles in the limbs, which are indistinguishable clinically from the follicular keratosis of vitamin A deficiency. Eventually in scurvy minute haemorrhages occur around the base of these hair follicles. The interdental papillae of the gums enlarge as swollen purple buds and they bleed easily. Other haemorrhages may occur in the mouth, large purpuric swellings may be seen in the limbs, occasionally there are internal haemorrhages. Anaemia is a variable feature, in many cases it is completely absent as in the experimental study of scurvy in adult volunteers.

Scurvy must be distinguished from other causes of purpura and haemorrhage, and in infants from other bone and joint diseases. The typical X-ray picture, the dietary history and the serum level of ascorbic acid are of great diagnostic value When vitamin C deficiency is clinically manifested, the serum levels of ascorbic acid are reduced to zero.

The treatment of scurvy at all ages is extremely satisfactory and prompt recovery thus constitutes one of the best criteria of the presence of the disease. In the established case large amounts, up to 1 g., may be given as tablets in a single dose; there is little to commend the traditional but cautious administration of 50–100 mg. thrice daily, unless a loading dose has been previously given. Treatment at this high level is necessary for only a few days; after this every effort should be made to supplement the diet with fresh foods. These are measures by which the disease is prevented in bottle-fed babies, who should receive daily the juice or purée of almost any fresh fruit or fresh vegetables. The tropical and subtropical areas offer, in addition to the citrus fruits, a large variety of fruits and vegetables which are excellent sources of ascorbic acid; since they are usually not available in the temperate zones, they do not appear in the classical text book recommendations and are frequently overlooked, their use should be encouraged; mangoes, pineapples, guavas, the cashew nut fruit can be mentioned as examples. Many of these fruits are, in addition, excellent sources of carotene. In older children, reliance must be placed on the inclusion of some fresh food in the diet.

The prevention of scurvy is important in babies reared on boiled cow's milk or dried milk powder; juice from almost any vegetable or fruit readily prevents this disease, as does administration of ascorbic acid tablets mixed with the feeds (30 mg./day).

Rickets

Rickets is prevented and cured by one of the D vitamins. In the sunny tropical and subtropical countries, rickets is usually prevented by the action of sunlight on the skin, as this acts on fat situated on the surface of the skin to form vitamin D_3, which is subsequently absorbed. Vitamin D also occurs naturally in most animal fats (butter, egg-yolk), liver fat is especially rich in

this vitamin, so that oil extracted from this organ has been used much in therapy. Vegetable oils usually contain no vitamin D, so that this vitamin has been added to margarine in certain countries in order that it may be taken safely in place of butter. In temperate regions, especially if there is little sun, and clothing protects the skin from the sunlight, children rely very largely on the diet for their vitamin D; this, however, is not necessary in most of the tropics. Calciferol (vitamin D_2) does not occur in nature, but is prepared artificially by irradiating ergosterol and is employed in the treatment of rickets. Other factors in the diet also influence the incidence of rickets; calcium and phosphorus should be present in balanced amounts in the food and it is essential that they should be absorbed. There is little knowledge concerning the way in which vitamin D exerts its influence, probably it acts primarily on phosphorus metabolism, aiding its combination with calcium and thus the ossification which is occurring along the epiphyseal line.

Owing to the fact that vitamin D is formed by sunlight acting on the bare skin, it is not possible to state how much should be taken in the diet. In sunless temperate regions it is considered that the diet of children of all ages should contain 400 IU daily of vitamin D (National Research Council, 1964).

Formerly, rickets was common in temperate regions and surveys early in the present century revealed that one-third of the children in Britain showed evidence of rickets as detected by radiological examination. As a result of health education, the enrichment of milk with vitamin D, the wide use of vitamin D concentrates as supplements for infants and small children; a rising standard of life and medical care, rickets has become uncommon in temperate regions. It is still frequently seen among children in the tropical and subtropical zones, especially the latter (Fig. 7.15). It is especially frequent in large towns where buildings may cut off much of the sunlight, and is uncommon in rural areas. Much may depend on local custom with regard to clothing, housing and exposure to the sun. Its high incidence in many tropical urban areas, especially those in Asia, was reviewed by Jelliffe (1955). More recently, it was also found by Jelliffe *et al.* (1961) in the Indians living in the tropical and sunny islands of San Blas on the Atlantic coast of Panama. It has also been described in the Middle East by Costeff and Breslaw (1962).

In Guatemala, a significant number of cases have been found not only in the cities, but also in the very tropical and sunny rural areas. These are usually toddlers who are kept constantly inside the house, frequently within a wooden box to prevent their wandering around, particularly when the mothers have to work and leave the children in the house without a responsible person to take care of them (see Fig. 7.15). More attention should be given, therefore to rickets in the tropical and subtropical areas; social changes now occurring in these areas with increased tendency for urbanization, in most cases inadequately, and with higher demand for the work of women, may result in the appearance of new problems, among them, rickets. It is also probable that if rickets is not more frequently seen in malnourished children in the tropical and subtropical areas, who frequently are not exposed enough to sunlight and do not receive external sources of vitamin D, is because their growth is greatly impaired by the calorie–protein deficiency

they usually suffer. When their inadequate diet is corrected by supplementary feeding or by other means, attention should be given to either sufficient sunlight exposure, which is much more practical in these areas, or if necessary, to vitamin D supplementation.

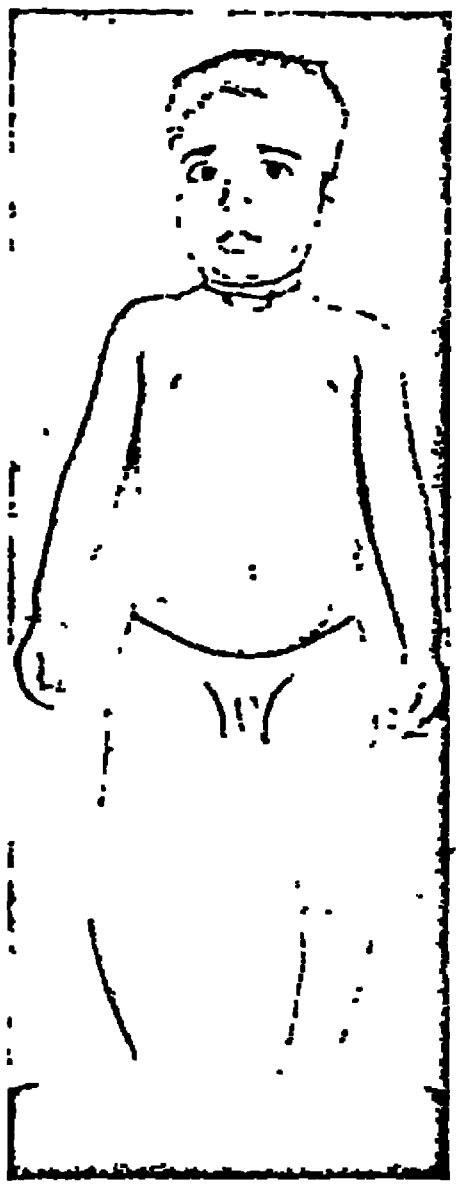

Fig. 7 15. Rickets in urban tropical child, showing bow-legs and epiphyseal enlargement (Calcutta, India)

Many general signs occur in rachitic infants, but possibly some of them are due to associated forms of malnutrition. The rachitic infant is said to be irritable and unhappy, the muscles are flabby, it is prone to attacks of diarrhoea and respiratory infections. Development is delayed and the usual milestones are passed late. The bony changes are, however, the distinctive features of this disease; they occur at situations where growth is more rapid and may result in deformities due to the action of muscles or of body weight or of posture.

Under 9 mnth of age, the earliest changes are seen in the skull where oval unossified areas can be made to crackle like parchment under the fingers (cranio-tabes). These occur in areas on which the infant lies and affect thus the upper occipital and posterior parietal regions. Cranio-tabes may occur in many other diseases and may even be detected in normal infants. There is delay in closure of the anterior fontanelle, which remains large in size. Bossing of the skull over the frontal and parietal eminences gives the 'hot-

cross-bun head'. Beading of the ribs occurs at the osteochondral junctions near the sternum and is due to an increase of osteoid tissue. The epiphysis of the limb bones are enlarged for the same reason; this is seen most characteristically in the wrists and ankles during the second year of life. Some bowing of the long bones of the limbs may occur, especially if weight is borne, resulting in various deformities which are most marked in the legs. Although these may tend to decrease as the child grows older, especially if the diet improves or more sunlight is available, pelvic deformities may persist into adult life. The pelvic brim is deformed in a characteristic manner, having a reduced antero-posterior diameter, and serious delay in childbirth may necessitate Caesarian section. There is little evidence to show that caries in childhood is related to deficiency of vitamin D, but rather to an excess of sugar and refined flours (p. 379). The lowered blood calcium sometimes found predisposes the child to various manifestations of increased nervous irritability and tetany.

The diagnosis of rickets is confirmed by the X-ray appearances and by the response to treatment. Radiological changes are seldom manifest before the end of the first yr; after this age, they are almost a constant feature and are seen most distinctively at the wrist. The lower ends of the ulna and radius enlarge, the diaphysis appears enlarged and cup-shaped, its lower margin is hazy and corresponds to a broad zone of irregular calcification. The serum alkaline phosphatase is constantly raised in all cases of active rickets above the normal figure of 5–10 units in children under 2 yr of age; any figure of over 15 units is pathological, but may occur in hepatic disorders or generalized bony disease. The serum phosphorus is usually reduced to 2–4 mg./100 ml. (normally 4·5–5·5 mg./100 ml.), the serum calcium is often normal (10–11 mg./100 ml.) or only slightly reduced in the nervous complications. All biochemical and radiological abnormalities should return to normal during treatment.

It is easy to confuse other diseases with rickets or to overlook genuine cases of this disease in tropical areas where this disorder is thought to be rare. Some bossing of the skull is common in many children; it may be very marked in sickle cell anaemia. Cooley's anaemia and other haemolytic anaemias (p. 540), but is seldom marked at as early an age as rickets. A marked bossing of the skull has been noticed frequently in young African infants who show no other signs of rickets: this disappears as the child grows older, and, occurring mostly at an age when chronic malarial anaemia is common, it may reflect a response of the marrow to this disease. The moth-eaten changes in the epiphysis and the osteitis of the long bones are features in which congenital syphilis (p. 731) differs from rickets. It should be borne in mind that some prominence of the forehead is common in newborn babies and again in plump 3-yr-old toddlers.

Treatment of rickets may be with cod liver oil (1 teaspoonful often contains 300 IU), or vitamin D concentrates, about 900–1200 IU should be given daily for 1–3 mnth or even longer. Severe cases may be given the liquid vitamin D concentrates—administering for 2–4 weeks 2000 IU daily, subsequently the dose is reduced to 1000 IU daily for several months. Very

ere cases, especially if little supervision can be given to their treatment, ay be given a single massive dose of 300,000 IU as an injection of calciferol. The continued administration of high doses of vitamin D is dangerous and leads to calcification of abnormal sites in the body of which the most important are the renal tubules.

The prevention of rickets must be considered as a public health problem in the larger towns of Asia and wherever children are shielded from sunlight, whether by excessive clothing or even more completely by tall buildings and dark rooms in congested slum areas. In these regions, it may be necessary to issue preparations of vitamin D at child welfare clinics, to encourage the consumption of any form of animal fat (vegetable fats contain none of this vitamin), and to advocate some form of sunbathing for infants, if practicable. The enrichment of supplementary foods such as skim milk should also be considered. In the tropical rural areas, health education in regard to housing and clothing may be needed.

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Prevalence of Malnutrition among Preschool Children of Developing Countries

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Clear-cut, reliable, and quantitative information on malnutrition in preschool children is extremely limited. One reason is lack of common agreement on what to recognize as true malnutrition. A second reason is the scarcity of systematic incidence studies in large population groups observed in their natural setting.

The world-wide effort expended on the study of malnutrition in young children during the past 15 to 20 years is both imposing and valuable. In the beginning, attention concentrated excessively on clinical studies of severe cases, to a large extent on the syndromes of kwashiorkor and marasmus. Subsequently came realization that these obvious illnesses constitute a small part of the over-all problem. Information on the remaining subclinical malnutrition in a general population is to be had only through costly and tedious investigation. Studies designed to acquire information under field conditions are not as appealing as clinical investigation, with the result that such data are scarce.

A recent review by Jelliffe[1] furnishes useful although limited information about conditions in developing countries. For instance, a single community survey in Haiti showed an extremely high prevalence of kwashiorkor in children 1 to 3 years old compared with the frequency in other similar areas. The average for the country was 7 per cent, and yet this high ratio in no way expresses the real magnitude of the problem in Haiti or generally. About two thirds of this same population suffered some degree of protein-calorie malnutrition as judged by deficiencies in height- and weight-for-age.

Similarly, 10 per cent of children less than 6 years old admitted to a large hospital in Kampala, Uganda, were patients with kwashiorkor. The proportion is certainly great. That it is representative of the general region is supported by the experience of outpatient clinics in the same area, where at least one half of all children between 6 months and 3 years of age gave some evidence of protein-calorie malnutrition.

Current country-wide nutritional surveys in Central America are

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providing similar information.* In Guatemala, for instance, in a sample of approximately 600 families living in 40 rural communities distributed throughout the country, only one case of frank kwashiorkor was observed among children under 5 years of age. If this case is added to 8 others classified as prekwashiorkor and to 3 with marasmus, the prevalence of severe cases is 1 5 per cent A total of about 13 per cent of the children were classified clinically as malnourished. By contrast, if body weight for age is used as the criterion of nutritional status, about 70 per cent of Guatemalan children less than 5 years old are malnourished. In El Salvador the prevalence of severe protein-calorie malnutrition at the same ages was 4 5 per cent A half of all children were classified clinically as malnourished, and again about 60 per cent of those aged 6 months to 5 years were underweight-for-age.

It is evident that more information is imperative if the magnitude and public health significance of malnutrition in early childhood are to be defined. One approach is a consideration of primary factors in the epidemiology of protein-calorie malnutrition. Dietary practices and the prevalence and effects of infectious diseases have first attention.

Dietary Patterns

A representative cohort of infants born in a Mayan Indian community of the Guatemalan highlands[2] has been followed by home visits from birth to the present time, about 3 years. The study continues In all, 80 children have been studied at intervals that varied from daily visits in the newborn period, then to weekly, and then fortnightly intervals for older children All were initially breast-fed and 21 are now completely weaned.

The dietary pattern of these children during infancy and weaning is summarized in Figure 1. The shaded part of a bar indicates the proportion of children receiving a particular food at a prescribed age. The intensity of shading is designed to show its nutritional significance, either by reason of amounts received or the kind of food.

Breast feeding continued until late in the second year unless termi-

*These studies have been carried out with the cooperation of the governments of the Central American countries and Panama, the Office of International Research (OIR) of the National Institutes of Health of the United States (NIH), the Institute of Nutrition of Central America and Panama (INCAP) This research was supported by the Advanced Research Projects Agency (Project AGILE) and was monitored by the Nutrition Section, Office of International Research, National Institutes of Health, under ARPA Order No 560, Program Plan No 298.

nated by pregnancy or birth of another sibling before that time. Liquids, usually water with sugar, were given to most children during the early weeks after birth; their use was subsequently less frequent. Supplementation of mother's milk began at about 6 months, with a progressively increased introduction of new foods. By age 1 year, the children received practically all foods within the general family diet. Liquid preparations (mainly coffee, thin starchy gruels, and broths) comprised an important part of the diet.

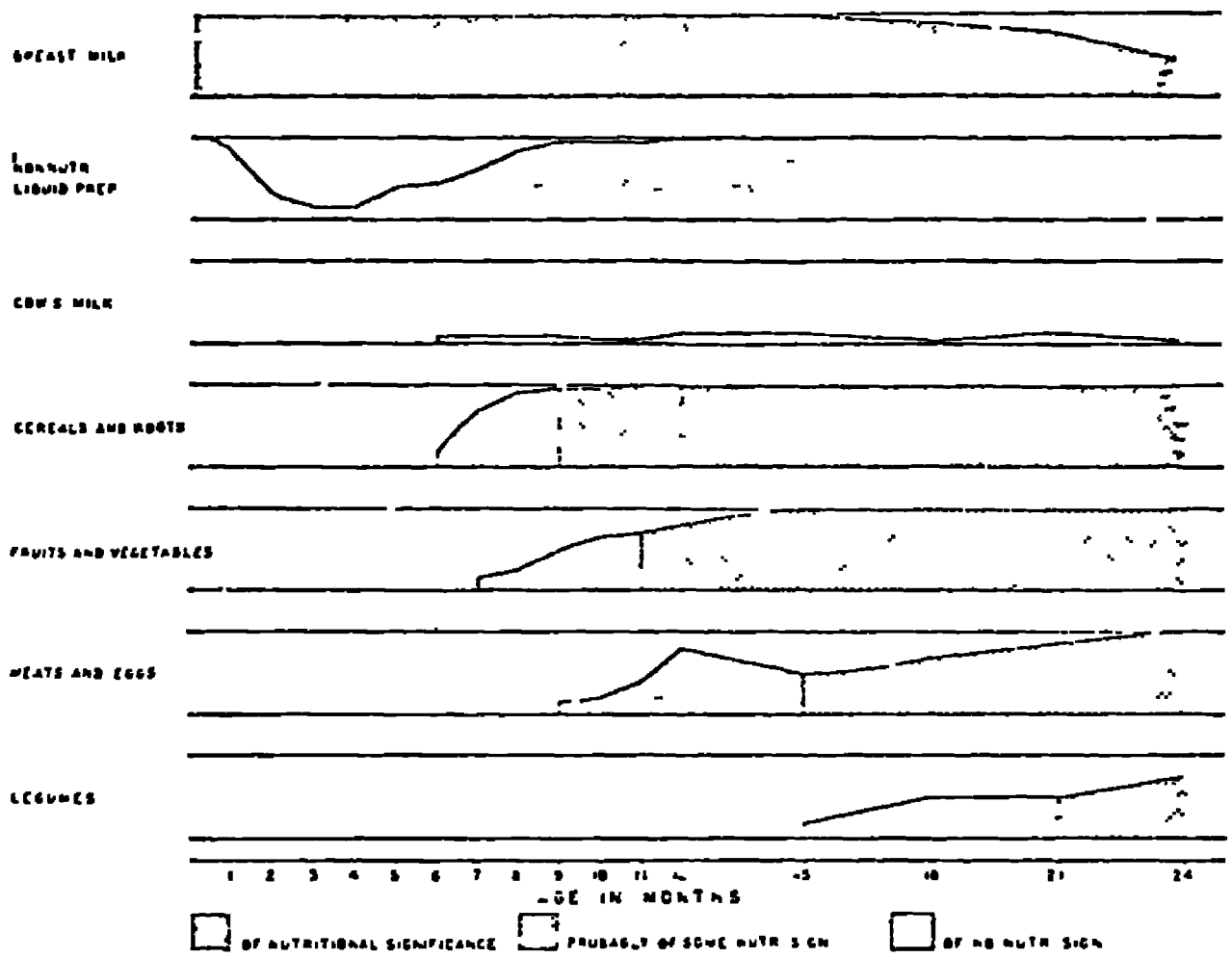

FIGURE 1
Dietary pattern of infants, by age in months, in a rural Mayan Indian community in Guatemala

Two features of supplementary feeding require emphasis, the first being the quantitative aspect. Most of the foods offered infants during breast-feeding, and even after weaning, were in conspicuously small amounts. The real intent of mothers was to develop in the children a taste for foods other than breast milk and to accustom them to their use, rather than to provide added nutrients.

The qualitative aspect is the second consideration. Meals were not prepared specifically for the infants, with the possible exception of starchy gruels, and then primarily when the children were ill. Other-

wise, they received the same foods the rest of the family ate, although in lesser amounts. The family diet was regularly low in protein, and that protein was of low biological value. Ordinarily it met the protein requirements of older children and adults, particularly if large amounts of food were consumed, but it was decidedly inadequate for the small child.

The dietary situation was further aggravated by exclusion from the infant's diet of certain items consumed by older children and adults, because they were considered unsuited to infants and small children. Such items included black beans, one of the more important and common sources of protein in the family diet, and also the occasional meat available to the family. Only the water in which these foods were cooked was believed satisfactory for the infant.

The potential ill effect of these dietary habits becomes evident through appraisal of the protein and calorie content of supplements received by infants during weaning, and the total diet after weaning.

At 24 months of age, as Figure 2 shows, the supplement provided only about one half of the generally accepted allowances for calories and 55 per cent of the required protein. Protein deficiency is indeed more serious than these cited values indicate, first, because the low-calorie intake limits utilization of proteins as essential nitrogen, and second, because the greater part of the protein is of vegetable origin and of low biological value.

Under field conditions, where these studies were made, the amount of mother's milk received by the children was impossible to measure. A variety of indirect evidence indicates that the breast milk received during late lactation is far from meeting the deficit in nu-

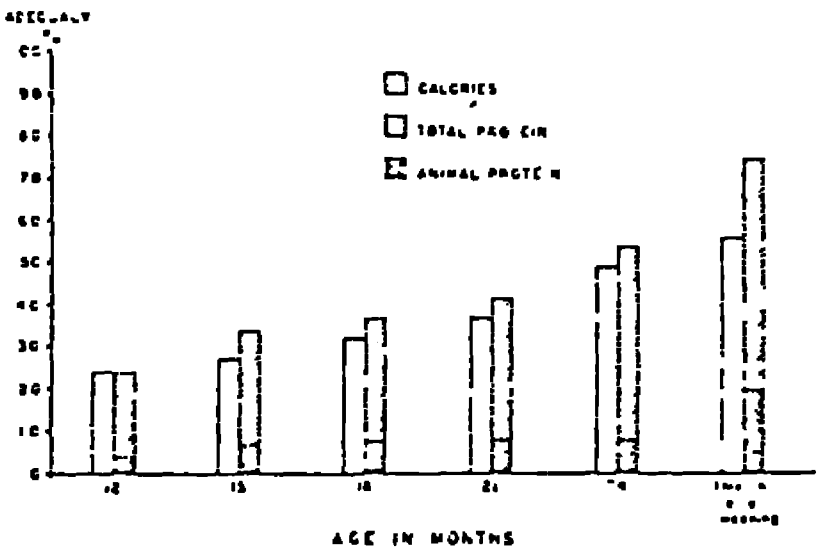

FIGURE 2
Calories and protein content of supplementary feeding of infants, by age in months, in a rural Mayan Indian community in Guatemala

trients The same poor dietary practices cont nue immeciately after weaning. Since all intake can now be measured, it becomes certain that foods consumed at this time are both insufficient and of poor quality

At approximately the fourth year of life a trend toward improved dietary intake is evident. Although low-protein and low-calorie intake continue, as judged by recommended allowances for normal children of this age,[3] the deficit is probably not as great as first appears, provided the reduced size and activity of malnourished children are taken into account

Better knowledge of the mechanisms by which the individual adapts to a diet low in protein and calories may explain why serious nutritional problems are less frequent after the fourth year of life. The effect on health, behavior, and socioeconomic welfare in adolescence and adult life of this "adaptation" to suboptimal nutrition is an equally cogent consideration

The dietary pattern of a Mayan Indian community in the highlands of Guatemala is of general interest It also illustrates a principle Throughout most of the underdeveloped world the same pattern prevails with little variation Jelliffe emphasizes this in his monograph on *Infant Nutrition in the Subtropics and Tropics*[4]

In widely different cultural groups, living in diverse areas and with different foodstuffs available, people have adopted strikingly uniform principles of infant feeding The kinds of food may be different: the "tortillas" of the Guatemalan Mayas may be replaced by "chupatti" in India, by "mehallabiah" in Egypt, by "sugi" or "delnys" in Pakistan, by "bubus nasi" in Indonesia, by "taro" or sweet potato in New Guinea, or by "matoke" in Uganda All are poor in protein.

From country to country, principles of infant feeding are in remarkable agreement The more important are (1) breast feeding is prolonged, usually until the second or third year of life, and sometimes even longer, (2) supplementary solid preparations are introduced late and in insufficient quantities, (3) supplementary foods are selected from the usual family diet, without individual preparation, and selection is based on what is considered "safest" for the child.

The conclusion is that these practices result from (1) unavailability of adequate and safe substitutes for mother's milk, (2) poor sanitary conditions, lack of basic concepts of hygiene, and erroneous concepts of disease causation and (3) the circumstances just noted. cultural concepts about foods are more closely oriented to disease than to health, thus leading to selection of foods for small children on the basis of safety tolerance, or adaptability, rather than nutritive value

While many different cultures have arrived at the same basic concepts and similar methods of practicing infant feeding, although using different foods, it is equally apparent that in many places these practices are being modified under the influence of a foreign culture. If this happens without cultural change, the results may be disastrous Repeated examples are to be found of the deleterious effect of early weaning, or the use of cow's milk preparations by populations that are culturally and economically not yet able to carry out these practices properly. This serious problem affects large sectors of the world's population, not only people still living under primitive conditions but also those who have migrated to more sophisticated urban societies without having adapted to their new environment culturally and economically. The problem is fundamentally social.

Infectious Diseases

A second factor strongly determining malnutrition in early childhood in underdeveloped regions is the high prevalence of infectious diseases, and, what is less well appreciated, the common synergistic interaction of nutrition and infection The communicable diseases of childhood, which include measles, whooping cough, and others, and particularly the diarrheal diseases, are extremely frequent in malnourished populations living in a poor and insanitary environment [5] They are also most prevalent at precisely the ages when children are most affected by dietary deficiencies Many factors enter into this situation. Measles, for instance, is a disease of early school age in large industrialized countries but a disease of preschool children in the semi-isolated and more homogeneous rural communities of developing countries The impact is therefore much greater, affecting younger children already in a poor nutritional state.[4]

The situation in respect to diarrheal disease is even worse The children of these underprivileged populations are contaminated with enteropathogenic agents almost from the moment of birth Guatemalan village studies[2] have demonstrated protozoa, including *Entamoeba histolytica*, enteroviruses, and bacteria in the feces of infants within days after birth Newborn infants are, however, relatively protected during the early months by transplacental immunity and breast feeding After the third to sixth month passive immunity diminishes; additional contamination occurs as unfamiliar foods are progressively introduced into the diet, direct contact with the insanitary environment increases, and the nutritional status of the child begins to deteriorate. The incidence of diarrheal diseases rises and reaches a peak as the weaning period ends These epidemiological

factors are well defined. Others are not so clear: questions relating to the anatomy and physiology of the intestinal mucosa, the interactions of the intestinal flora, and the nature of the diet. Malnutrition is thus both a consequence and a causative factor in this widespread and lethal disease of developing countries. It has been defined epidemiologically as weanling diarrhea.[5,7]

The introduction of new people and customs within the population of a developing country also influences infectious disease, as already shown with respect to dietary patterns. The mechanisms are different, but the effect is just as certain. An infectious agent not previously present in a native population, and to which it has not adapted, disturbs the existing ecology, causes epidemics, or becomes implanted as an endemic process. This is especially likely if the population is in a state of cultural and social change; and that happens to be the present status of large sectors within developing countries.

Synergism of Nutrition and Infection

The immediate results of the synergistic interactions of nutrition and infection[6] are well known and documented by the high incidence of disease and deaths among children throughout large areas of the developing world. Of more direct concern for this Conference on

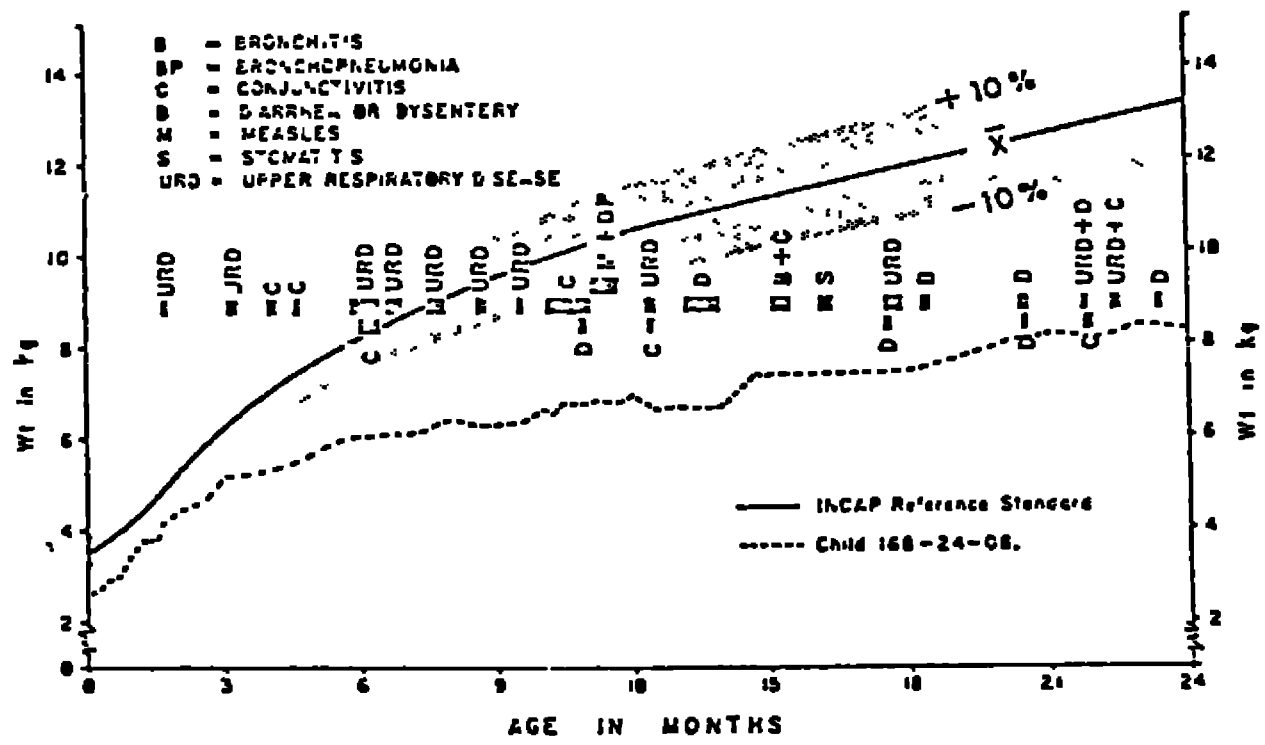

FIGURE 3
Acute infectious diseases in a Guatemalan village child, by age, and subsequent gain or loss of weight. The shaded zone shows mean weight gain of well-nourished Guatemalan children (x) and 10 per cent deviations (INCAP reference standard).

growth and development, physical and mental, is the situation of the surviving child. The large majority will continue to live in a state of chronic subclinical malnutrition, usually not recognized. This is clearly manifested in lesser physical growth, whether in relation to the individual child or to the community of children. Figure 3 presents the weight curve of a typical child from among those studied over a period of years in the rural Guatemalan village already mentioned.[2]

The child did well for the first 3 months of life, with a single illness of minor consequence; the gain in weight kept pace with the INCAP reference standard[9] and was close to that for infants generally. Thereafter the tempo of illnesses quickened and with it a halt in weight gain. Throughout the next 2 years, the gap widened progressively between observed and expected weight for age. This child was no exception. His experience was duplicated by child after child in the study group, as the composite of the other 45 children (Fig. 4) well demonstrates.

Nor is rural Guatemala unique. The growth pattern of these village children coincides with that of children in most underdeveloped areas. Gain in height and weight is satisfactory for the first 3 to 6 months. The rates then drop and throughout the preschool years do not again approach the standard set by well-nourished children of an industrialized country where economic and social conditions are more favorable. Figure 5 illustrates weight curves for southern India,[10] Figure 6 for Thailand,[11] and Figure 7 for New Guinea.[12] Similar weight curves by age were charted for Uganda children,[13] children in Mexico,[14] Chinese children in Malaya,[15] and other regions. The results were strikingly uniform. Obviously, the observed behavior related to no racial characteristic. It was the result of an interaction between a host and its environment, in a universe of malnutrition and infectious disease.

The regularity of this situation in so many parts of the world and the uniformity of its effects require an attempt now to quantitate the worldwide prevalence of protein-calorie malnutrition in preschool children. The estimates to be presented are based on two premises first, that the presence in a given area of the syndromes of kwashiorkor or marasmus is to be taken as indicative of the occurrence of protein-calorie malnutrition in its varying forms and extent of severity; and second, that retardation in body weight for age is a practical index of the magnitude of the problem.

Areas where kwashiorkor and marasmus are known to occur are shown in Figure 8. On the basis of studies on body weight of children in many of the developing areas, an estimate that 75 per cent of

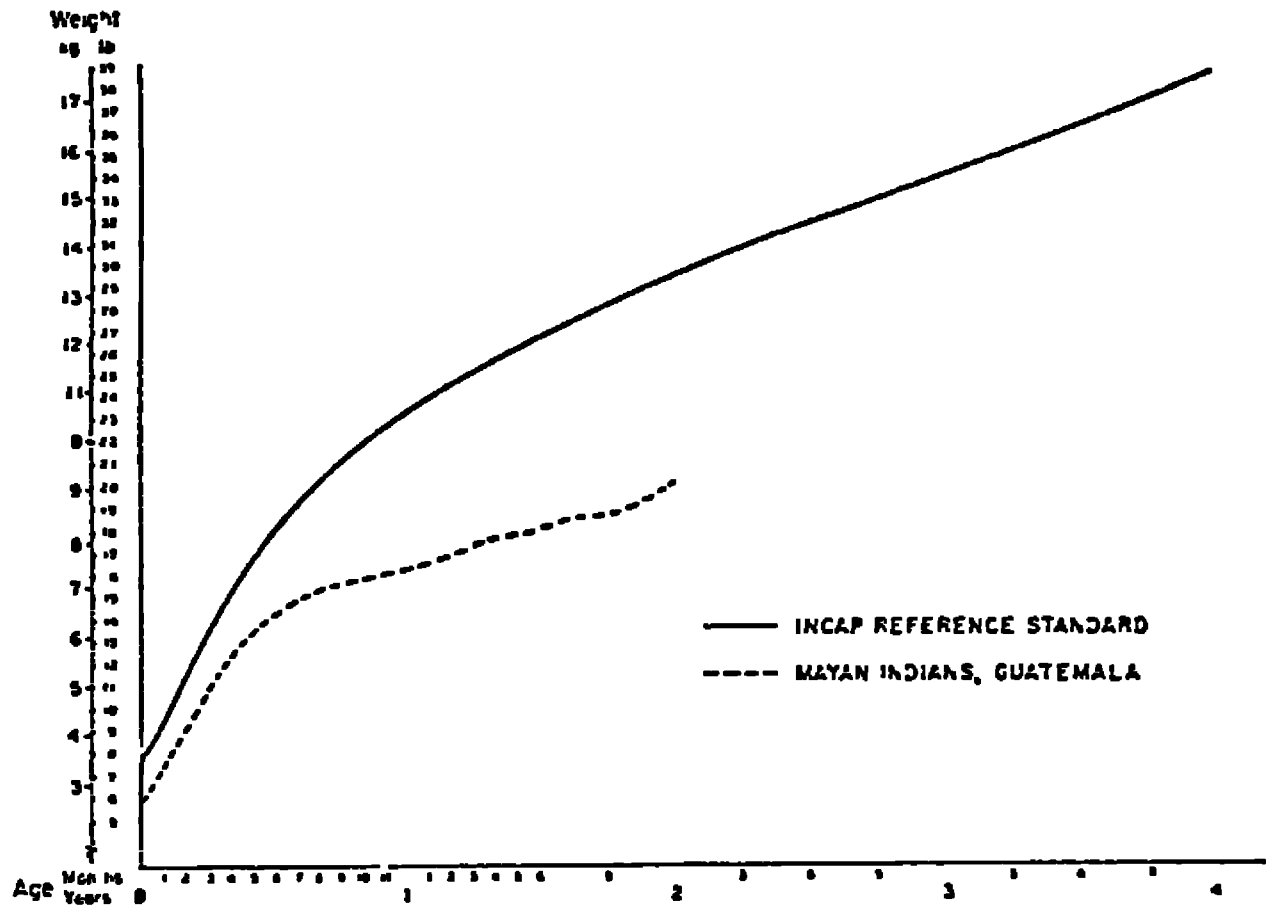

FIGURE 4
Average weight-for-age (kilograms and pounds) of 45 Mayan Indian children in Guatemala, and corresponding values of the INCAP reference standard.

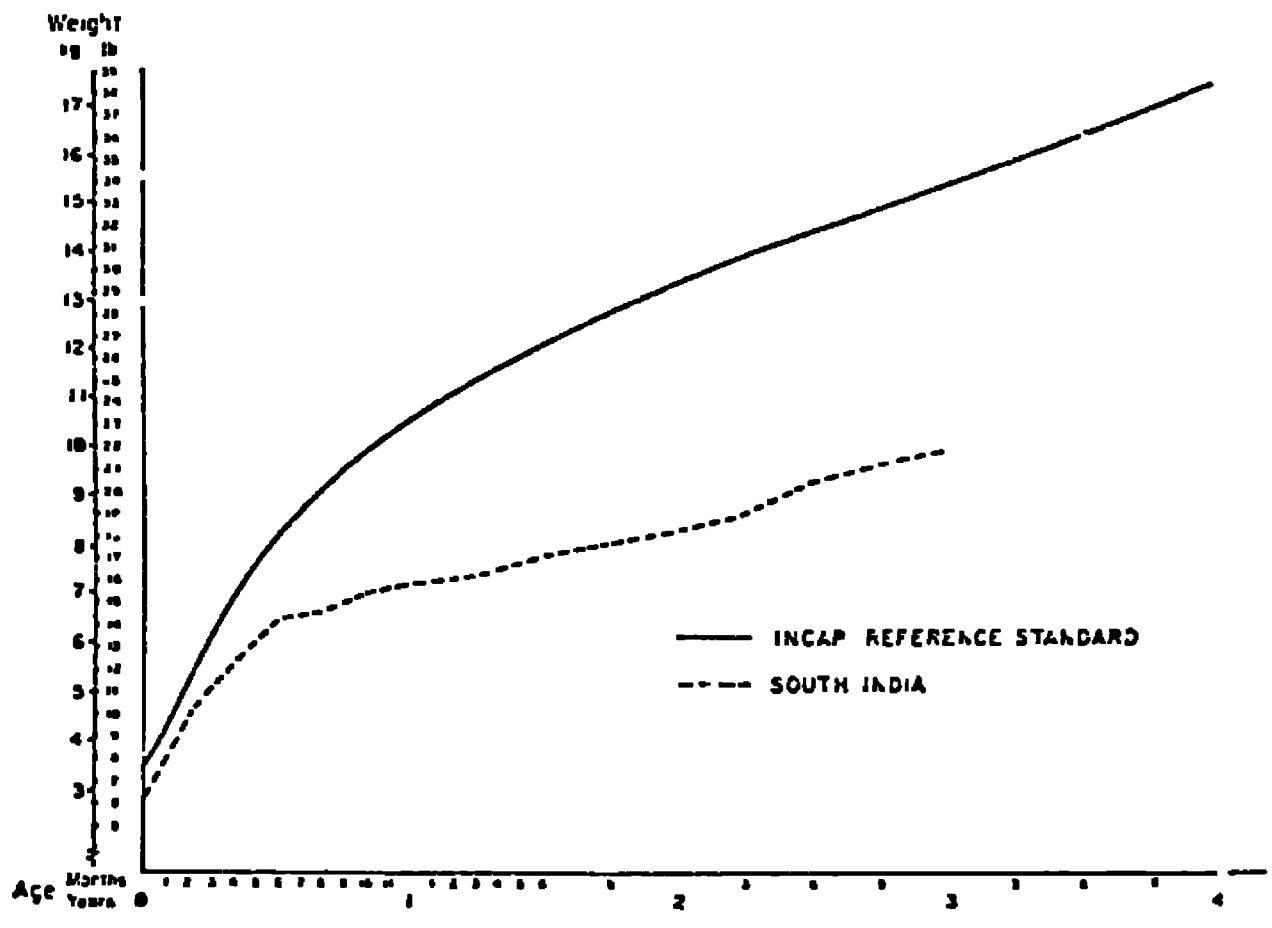

FIGURE 5
Average weight-for-age (kilograms and pounds) of children in southern India, by age, and corresponding values of INCAP reference standard

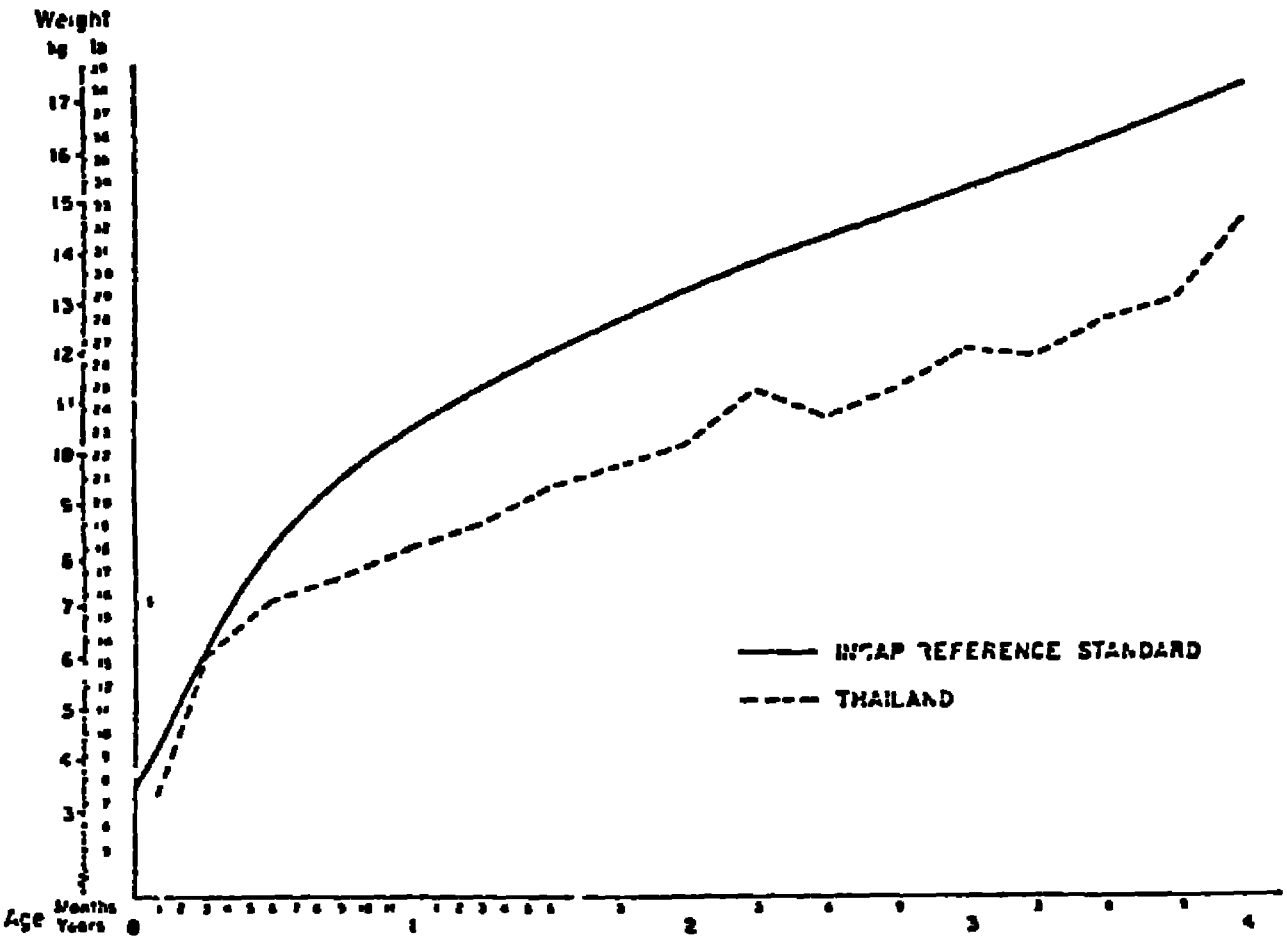

FIGURE 6
Average weight-for-age (kilograms and pounds) of children in Thailand, and corresponding values of INCAP reference standard.

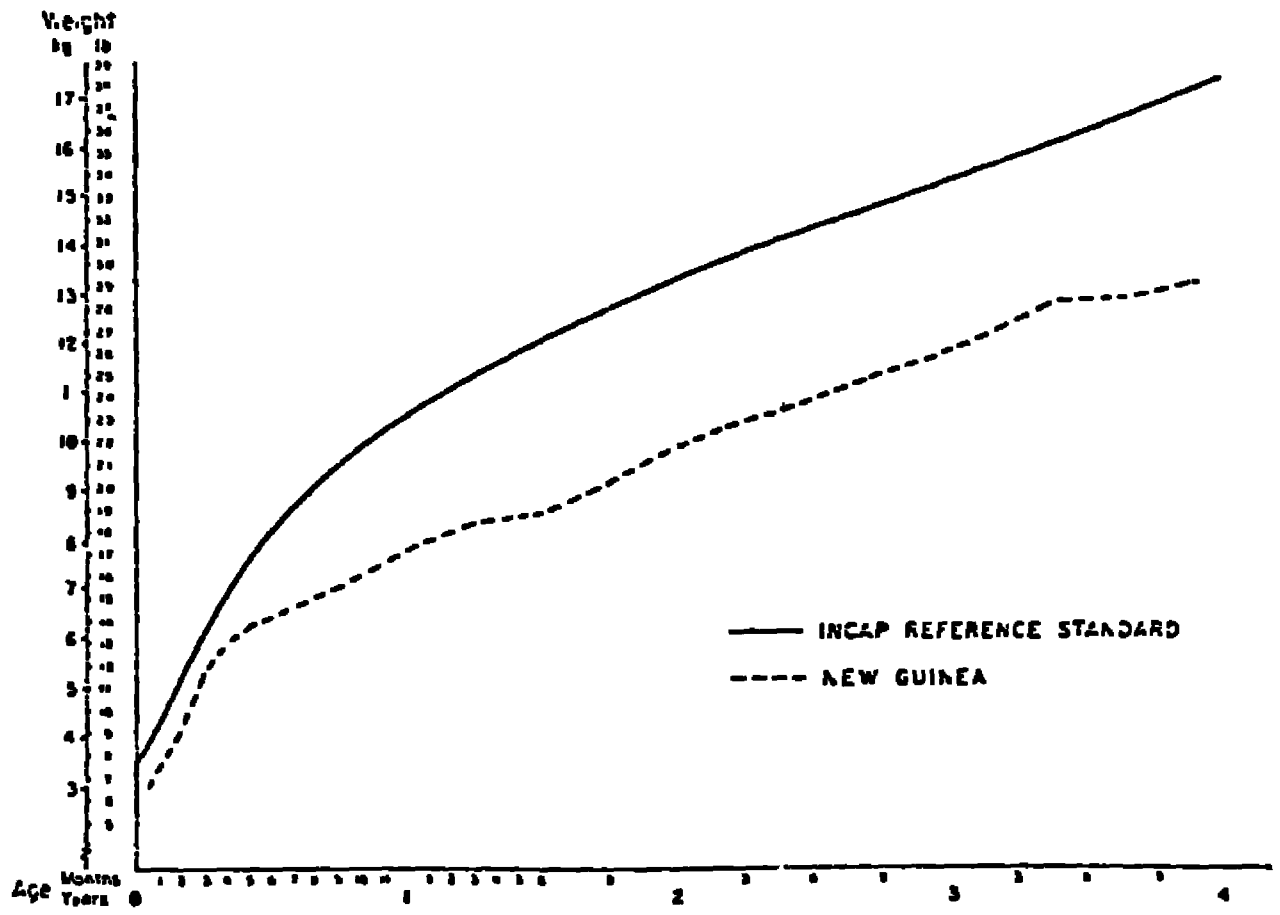

FIGURE 7
Average weight-for-age (kilograms and pounds) of children in New Guinea, and corresponding values of INCAP reference standard.

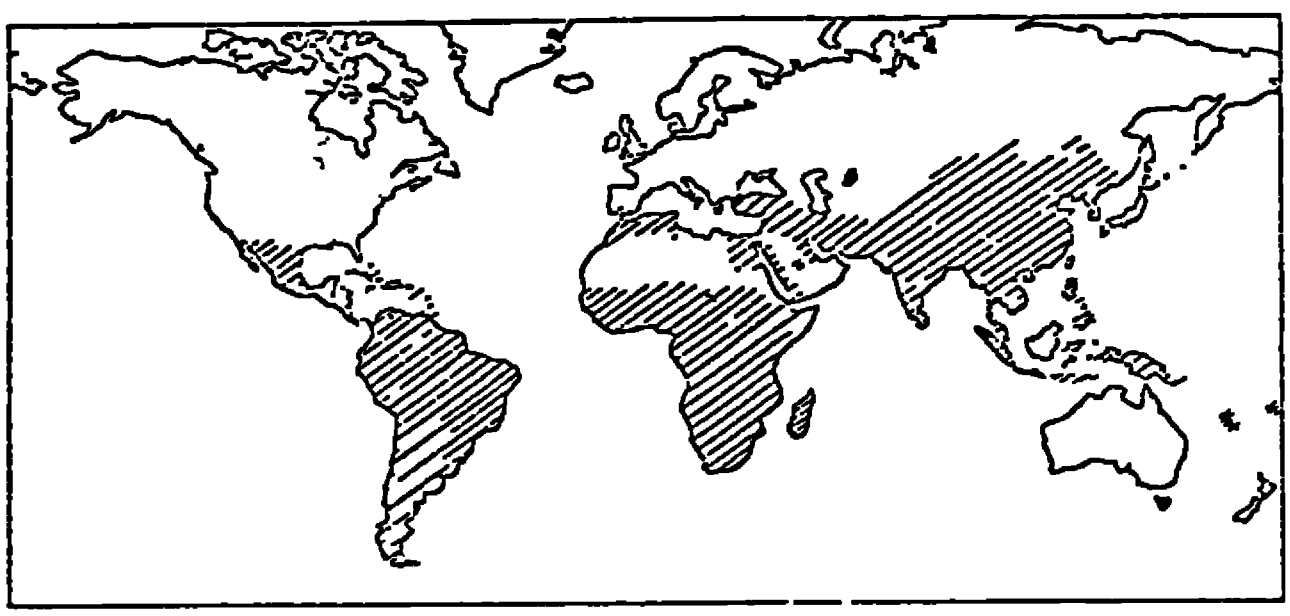

FIGURE 8
Geographic distribution of protein-calorie malnutrition (PCM).

preschool children are underweight-for-age is conservative. About 400 million children less than 5 years old live in these areas; from which it follows that about 300 million preschool children suffer currently from mild to moderate forms of protein-calorie malnutrition. This corresponds to about 60 per cent of the total preschool age population of the world (500 million). The numbers affected will tend to be greater because populations in underdeveloped areas are growing at a faster rate than food supplies increase.

Conclusions

Increasing evidence supports a solid effect of nutritional disorders on physical growth and development of preschool children. The assumption of an effect on mental growth and development, and on learning and behavior as well, is wholly reasonable. The brain is as much an organ as any other, and presumably shares in the effects of malnutrition. The preschool children of today are the young adult population of 20 years from now. The future social, economic, and political well-being of man may well depend upon an enlarged understanding of the effects of malnutrition and an attempt to eliminate the causes of that condition.

Acknowledgments

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Eds. *Béhar's observations derive mainly from a series of field studies conducted by the Institute of Nutrition of Central America and Panama (INCAP) during nearly two decades. The investigations were among children less than 5 years old, most of them from the rural populations which predominate in that developing country. Enough urban communities were studied to permit reliable comparisons.*

While estimates of health conditions in developing countries are at best untrustworthy due to limited factual information, the number of children experiencing an appreciable deficiency in physical growth and development easily includes the hundreds of millions calculated by Behar. The finding that 70 per cent of children of lower-income, rural populations in Guate-

mala are 10 per cent or more below expected weight for age according to a reference standard is impressive and even astounding. However, by clinical criteria, Béhar's extensive survey gives a prevalence of only 13 per cent. This is because weight-for-age measures both existing malnutrition and evidence of a preceding deficit in children now gaining weight at a normal rate for actual height. It is a matter of distinguishing between incidence and prevalence. Behar's figures represent the number of children who either are or have been malnourished between the ages included.

The occurrence of kwashiorkor can also be used as an indicator of all degrees of protein-caloric malnutrition, but the same lack of exactness exists as in attempted evaluation of inapparent infection by the frequency of clinical manifestations. Protein-calorie malnutrition is like a huge undersea mountain, a small fraction visible above the surface, while the great bulk is submerged and unseen. To the public health worker, kwashiorkor and marasmus are the evident part of protein-calorie malnutrition; the majority of cases remain clinically inapparent except for smaller body size

The practical need is a reliable method to differentiate existing malnutrition from past malnutrition. The ratio of present weight to present height is one answer Current and past incidence are independent questions, in which case the age at onset, and duration and extent of active malnutrition, may well be the useful determinants of long-term health effect.

A second major contribution of Béhar's studies is the proof they give that the more marked deficiencies in height and weight for age are associated with inadequate food intake during weaning from breast feeding and shortly thereafter. The resulting malnutrition acts synergistically with the infectious diseases so frequent at these ages, promoted as they are by the prevailing poor sanitation and unsatisfactory personal hygiene.

The general acceptance of multifactorial causation furthers understanding but complicates the separation of individual biological, social, and cultural components of the causative complex. Still more difficult is the evaluation of their mutual interaction. Multifactorial analysis is hard enough for physical growth and development; the difficulties multiply when the issue is mental maturation

The next paper, by Guzmán, also of INCAP, systematically examines country after country in developing regions to establish how widely characteristic are the conditions described for Guatemala.

I-469 Scrimshaw, Nevin and Moisés Béhar. "Malnutrition". Section III (Chapter 11). In:Human Ecology and Public Health. E.D. Kilbourne and W.G. Smilie (Eds.) 4th. ed. New York, The Mcmillan Co., 1969, p. 284-307

11

Malnutrition

Nevin S. Scrimshaw and
Moises Béhar

INTRODUCTION

Advances in public health and parallel social and technological changes paradoxically have increased the prominence of malnutrition in both less developed and industrialized countries. In the less-developed countries, control of the mass diseases that once decimated whole populations has left evident the underlying malnutrition, particularly among young children, that retards growth and development and increases the severity of common infections (Scrimshaw and Béhar, 1965).* It has also contributed to the higher rates of population increase, which, in turn, have led to an actual decrease in *per capita* food availability in some countries. In the industrialized countries prosperity and an abundance of food have resulted in the rise of obesity as a public health problem and contributed to the increase in coronary heart disease.

NUTRITIONAL PROBLEMS OF LESS-DEVELOPED COUNTRIES

Protein-Calorie Malnutrition

Various degrees of protein and calorie malnutrition are universal among the lower income populations of the less developed countries (Scrimshaw and Béhar, 1961). They are a major factor in the high infant and preschool child mortality in these countries. Protein-calorie malnutrition is more than a medical problem. In those countries where large proportions of the population are living under conditions of limited social and economic development, malnutrition arises from a combination of two main factors: a diet that is quantitatively and qualitatively inadequate, and

* Parts of this chapter are adapted from N. S. Scrimshaw, and M. Behar: Malnutrition in underdeveloped countries. *New Eng J Med*, 272 137–144, 193–198, 1965.

superimposed stress, commonly of infectious origin. The deficient diet results in turn from various combinations of low food production, inadequate preservation and distribution of foods, restricted purchasing power, poor food habits, and deficient knowledge of the relation between diet and health. The excessive incidence of infectious disease is consequent to a lack of environmental sanitation, and to poor personal hygiene, inadequate control of vectors, insufficient health services, and lowered resistance due to malnutrition.

The two main factors are, therefore, interrelated and act synergistically to the detriment of nutritional status (Scrimshaw, *et al.*, 1968). Their relative influence determines the clinical results. Of particular significance are the severity and duration of the nutritional deficiencies of protein and calories, and the extent to which protein is deficient relative to calories, the nature and severity of other associated nutritional deficiencies, the age and physiological state of the person affected, and other diseases that have preceded or are concurrent. The mild and moderate forms of protein-calorie malnutrition are frequently unrecognized because they are characterized primarily by retarded physical growth and development (NAS–NRC: *Pre-school Child Malnutrition* ... 1966). Unfortunately, at early ages mental development and subsequent learning and behavior can be affected as well (Scrimshaw and Gordon, 1968).

Mild and Moderate Forms. In underdeveloped countries the average weight and length of children at birth are close to the values for North American or European children. Most infants grow normally during the first four months of life because they are breast fed. Beginning as early as the fourth month, however, rates of growth decrease and height and weight values depart progressively from established values for well-nourished children. During the second and third years, growth and maturation may be almost at a standstill. Only after this crucial weaning and postweaning period do children partake sufficiently of the family food and acquire enough resistance to infectious diseases so that their growth rate again approaches that of well-nourished children. During the school years rates of growth generally parallel those of well-nourished children, but lost ground is not recovered.

In some populations this amounts to a retardation of two to four years in bone age at the time of entering school, at about age seven. Consequently, when growth stops with the closing of epiphyses the final stature is smaller. Epiphyses seem to close at much the same chronological age despite the lesser size of the child. It is mainly for this reason that adults in underdeveloped countries tend to be smaller than those in industrialized ones. Genetic differences in growth potential are probably of lesser importance.

The period of retarded growth coincides with the increasing inadequacy of breast milk as the sole source of protein and other nutrients and insufficient or improper supplementation of the breast-feeding regimen (Jelliffe, 1955). After full weaning, which may not occur until the third year, the diet given the young child in less-developed countries is still commonly cereal gruels, starchy roots, overdiluted milk, and even cornstarch, with no opportunity provided the child to share in the full adult diet. In most cases this regimen not only fails to provide the needed protein and calories but is deficient in other essential nutrients. Legumes, vegetables, and occasional

meat, cheese, or other animal products are usually too few to provide the additional proteins needed. Only toward the latter part of the preschool period, when the child is permitted an adult type of diet, does protein-calorie malnutrition become less common.

Unfortunately, this period of greatest dietary inadequacy coincides with a high exposure to an unsanitary environment at a time when passive immunity from the mother has been largely lost, and acquired immunity is limited. This is the age of highest frequency of diarrheal, respiratory, and parasitic diseases as well as the common communicable diseases of childhood: measles, whooping cough, chicken pox, rubella, and mumps. The second year death rate in a country is the best single index of the extent of malnutrition among young children (Gordon, *et al.*, 1967). The adverse consequences of infectious disease on nutritional status are described later in this chapter.

Because stunting during the period of malnutrition is most marked in those parts of the body that normally grow faster, disproportion develops in anthropometric measures. The shorter limb-to-trunk ratio observed in some poorly nourished population groups is largely from this cause. Moreover, 80 per cent of adult brain growth is achieved before three years of age. It is not surprising, therefore, that early malnutrition has been shown in many less-developed countries to be associated with a smaller permanent head circumference

The common assumption that genetic factors are responsible for a substantial part of the size differences among adult populations is untenable. Well-nourished children in a healthy environment usually follow the growth patterns of well-fed North American or European children, regardless of their genetic origins Conversely, children of European racial origins living under adverse conditions consistently show reduced growth.

Adult Protein-Calorie Malnutrition. The consequences for adult populations of predominantly cereal diets low in protein quality have been little studied. It is presumed that such diets reduce resistance to stress, particularly that resulting from infectious disease and trauma. Calorie deficiency seriously reduces work capacity and thereby interferes with social and economic development, but there is little evidence that many adult males require more protein than they now receive.

For pregnant women and lactating mothers, however there is widespread indication of a progressive nutritional depletion with repeated reproductive cycles (WHO: *Nutrition in Pregnancy and Lactation*, 1965). Many women fail to gain a normal amount of weight during pregnancy and therefore suffer a net loss of weight after parturition, though the average weights of children at birth are not much affected A further loss of weight is associated with the usual prolonged breast feeding, largely because body protein is consumed to supply the protein in breast milk The consequences of repeated pregnancy and lactation on poorly nourished mothers have received far too little attention It is noteworthy that such women look much older than their chronological age by the standards of more privileged populations

Marasmus. Marasmus in children is the result of insufficient food and is therefore a form of starvation (Scrimshaw and Behar, 1961) The extreme low-calorie diets responsible for the syndrome are obviously also markedly deficient in protein and many

other essential nutrients. To compensate for the lack of food, the child utilizes the stress mechanism to mobilize, for gluconeogenesis, amino acids from the skeletal muscle and other tissues, and these essential amino acids are also available for necessary protein synthesis in the liver. Fat stores are also used maximally as an energy source until they are exhausted. Growth stops, but the amino acids and other nutrients liberated from the child's tissues make possible a continuing synthesis of serum albumin, enzymes, and other essential metabolites. For this reason, no serious biochemical changes are observed until fat stores and available tissue amino acids have been exhausted. The child with marasmus becomes, however, extremely emaciated owing to a loss of subcutaneous fat, severe muscle wasting, and atrophy of most organs and tissues (Figure 11-1). Despite the apt description of being reduced to "skin and bones," the child remains clinically alert and has a good appetite.

Infantile marasmus is generally associated with early weaning. It is increasing in

FIGURE 11-1. Moderate marasmus in a Guatemalan child

frequency as the urban populations of developing countries grow disproportionately. Under urban circumstances, the mothers frequently wean their infants when they are very young, either in imitation of the practice of women of upper socioeconomic status, or in order to work In either case, the substitute for breast milk is likely to be a watery gruel, thin cornstarch beverage, or overdiluted milk, all extremely deficient in both calories and protein.

Because children under one year grow more rapidly and require more calories and protein per kilogram of body weight than later, marasmus is particularly likely to develop under these circumstances. Later, if more calories are given without added protein, kwashiorkor is likely to be superimposed on a varying degree of marasmus, especially when infectious diseases further increase protein needs and induce a decrease in protein intake

Kwashiorkor. In contrast to marasmus, there is a lack of essential amino acids available to the liver in kwashiorkor (Scrimshaw and Béhar, 1961; Viteri *et al*, 1964). When dietary protein is deficient relative to calories, the mechanism that maintains blood glucose levels through amino acid mobilization for gluconeogenesis in the liver does not function. This results in profound physiologic and pathologic alterations.

Clinically, the kwashiorkor syndrome is characterized by edema of varying degree, from a mild form limited to the feet and ankles to severe and generalized, with eyelids swollen shut (Figure 11-2) Movement of the extremities may be limited by the fluid accumulation. Children with kwashiorkor are usually extremely apathetic, with a weak and monotonous cry if disturbed They may be quite irritable when aroused. Anorexia is usually present and is frequently profound. Diarrhea is an almost constant finding

The characteristic alterations of the skin resemble the dermatoses of pellagra with which they have often been mistakenly identified. The lesions are pigmented, dry, hyperkeratotic, and often desquamating, varying in size from punctiform to large confluent areas. They are most numerous on those parts of the body most subject to irritation, particularly the perineal region, trunk, and buttocks, although they frequently occur on the extremities and may extend to the face. In severe cases the skin of the entire body is involved.

The hair becomes discolored dry, fine, and brittle (Figure 11-3). It is generally easily and painlessly pulled out, or may even fall out In Negro children it may become reddish, but in Indian children, both Asiatic and American, whose hair is normally black, it becomes pale and even white. Successive periods of normal and abnormal growth of the hair can produce pigment changes in stripes. The extremities are frequently cold and cyanotic The abdomen may be distended owing to flaccid abdominal muscles and to fluid accumulation

The principal biochemical characteristics relate to alterations in protein metabolism. Low serum concentrations of albumin, β globulin, β lipoproteins and cholesterol, and the carrier proteins, transferrin and ceruloplasmin are found As a consequence, serum iron and copper concentrations are lowered as well as serum levels of vitamin A, zinc, magnesium and phospholipids The activities of pepsin trypsin, and amylase in samples of duodenal fluid are reduced to nearly zero, although upon feeding these increase immediately Serum levels of amylase, lipase, pseudocholinesterase and

FIGURE 11-2. Kwashiorkor with characteristic skin lesions and edema in a Guatemalan child with some previous marasmus.

alkaline phosphatase are also markedly lowered. While the most essential liver enzymes are resistant to protein depletion, the activities of xanthine oxidase, D-amino acid oxidase, phenylalanine hydroxylase, and urokinase are depressed Reduced succinate and glycolic oxidase activity, together with decreased oxidative phosphorylation and increased nucleic dehydrogenase, indicate disturbances in carbohydrate metabolism, and fatty acid synthesizing enzymes are also depressed

The essential amino acids in plasma are consistently and markedly decreased, especially the branched chain amino acids, valine, leucine, and isoleucine The total free amino acid level is less altered, however, because nonessential amino acids tend to increase. Advantage has been taken of this observation by Whitehead and Dean (1964) to develop a simple test for protein malnutrition utilizing the ratio of several key essential amino acids to selected nonessential ones measured by paper chromatography

Abnormal nitrogen metabolites such as B-amino isobutyric acid and ethanolamine suggestive of alterations in amino acid metabolism, are also found in the urine Concurrent with the cessation of growth in kwashiorkor and in other malnutritional states the urinary excretion of hydroxyproline falls Diminution of muscle mass also results in lowered creatine excretion Both urinary creatinine and hydroxyproline relative to appropriate standards can be used as indices of malnutrition Low plasma

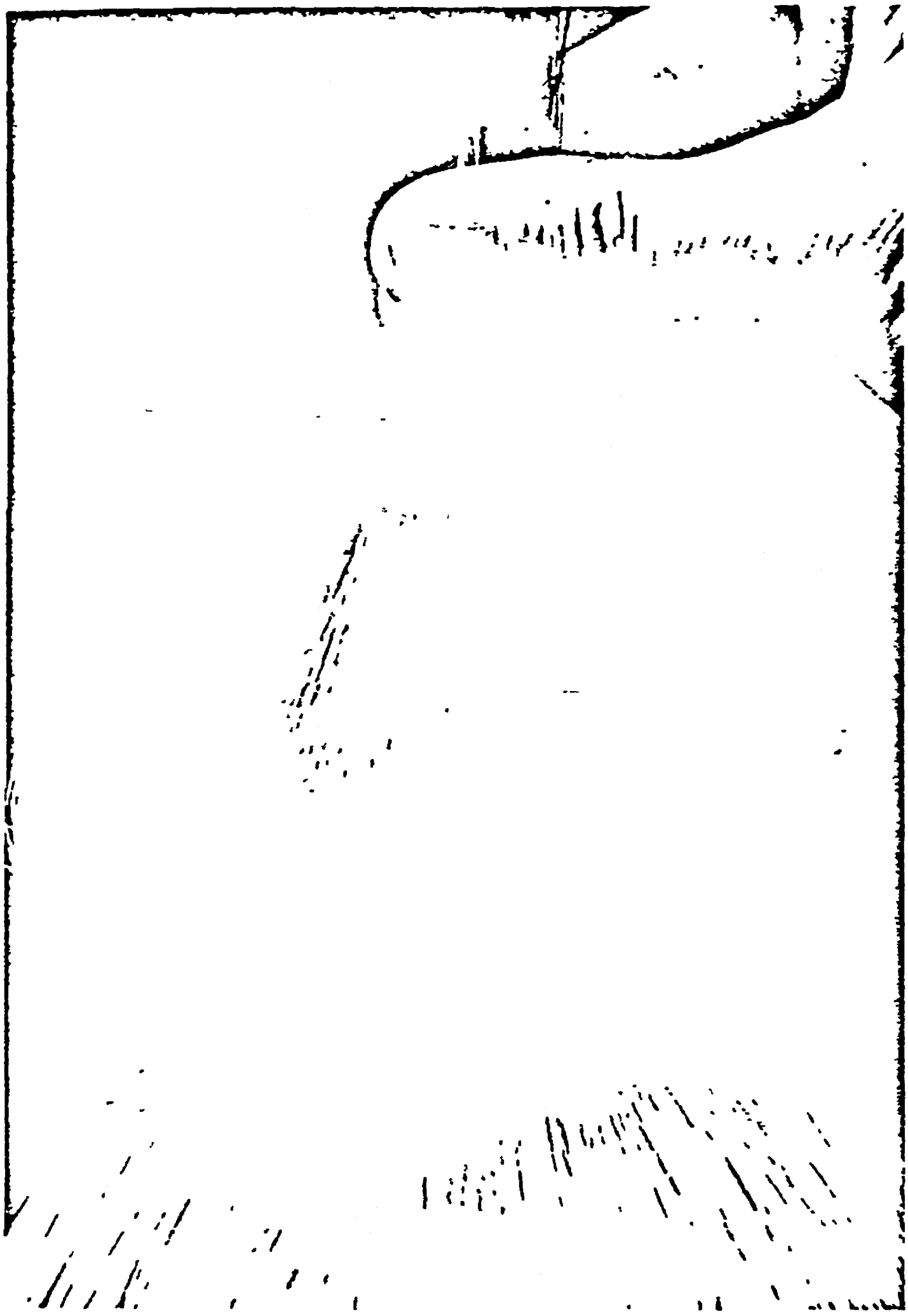

FIGURE 11-3 Extreme example of the hair depigmentation associated with severe protein malnutrition in a child recovering from kwashiorkor as the result of appropriate dietary treatment

urea values correlate with a low urinary excretion of this substance, and both reflect reduced dietary protein intake

An increase in total body water with sodium retention and potassium depletion is a constant occurrence and magnesium deficit has been reported Reduced basal

metabolism, renal plasma flow, glomerular filtration rate, and low electrocardiographic voltages are other physiological changes.

The main pathologic alterations include extensive accumulations of fat in the liver, beginning in the periportal portions of the lobules and extending progressively to the central vein. The pancreas and other exocrine glands become atrophic and the marked atrophy of the intestinal mucosa leads to symptoms resembling those of primary malabsorption. The skin shows atrophy of the epidermis with varying degrees of hyperkeratosis and parakeratosis.

The initial management of kwashiorkor requires correction of dehydration and electrolyte imbalance. Serious complicating infection is also likely to be present despite the absence of fever, leukocytosis, and other common diagnostic signs For this reason, an antibiotic should generally be administered. The basic requirement, however, for both kwashiorkor and marasmus is a diet providing sufficient protein and all other essential nutrients.

Care and patience are required to administer a satisfactory therapeutic diet in the treatment of the severe protein-calorie malnutrition of the kwashiorkor type in children because of the severe anorexia and vomiting associated with the condition. In the ordinary overcrowded and understaffed hospital ward in the areas where the syndrome is common, the food ordered by the physician frequently is not actually consumed by the child. Also, the child is exposed to multiple cross-infections at a time when he is highly susceptible to them Under these circumstances, recovery may take many months or not occur at all. If adequate food can be administered with regularity, the anorexia soon disappears and food is well accepted thereafter.

Although the edema and most of the biochemical abnormalities disappear within about two weeks, intestinal absorption of lipids improves more slowly and complete recovery usually requires at least three months When comparison is made with the creatinine excretion of a well-nourished child of the same height, the daily excretion of creatinine provides the basis for a more reliable indication of recovery than the usual weight-to-height ratio

Vitamin Deficiency Diseases

The clinical manifestations of protein-calorie malnutrition are frequently complicated by the presence of other nutritional deficiencies Vitamin A deficiency with serious eye lesions is frequent in both marasmus and kwashiorkor In kwashiorkor serum vitamin A levels are low and intestinal absorption of vitamin A extremely reduced, even when liver stores of vitamin A are adequate, because of a deficiency of carrier protein.

The diet responsible for protein-calorie malnutrition is also likely to be deficient in B vitamins, particularly riboflavin The mild normocytic normochromic anemia attributable to protein deficiency is often complicated and more severe because of simultaneous deficiencies of iron, vitamin E, folic acid, and possibly other hematopoietic factors

Avitaminosis A. Vitamin A deficiency is responsible for thousands of cases of blindness in young children in South and East Asia Africa and the Middle East (Kinney and Follis, 1958 pp. 103–143) Furthermore, children with such a deficiency suffer

an exceedingly high mortality owing to the increased susceptibility to infections, especially bronchopneumonia In some areas as many as 1 per cent of all children have residual corneal damage sufficient to interfere with vision, and about one fourth of the children in whom xerophthalmia develops do not reach adulthood because of death from secondary infections. Loss of dark adaptation appears widespread among adults in the same areas, although the condition has not been systematically studied.

Wille (Kinney and Follis, 1958, p 112) describes the

> ... too, too frequent case in which a mother, after long hesitation, ventures to the doctor, because her small child did not open his eyes for 10 days. The doctor then finds two corneas irretrievably gone But xerophthalmia is also seen in the case of the school child, ... with a big contusion on his forehead. He ran into a pole the preceding evening at dusk, because he is night-blind, and he has Bitot spots on his eyes

Much the same conditions that are responsible for the world-wide occurrence of kwashiorkor and marasmus also account for the geographic distribution of xerophthalmia and their often simultaneous presence in the same child Supplementary foods for young infants are prepared from rice or other cereals deficient in β-carotene and vitamin A as well as protein. Families of unskilled laborers without land, whether urban or rural, tend to subsist on satiety-producing cereals to the neglect of vitamin-containing vegetables and fruits Vitamin A deficiency occurs in some of the greenest places on earth, where carotene-containing leaves should be readily available, but the end result is the same as in arid rural areas with a sheer lack of carotene sources for most of the year Parts of North Africa and northeast Brazil are examples of the latter.

Clinically, xerophthalmia is an affection of the conjunctiva and the cornea A fatty dryness of the conjunctiva is typical, with thickened wrinkles at the corners and hyperpigmentation Thick, whitish flecks may be seen on the surface, where they accumulate as the frothy-appearing Bitot spots With adequate vitamin therapy the conjunctiva at this stage can again become transparent and moist within a few days, but the Bitot spot, lacking living cells, may remain for weeks and the hyperpigmentation may become even more pronounced

Involvement of the conjunctiva is often accompanied by xerosis of the cornea, which becomes hazy, rough, dry, and sensitive Punctate, superficial infiltrations or small surface erosions may lead, within a day or so, to protrusion of the iris and even prolapse or expulsion of the lens The late stages are accompanied by inflammatory symptoms.

Keratomalacia, a colliquative necrosis of the whole cornea follows xerosis. A rather sudden spongy swelling and melting down of the cornea progresses to eventual shrinkage of the eyeball Because corneal changes are minimal in the germ-free rat with vitamin A deficiency, it may be inferred that secondary infection probably plays a part in the later stages of the disease in man

Rickets and Osteoporosis. Rickets develops in growing children as a result of vitamin D deficiency Because vitamin D is supplied both by breast milk and the action of sunlight on the skin it has been rare in tropical countries except for occasional children kept from the sun either because of illness or accompanying their mothers, who work all day in covered markets Urbanization of tropical populations however

is increasing the frequency of rickets because children get less direct exposure to the sun and air pollution cuts down its effectiveness There are also reports of osteoporosis in adult Moslem women whose clothing shields them completely from sunlight and whose diet is poor in vitamin D.

Beriberi Beriberi is almost entirely limited to underdeveloped areas of the Far East, where highly milled rice is the principal food staple (Kinney and Follis, 1958, pp. 3–56). In Japan, rice enrichment and a more diversified diet have virtually eliminated the disease. In the Philippines and Indonesia the incidence has also decreased, probably owing to an increase in variety of diet. In Thailand, Malaysia, and Vietnam, however, beriberi has increased as more efficient small mechanical mills replace hand pounding, which left some of the germ and hull. Moreover, most of the increase has been in infantile beriberi, with its high fatality.

Beriberi in both adults and older children is of three main types. The chronic, dry, atrophic form and the acute, fulminating type are more serious and dramatic, but most cases are mild and subacute. The chronic, dry, atrophic type, with wrist and foot drop, is generally found only in the older adult, often associated with prolonged consumption of alcohol.

The third type, the mild and subacute form, has characteristic nervous manifestations, including alterations in tendon reflexes. Paresthesia is common. The extent of muscular involvement relates to length of the nerve, amount of work done by the muscle group involved, and possibly the blood supply. Sensations of fullness or tightening of the muscles and muscle cramps are common at night. Cardiovascular signs and symptoms range from breathlessness on exertion and palpitation to tachycardia, cardiac dilatation, and some degree of congestive heart failure. Coexisting deficiencies of ascorbic acid, riboflavin, niacin, and vitamin A are common.

The development of infantile beriberi is due to low thiamine levels in breast milk. Among all deficiency diseases it is one of the most dramatic, for a child may be apparently well and yet die from this condition a few hours later. Recovery with parenteral administration of thiamine is equally dramatic The initial stage is characterized by vomiting, restlessness, pallor, anorexia, and insomnia. In acute infantile beriberi cyanosis, dyspnea, and death ensue rapidly. In the subacute form vomiting, puffiness of the face and extremities, oliguria, abdominal pain, dysphagia, aphonia, and convulsions may appear. This type may go on to a fatal acute episode or may become chronic.

Chronic infantile beriberi sometimes evolves from the initial state without an intervening subacute stage. Vomiting, inanition, anorexia, aphonia, neck retraction, opisthotonus, edema, oliguria, constipation and meteorism are variously seen There need be no signs of beriberi in the mothers of infants affected. To contract beriberi or to transmit it to a nursing child, a mother must generally derive a high proportion of calories from polished rice.

Pellagra. Pellagra is still found seasonally in Egypt, Yugoslavia, and some parts of Africa, where corn supplies more than 60 per cent of the daily calories Because of the niacin supplied by beans and coffee, as well as the increased availability of tryptophan from lime-treated corn, it is not seen in Mexico and Central America, even among populations deriving up to 80 per cent of their calories from corn Persons whose

diets are deficient in niacin and contain no excess of tryptophan acquire, on exposure to the sun, a scaly, pigmented dermatitis over the uncovered areas of skin (Goldsmith, 1964). Depending on the type of clothing and occupational activities, the areas most affected are the face, neck, back of the hands, knees, and front of the ankles. Patients with severe cases have atrophy and thinning of mucosal surfaces, leading to sore mouth and diarrhea.

Dementia, one of the classic "three Ds" of pellagra, along with dermatitis and diarrhea, is rarely seen today. Anemias are frequent, presumably owing to associated deficiencies of other components of the vitamin B-complex and/or iron. The so-called "infantile pellagra" once reported from Yucatan and Africa is now recognized as kwashiorkor, the similarity of the skin lesions having led to the confusion.

Ariboflavinosis. Clinical deficiency signs of riboflavin deficiency of mild degree are common in developing countries, particularly in association with other deficiency diseases of the vitamin B group and with various forms of protein-calorie malnutrition. Glossitis and ocular changes are seen in patients with riboflavin deficiency, but the signs are neither constant nor specific to riboflavin deficiency alone.

Lesions of the lips begin with redness and may develop to shallow ulcerations and crusting. Sore, reddened fissures and encrustations of the corners of the mouth, the so-called angular stomatitis, are classically attributed to riboflavin deficiency, but may also result from deficiency of niacin or iron and may occur idiopathically in well-nourished individuals. A seborrheic dermatitis is also common in this deficiency, characterized by a greasy appearance with erythema at the nasolabial and nasomalar folds, the alae nasi, vestibule of the nose, or around the outer and inner canthi of the eyes, and on the ears.

The swollen, reddened tongue seen in riboflavin deficiency is not clearly separable from that caused by lack of niacin, folic acid, or vitamin B_{12}, and the scrotal and vulval dermatitis is seen in niacin deficiency as well. The circumcorneal vascularization, once considered pathognomonic of riboflavin deficiency, can be produced by many other factors as well. So can such symtoms as soreness and burning of the lips, mouth and tongue and visual symptoms such as photophobia, lacrimation, and burning and itching of the eyes.

Aside from the physical discomfort of ariboflavinosis, the most serious consequence is a decreased resistance to common infection. In the industrialized countries clinical signs attributable to riboflavin deficiencies are often seen in alcoholics along with other B vitamin deficiencies, and in some food faddists

Consequences of Mineral Deficiencies

Endemic Goiter. Until recent years, endemic goiter was primarily a place disease, peculiar to areas where geologic factors resulted in a lack of sufficient iodine in the local water and food supply (WHO. *Endemic Goiter*, 1960). Historically, endemic goiter has occurred on every continent and in most countries. In the developed countries, however it has largely disappeared, in part because of the widespread availability and use of iodized salt, compulsory in many countries and also because of the increasingly heterogenous origin of the food supply from iodine-rich as well as

iodine-poor areas. In most goitrous areas of the underdeveloped countries neither of these factors has yet come into play.

In surveys, goiter is classified as Grade 3 if the thyroid enlargement is visible at a distance, Grade 2 if it is visible on close inspection with the head in a normal position, and Grade 1 if it is smaller, although more than four or five times the normal size. The presence of nodules suggests fetal deprivation of iodine. Most goiters in school children are Grade 1, but Grade 2 and even Grade 3 goiters occur in older children. Rarely is there a suggestion of thyroid dysfunction; in children, at least, enlargement of the gland seems to be a successful compensatory hypertrophy. Goiter may become progressively larger in adults to the point where it is disfiguring, interferes with respiration, and becomes so fibrotic that it cannot be eliminated by iodine therapy. In children simple goiter usually disappears some weeks after iodine administration, but will reappear if iodine is no longer supplied.

Preventive action is desirable in areas where goiter is prevalent. Cosmetic reasons are minor compared to the increased frequency of cretinism, and evidence that an increase in feeble-mindedness and deaf-mutism can be associated with endemic goiter. Furthermore, thyrotoxicosis parallels endemic goiter in most such areas. A relation to thyroid carcinoma is less certain.

The relative contributions to the frequency of endemic goiter of primary iodine lack and the presence of goitrogenic factors in food and water are not well defined. The thiocyanates and thiocyanate precursors present in many members of the cabbage family are known food goitrogens, and a wide variety of other foods, including peaches, pears, strawberries, spinach, and beans, have goitrogenic activity in laboratory animals. Hardness of the water, vitamin A deficiency and polluted water supply have been reported to be goitrogenic in man. The combination of environmental iodine lack and the monotonous, mainly vegetarian diet of foods with goitrogenic activity is sufficient to explain the high prevalence of endemic goiter in so many of the underdeveloped countries.

Other Consequences. Of the trace minerals, only zinc, magnesium, and copper deficiencies have been specifically identified. Recent studies in the Near East report zinc deficiency to be a responsible factor in a syndrome of dwarfism and hypogonadism in male adolescents. The deficiency of zinc may result either from a low intake or from impaired absorption due to a high dietary content of phosphates and phytates, as in diets predominantly of cereal grains. Similar syndromes in other areas have been attributed to anemia, to liver dysfunction caused by schistosomiasis, or to general undernutrition. Because these factors do not always provide a satisfactory explanation, further studies on zinc deficiency in representative areas are needed.

Iron and copper deficiencies are discussed under Anemias of Nutritional Origin, and calcium deficiency is referred to under "Rickets and Osteoporosis."

Synergism of Malnutrition and Infection

The role of infectious diseases in precipitating kwashiorkor, marasmus, and keratomalacia in children consuming diets of borderline adequacy has already been emphasized. Diarrheal diseases are especially frequent in underdeveloped countries because of poor environmental sanitation and deficient personal hygiene (Scrimshaw

et al., 1968). Respiratory infections are also common and tend to be more severe than in more favored regions. These infectious diseases, along with the common communicable diseases of childhood, decrease appetite and cause extra metabolic loss of nitrogen and a number of other essential nutrients. Equally important, attendants commonly reduce the food intake of persons who are ill, especially children, by substituting thin carbohydrate gruels or cereal infusions for the usual solid food. The frequent administration of strong purgatives to children with diarrhea adds to the disastrous nutritional consequences.

Of equal or greater concern is the fact that malnutrition severe enough to interfere with growth and development is also able to interfere with resistance to infections. The common childhood diseases, rarely fatal in well-nourished children and scarcely requiring medical care, are major causes of death in areas where malnutrition prevails in childhood. Despite incomplete reporting of such deaths, mortality from measles in 1962, for example, was approximately 255 times higher in Guatemala, 155 times higher in the United Arab Republic, and 140 times greater in Chile than in the United States (WHO: *World Health Statistics Annual*, 1965). Nevertheless, measles caused no special problems among the better nourished children of families with middle and upper incomes in the same countries.

An analysis of the deaths of children in four Guatemalan highland communities in a two-year period indicated that diarrheal disease and common childhood infections were apparently responsible for nearly two thirds of the mortality in the group from one to five years of age (Béhar, *et al.*, 1958). Few of these infections would have been fatal in well-nourished children. Conversely, approximately two fifths of the children of this age group who died during the period of observation had symptoms of kwashiorkor, but the syndrome appeared to have been precipitated in every case by a preceding episode of diarrhea, measles, or other infection. Over-all mortality in children of this age in the four communities, as in Guatemala as a whole, was over 40 times higher than in the United States and Western Europe, and the difference could be accounted for largely by the synergism of nutrition and infection.

In a five-year study by the Institute of Nutrition of Central America and Panama (INCAP) in the rural Guatemala highland village of Santa Catarina Barahona, children under five years and all pregnant and nursing mothers were offered a supplement providing 15 gm of protein and 450 calories five days a week. No medical care was given. Mortality of preschool children decreased as compared with preceding years, whereas no change occurred in the control village of Santa Cruz Balanyá (Ascoli *et al.*, 1967).

It is now increasingly recognized that the acute diarrheal disease of infants and young children so common in developing countries during and shortly after weaning is microbiologically nonspecific and constitutes an epidemiologic entity to which the name "weanling diarrhea" has been applied (Gordon *et al.*, 1963). Throughout the world a known pathogenic agent can be identified in only about 20 to 30 per cent of cases of weanling diarrhea. The remainder defy expert microbiologic investigation, including a search for causative enteroviruses. Infectious agents identified are mainly various strains of enteropathogenic *Escherichia coli*, shigellas, and occasional salmonellas.

The hypothesis is advanced that many weanling diarrheas are the consequence of organisms not normally pathogenic in a well-nourished child. Even those strains of *Escherichia coli*, *Shigella*, and *Salmonella* with accepted pathogenic properties are known to invade the well-fed nursing infant under four months of age without necessarily causing diarrhea. The incidence of diarrhea is relatively low at this time, as is the mortality rate. After the mother's milk is no longer a sufficient source of protein, the same organisms may then be associated with diarrheal disease. Cases and deaths increase, and rates continue high throughout the long weaning period and for the months immediately thereafter. It is noteworthy that weanling diarrhea is spread by direct and indirect contact rather than by food or water of common origin.

Progress in identifying the mechanisms whereby malnutrition exaggerates infection has been slow (Scrimshaw *et al.*, 1968). It is well known from studies in laboratory animals that a variety of nutritional deficiencies will interfere with antibody formation and with leukocyte response and activity. In kwashiorkor the antibody response is inhibited. This has also been observed in malnourished patients with chronic infections and in experimental pantothenic acid and pyridoxine deficiency in human volunteers. Children with kwashiorkor may show no febrile or leukocytic reaction to infection. Nothing is known, however, of the extent of involvement of any of these mechanisms in the lowered resistance of subclinical deficiency states.

Alterations in tissue integrity, especially of mucous membranes and other epithelial structures, so characteristic of kwashiorkor, vitamin A deficiency, scurvy, pellagra, arboflavinosis, and some other deficiencies, also are partly responsible for increased susceptibility to some infections. Other potential but unproved means by which resistance is decreased in malnourished inhabitants of underdeveloped countries include interference with general resistance factors such as lysozymes, interferon, and properdin, decreased nonspecific resistance to bacterial toxins, endocrine imbalances, and altered intestinal flora.

Nutritional Anemias

Nutritional anemias due to insufficient intake of hematopoietic factors, to their poor absorption, or to increased demands because of abnormal blood losses are frequent in tropical and subtropical areas (International Symposium on Vitamin-Related Anemias, 1968). Pregnant women, infants, and small children are most seriously affected in the areas where the problem exists. Mild-to-moderate cases in the general population are often highly prevalent and yet unrecognized A deleterious effect of anemia on work performance and general well-being is suspected but not quantitatively determined.

Iron deficiency anemia is the most common type in tropical and subtropical areas. A good correlation is found between the number of worms and the level of hemoglobin in heavy hookworm infections In a significant number of cases, however, the same type of anemia is observed without hookworm disease, and similarly, although less frequently, in areas where hookworm does not exist. Venezuelan studies suggest that less than a third of the iron deficiency anemias observed in hookworm-infested areas are due solely to the parasites.

Increased loss of iron by sweat and dermal desquamation is a factor of unknown significance in areas where environmental conditions favor profuse sweating. Other possible factors interfering with iron absorption and requiring further study are the frequently associated infections and protein deficiency.

Total iron intake, as estimated by dietary surveys, is usually within recommended amounts or even higher in areas where iron deficiency anemia is prevalent, either with or without hookworm disease. The extent of absorption of the iron contained in the diets is less well known. Diets in developing countries ordinarily include a large proportion of cereal grains and legumes as the principal sources of iron. Recent studies suggest that the iron of cereals is not well absorbed, at least by anemic persons.

Megaloblastic anemias are less common than the microcytic hypochromic type associated with iron deficiencies. They are reported particularly in pregnant women and in severely malnourished children. Folate deficiency, either of dietary origin or from other factors interfering with its metabolism, seems to be a frequent cause. Vitamin B_{12} deficiency has also been reported, particularly in populations with a predominantly vegetarian diet, and in pregnant women. In addition, anemias responding to vitamin E have been described in several developing countries. The anemia of kwashiorkor has been mentioned earlier.

Malnutrition, Learning, and Behavior

There is increasing evidence that the degree of malnutrition responsible for the early retardation of growth and development among infants and preschool children in developing countries is sometimes also sufficient to interfere with brain development, learning, and behavior (Scrimshaw and Gordon, 1968). Data from many investigators indicate that such children have a smaller head circumference at maturity than do those who have not experienced such early malnutrition. Although differences in head circumference are of little significance among well-nourished individuals, the smaller head circumference associated with early malnutrition does indicate smaller brain size. Recent work has shown that the number of brain cells is reduced as well (Winick, 1968).

In addition, several field studies have shown that preschool children who are most retarded in height and weight for age also tend to have the lowest scores on tests of intersensory perception and cognitive behavior. Because the social deprivation so commonly associated with malnutrition in underprivileged populations may have similar effects, the relative importance of these two major factors is still to be determined and indeed must vary with the circumstances. Nevertheless, the implications are clear. There is a risk that early malnutrition of children in the first one to two years of life today may adversely influence the capacity of this generation upon whom developing countries must count for future progress.

Caries and Periodontal Disease

Dental caries is exceedingly prevalent in most of the underdeveloped countries (Scrimshaw and Béhar, 1965). Comparatively young persons with teeth broken off at the gums or entirely absent are a common sight. Tooth decay is presumably not

more active in such areas than in many highly developed countries, but because of the lack of dental care, its consequences are more serious. Indeed, some malnourished populations enjoy remarkably good teeth, particularly when the natural fluoride content of soil and water reaches prophylactic levels. Periodontal disease is also a serious public health problem, again owing more to poor dental hygiene and lack of dental care than to malnutrition.

NUTRITIONAL PROBLEMS OF INDUSTRIALIZED COUNTRIES

In industrialized countries, malnutrition due to nutritional deficiency is rare, but obesity is very common (Van Itallie, 1960). Whether or not obesity is regarded as a disease state, it has a direct relationship to the development of cardiovascular disease. It is also clear that the combination of a high proportion of calories from fat in the diet and limited physical exercise make for a relatively early development of atherosclerosis and a relatively high prevalence of coronary heart disease.

In countries like Japan, where many of the foods are very high in salt content, this is a distinct factor in producing a high national incidence of hypertension. There is also a relationship between the high intake of calories, particularly from carbohydrates, and the relatively greater frequency of diabetes in the industrialized countries. Finally, as already mentioned, diets high in refined carbohydrates are conducive to the development of dental caries.

In addition to these diseases of dietary excess, nutritional anemias are also much more prevalent in industrialized countries than is generally realized (International Symposium on Vitamin-related Anemias, 1968). They are particularly associated with faddist diets, teen-age neglect of nutrition or adoption of bizarre diet patterns, and self-prescribed reducing regimens. Two periods are particularly vulnerable to anemia: infancy and pregnancy. Because few infants are breast fed in the industrialized countries and because cow's milk is much lower in iron, anemia has been fairly common. There is now a growing concern for the prevalence of microcytic, hypochromic anemia in infancy associated with cow's milk formulas that are not enriched with iron. In addition, the diets of some women are apparently inadequate in folic acid for the demands of pregnancy and lactation, and they develop a megaloblastic anemia for this reason.

FACTORS RESPONSIBLE

The public health approach to the causes of malnutrition must be an ecological one, taking into account the interaction of host, agent, and environment (Scrimshaw, 1964; Scrimshaw and Behar, 1964). This approach permits the selection of those preventive measures that are most likely to be successful. Moreover, effective prevention of most malnutrition requires attention to several factors concurrently.

In the case of nutritional disease the agent must be thought of as either the deficiency or the pathological excess of a specific nutrient or nutrients. Environmental factors are those of the physical, biological, and social environment, and each may affect availability, consumption, or host requirement of a nutrient.

To the extent that the availability of food is the limiting factor, measures must be those that will increase the production of food from plant and animal sources or increase its availability through storage and handling practices that will reduce unnecessary losses to rodents, insects, mold, and spoilage. The problem may be primarily one of distribution and marketing rather than total production. On the other hand, actual production may be so inadequate that food will need to be imported in order to avert widespread malnutrition.

Most often, malnutrition is caused not by an absolute scarcity of food but by social and economic factors that result either in inadequate knowledge of proper food selection or insufficient purchasing power to acquire the foods needed for optimal nutrition. It is not just lack of knowledge that results in malnutrition, but also belief in food practices that are nutritionally unsound. As mentioned earlier, a major factor in the occurrence of protein-calorie malnutrition in children is the tendency to give watery or starchy gruels of little or no protein content to the young child who develops diarrheal disease (Jelliffe, 1955). Meat and eggs are often thought "too strong" for the weanling infant and cow's milk is believed dangerous because it results in diarrhea or "causes the worms to rise." Added to the effect of less nourishing diets is the administration of strong purgatives, which accentuate the diarrhea and worsen the nutritional situation. Similarly, various prejudices and taboos relating to the diet during pregnancy and lactation contribute to malnutrition.

The role of infection in producing the degree of malnutrition characterizing the majority of children in developing countries has already been discussed along with the frequency with which clinical nutritional disease is precipitated by an episode of acute infection. It follows, then, that lack of environmental sanitation and personal hygiene are major factors in the occurrence of malnutrition because they contribute so importantly to the high frequency of diarrheal disease in less-developed countries. Similarly, physical, biological, and social circumstances that favor the occurrence of malaria, schistosomiasis, cholera, hookworm, and other mass diseases significantly increase the frequency of malnutrition. Conversely, the relatively good environmental sanitation characterizing most populations in the industrialized countries has contributed to the virtual disappearance of malnutrition.

Another reason for the prevalence of malnutrition in developing countries is the limited degree to which medical and public health services reach the majority of the populations. Effective maternal and child health programs can do a great deal to reduce the frequency of severe malnutrition by their educational impact, their roles in the prevention of diseases, and by direct nutritional measures such as supplementary feeding or nutritional rehabilitation where these are required.

The physician dealing with underprivileged populations in private or public health practice also has an opportunity to recognize the possible development of specific and dangerous nutritional disorders such as marasmus, kwashiorkor, xerophthalmia and keratomalacia, pellagra, beriberi, rickets, and scurvy and to see that proper treatment is instituted promptly. It is where the population does not have access to medical services that these diseases so commonly go on to their tragic consequences of disability or death.

Unfortunately, medical practices sometimes have their adverse effects on nutri-

tional status. For example, food is withheld from children with diarrhea as a temporary therapeutic measure and this is interpreted by the mother as the proper treatment for the symptom. Pediatricians must also share some of the responsibility for the overfeeding of children in more favorable social and economic conditions.

In the industrialized countries members of the medical and public health professions have a special obligation to promote those measures that will contribute to improved nutritional status, such as a moderate food intake to avoid obesity, and regular physical exercise, as a preventive measure for both obesity and coronary heart disease. They should also oppose harmful faddist diets and nutritional quackery of all types. In both industrialized and developing countries they have an obligation to support administrative measures that will contribute to the nutritional health of the population, such as fluoridation of water, iodization of salt, and fortification of cereals.

Finally, the importance of medical and public health support in the promotion of family planning can scarcely be overestimated. The health implications of present rates of population increase are discussed in Chapter 1. It is sufficient here to point out that *per capita* food supplies are actually decreasing in many developing countries as population increases faster than food supply. Furthermore, rapid urbanization with its disruption of traditional food practices is creating nutritional problems that have reached alarming proportions in some countries. The problem of malnutrition is inseparable from that of population growth. It is not sufficient for food supplies to match population growth; they need to exceed it in most developing countries in order to improve present diets and to meet the rising expectations for more and better foods as improved economic and social status is achieved. Moreover, the problem is not just one of food production; distribution to and consumption by vulnerable population groups must be assured.

CONTROL AND PREVENTION

Emergency or Palliative Measures

A common response to the existence of malnutrition is the initiation of a supplementary feeding program. This may or may not alleviate the immediate problem, but it is seldom a satisfactory long-term solution. Participation in such programs by those most in need, even when the programs are free, is usually far from satisfactory. They tend not to reach the most vulnerable group, preschool children, because the mother is too busy to bring the child regularly to a feeding station or is unconvinced of its importance. Distributing food for the mother to take home also has its limitations because it is generally shared with the family or even sold. Moreover, termination of the program results in a return to the original conditions unless it is used for nutrition education and arrangements are made for nutritious foods within the purchasing power of the people to be available on a permanent basis

Two kinds of successful supplementary food distribution deserve special mention. One is providing sufficient food, to be taken home every one or two weeks, for poorly nourished children, or preferably, for all young children in a family, combined with instruction in nutrition and personal hygiene and accompanied by periodic visits

to the home to see that the food is being used properly. Such programs have been effective in improving growth and development and decreasing disease morbidity of poorly nourished young children. A second is the association with a health center of a nutritional rehabilitation unit where a child with malnutrition who might otherwise need hospitalization can be left each day to receive two or three complete meals. The mothers are expected to participate in the running of such a center primarily as a means of educating them as to the benefits of a proper diet for their children.

Corrective Specific Measures

Sometimes specific measures will effectively wipe out a nutritional disease in a manner analogous to that which can be achieved by immunization or vector eradication for the control of some infectious diseases. These measures generally consist of enrichment or fortification of a basic food staple. Endemic goiter, even where it is severe, can be effectively eliminated as a public health problem among children and young adults in a few months if effective iodization of all salt for human consumption is introduced Because this measure can be introduced by administrative action, adds only negligibly to the cost of the salt, and does not require education of the public, there is little justification for the continued persistence of endemic goiter in many countries

Enrichment of rice with thiamine and other essential nutrients is an effective and economical way of preventing beriberi (Williams, 1961) Unfortunately, political and economic obstacles have prevented the widespread adoption of this measure in rice-eating countries. Increasing the thiamine content of milled rice by parboiling is feasible but increases the hazard of producing the potent toxin aflatoxin from the growth of *Aspergillus flavus*. The technique involves coating some of the rice grains with a mixture of riboflavin, thiamine. niacin, and calcium. This combination of nutrients can be added to corn where this cereal is the staple and has been demonstrated to be effective in preventing pellagra The enrichment of wheat in this manner serves to eliminate the likelihood of deficiencies of such nutrients in populations consuming significant quantities of wheat.

The main factor in the disappearance of beriberi from regions in which it was once highly prevalent is the introduction of greater variety into diets that were previously based largely on rice To the extent that beriberi in industrialized countries is associated with alcoholism, parenteral thiamine may be required therapeutically and the excessive use of alcohol terminated.

Recently the addition of the essential amino acid lysine has been recommended as a means of improving the protein quality of wheat and lysine fortification of wheat bread and flour has already begun in India on a substantial scale. Amino acid fortification of corn with lysine and tryptophan could double the protein quality of this cereal, but with the present high cost of tryptophan, the introduction through cross-breeding of one of the genes opaque-2 or floury-2 seems a more promising way of achieving this end (Mertz and Nelson. 1966)

There have been recent spectacular increases in cereal yields in a number of developing countries through the use of improved varieties of seeds combined with the

necessary fertilizer and pesticides (*Strategy for the Conquest of Hunger*, The Rockefeller Foundation, 1968). Because these varieties are not improved in protein quality, it is still important to improve protein value of diets based on these cereals through appropriate fortification and supplementation.

In most industrialized countries the irradiation of cow's milk serves to increase its vitamin D activity and this measure is sufficient to prevent rickets in children. Vitamin A and D concentrates are universally prescribed by pediatricians and health centers for children under one year of age. In the tropical countries adequate vitamin D has in the past been supplied by breast milk and by exposure of the child to sunshine. In view of growing urbanization, which leads to earlier weaning and less exposure to sunshine, specific ways need to be found to add vitamin D to the diets of mothers and children in tropical cities NAS–NRC: *Progress in Meeting Protein Needs of Infants and Preschool Children*, 1961).

Simultaneous administration of capsules containing vitamins A and D is now standard policy of the United Nations Children's Fund (UNICEF) for milk distribution to children in areas with possible vitamin A deficiency. Alternatively, powdered milk for use in such circumstances can be enriched with water-miscible synthetic vitamin A. In many tropical areas, red African palm oil is readily available as a rich source of carotenes with vitamin A activity. Nutrition education programs in such countries place particular stress on green and yellow vegetables and on certain fruits, such as mangoes, papaya, squash, and melons as important sources of active carotenes in a balanced diet.

There are specific as well as general nutritional measures that can contribute directly to the reduction of dental caries (Nizel, 1966). The addition of fluoride to water supplies of communities without natural fluorine in the water to levels of about one part per million generally reduces caries in children by at least half. Not only is dental caries in adults also reduced to some extent by fluoridation, but there is also suggestive evidence that osteoporosis is decreased. Some recent experimental studies suggest that phosphate enrichment of cereal staples or other foods may have an effect additive to fluoride and bring about further caries reduction. Diet patterns relatively high in soluble carbohydrate promote dental caries.

In areas where no low-cost protein-rich food is already available that is suitable for the supplementary feeding of young children during and after weaning, the production and marketing of such a protein source can be an important specific measure in reducing the incidence of protein-calorie malnutrition (UN: *International Action to Avert the Impending Protein Crisis*, 1968). These are usually based on a combination of an oilseed meal and a staple cereal such as corn or wheat. A meal containing approximately 50 per cent protein is left after the oil is extracted from soy beans, peanuts, or cotton, sesame, and sunflower seed. Examples are Incaparina in Latin America, Bal-Ahar in India, and ProNutro in South Africa.

Bland, deodorized fish protein concentrates containing approximately 80 per cent protein can be produced from fish not otherwise valued for human food, but have not yet been utilized to a significant degree. Such concentrates are highly effective in improving the protein value of cereal-based foods and will eventually be widely used

Food yeast grown on molasses or sulfite liquor and containing approximately

50 per cent protein is already used to a limited degree in a wide variety of processed foods, including those for infants and young children. Other single-cell sources of protein produced on petroleum fractions as an energy source are under development, utilizing ammonia-nitrogen fixed from the air. Single-cell organisms have the great potential of growth in enormous quantities without the use of agricultural land and they contain protein of demonstrated usefulness. If, however, they are to be used in large quantities in order to supply a major proportion of the dietary protein, their high nucleic acid content will need to be reduced somewhat in order to avoid the possibility of producing abnormally high serum uric acid levels, and extensive biological testing will be required.

General Measures

Because the causes of malnutrition are multiple, general control measures are equally broad and must involve social and economic as well as medical and public health improvements. Some malnutrition is due to a primary lack of available foods of sufficient nutritive value. Therefore, increased agricultural production of food crops may be necessary (UN: *International Action to Avert the Impending Protein Crisis*, 1968). It is necessary to distinguish, however, between human need for food and what the economists call effective demand for it. More often malnutrition results from lack of resources for the purchase of protective foods. The solution is either to make available foods of adequate nutritive value at lower cost, or to improve the purchasing power of the family. In either case nutrition education is essential so that the right foods will be chosen, especially for the feeding of the young child during and after weaning.

The extent to which ignorance of nutritional principles and food values is responsible for malnutrition, even among the low-income populations of developing countries, should not be underestimated. It is exceedingly common for kwashiorkor to occur primarily because the food available for the rest of the family is not shared with the young child because it is thought inappropriate or even dangerous for him. The most valuable type of nutrition education for mothers in developing countries stresses the appropriate and increasing supplementation of breast milk beginning at about the fourth month of life. For the older child and adult, emphasis is on a balanced diet each day, incorporating protein foods, green and yellow vegetables, and fruits, as well as the cereal or root staples commonly making up the bulk of the diet.

For the industrialized countries the problem is quite different. For most of the population food is available in abundance and purchasing power allows them to buy more of it than is really needed. Even children are given the money to buy candy and soft drinks that replace nutritious foods with "empty calories" and contribute to the incidence of dental caries. For this group also education in nutrition must emphasize a balanced diet containing a supply of each of the basic food groups every day. It must also include the undesirability of overweight for both children and adults and its control by appropriate caloric intake and physical activity. The taking of vitamin concentrates should not be encouraged, because this is generally a waste of money as well as a poor substitute for a proper diet.

Because a major factor in the occurrence of malnutrition in less developed countries

is the high incidence of acute and chronic infections, it follows that measures to control infection have an important place in the prevention of malnutrition. As already indicated, diarrheal disease is probably the single most debilitating factor for the preschool child, and measures to reduce its incidence include constructing privies and toilets, improving the quality of the water supply and, desirably, supplying adequate water for sanitary purposes directly to each household.

These measures will also reduce the burden of intestinal parasites, which are almost universal among rural children in developing countries and are common in the poor urban districts as well. The specific burden of hookworm disease can be largely eliminated by the wearing of shoes.

Health education can help to encourage sanitary disposal of feces, to reduce the numbers of flies and their contact with feces and food, and perhaps most important of all, to improve personal hygiene. The agents of diarrheal disease are most commonly spread by the mother's hands from feces to food, nipple, and the child's mouth. Personal cleanliness including appropriate washing of hands would help to reduce weanling diarrhea.

Other infections that serve to precipitate acute nutritional disease in chronically malnourished children are the common communicable diseases of childhood: measles, whooping cough, chicken pox, rubella, and mumps. The first two can and should be prevented by immunization. To the extent that respiratory disease and tuberculosis are associated with overcrowding, better housing can be a factor in reducing the frequency of respiratory infections in children. Where major endemic diseases such as malaria and schistosomiasis are a factor, campaigns for their prevention will have favorable repercussions on the nutritional status of the population.

Role of Medical Services

Medical care is important in the treatment of individuals with severe malnutrition and in reducing mortality from this cause, but medical treatment is a poor approach to malnutrition. To an even greater extent than with infectious disease, the emphasis must be on prevention. When cases of malnutrition do come to the physician for treatment, he has a particular obligation to use the opportunity to explain the cause and prevention of the condition.

In less-developed countries the role of the public health center and clinic is primarily one of promoting better nutritional practices, especially for the growing child and the pregnant and lactating mother. Many cases of malnutrition will be observed that will not require later nutritional rehabilitation or hospitalization if the public health physician and nurse are alert and properly discharge their obligation for nutritional counseling.

Although education should be the main reliance, it may also be desirable for maternal and child health centers in developing countries to make food available for malnourished children at a reduced price or without charge. Otherwise these children progress to require more costly rehabilitation or hospitalization, or may suffer permanent damage. Moreover, the future social and economic development of all countries depends upon the adequate physical and mental development of their young children.

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PROTEIN–CALORIE MALNUTRITION

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1. Introduction

Protein–calorie malnutrition (PCM) in its different forms and degrees, is still one of the most prevalent and widespread nutritional deficiencies particularly in infants and young children in the underdeveloped areas of the world (Scrimshaw and Béhar, 1961). Various degrees of PCM have also been observed in the low socioeconomic classes of highly developed nations (Taitz and Finberg, 1966), and in significant numbers of adults in developing areas. The high incidence of the severe, clinically recognized forms of PCM (kwashiorkor and marasmus) affecting from 1 to 10% of infants and preschool agers in developing regions, does not in itself indicate the true magnitude of the problem. This is because of the much higher proportion of children affected by the mild-to-moderate forms of PCM who can be identified only by retardation in growth and development If retardation in growth is taken as an indicator of the magnitude of the problem, more than half of the preschool child population of underdeveloped areas of the world may be considered as affected by PCM (Béhar, 1968).

The severe, advanced forms (kwashiorkor and marasmus) are dramatic diseases which usually require hospitalization and are generally fatal if the children do not receive adequate treatment The less dramatic but much more prevalent mild-to-moderate forms are not less significant as health problems because, as a component of the 'social deprivation syndrome', they contribute to the manifestations of this 'syndrome', which include high morbidity and mortality rates and inadequate physical and mental development.

2. Classification

The clinical syndromes described under the names of kwashiorkor, marasmus, marasmic kwashiorkor, protein deficiency, undernutrition, nutritional dwarfism, and many others, are all different types or degrees of PCM. The different manifestations of PCM result as a consequence of (a) the relative degree of calorie and protein deficiencies, (b) age of the subject, (c) magnitude and duration of the deficiencies, and (d) nature and severity of concurrent diseases.

2.1. Relative degree of calorie and protein deficiencies

When children are fed a well-balanced food such as milk, but in very insufficient amounts, or thin diluted cereal gruels, sweetened water, or other starvation-inducing diets, the net result is a progressive calorie deficiency. These children lose weight rapidly and, in order to survive, utilize their lipid reserves and their muscle and other nonvital tissues as calorie sources. The resulting extreme clinical picture is that of emaciation known as marasmus.

On the other hand, and usually after weaning, when children are forced to consume large amounts of starchy foods (cereal flours, roots, bananas, gruels made of refined starches), their calorie requirements may be satisfied but with 'empty calories'. Under these circumstances, a clinical picture of severe protein deficiency rapidly develops. This syndrome was known in Europe earlier in the century and was described by Czerny and Keller under the name of Mehlnarschaden (Czerny and Keller, 1925–8), and more recently by Jelliffe in Jamaica, as 'sugar baby' (Jelliffe *et al.*, 1954). These children develop edema and other manifestations of severe protein deficiency without significant growth retardation or loss of subcutaneous tissue. Since children fed such imbalanced diets naturally reduce their calorie intake because of anorexia, the 'sugar baby' syndrome develops only when they are forced to consume their food. This explains why the syndrome is only rarely observed. In most cases, in addition to the protein restriction, children subject to diets of this type will show a certain degree of caloric deficit and will develop a mixed syndrome with components of the two previously described. This is the syndrome usually described as kwashiorkor or, when the marasmic component is more obvious, as marasmic kwashiorkor.

2.2. Age

PCM of any type can occur at all ages. Kwashiorkor has been observed in ages ranging from young infants to adults, and the same is true for marasmus. However, marasmus is seen much more frequently in infants, mostly as a consequence of insufficient breast feeding or the use of overdiluted cow's milk, cereal water, or other diets with low energy density. Kwashiorkor is more commonly observed during the second and third years of life when weaning has occurred, and it is more likely for children to be fed starchy foods high in calories and very low in protein. Furthermore, the relatively greater energy and protein requirements, and smaller protein mass and calorie reserves of rapidly growing infants, make them more susceptible to the development of marasmus.

2.3. Magnitude and duration of the deficiencies

When nutritional deficiencies in children are not very severe but are of long duration, the growth rate will be primarily affected; however, the child will show little or no evidence of tissue loss. On the other hand, a severe and acute restriction of calories will result in emaciation (marasmus). The severe and acute restriction of proteins provokes edema as well as other signs and symptoms of kwashiorkor. Nevertheless, in either case, the child's size may not be significantly retarded for his age. In the case of acute and severe protein deficiency, even weight may not be drastically reduced after disappearance of edema. More frequently, severe protein deficiency develops in a child already markedly retarded in physical growth and very often with various degrees of emaciation as a consequence of chronic and moderate PCM. The resulting picture is that which has been described as marasmic kwashiorkor

2.4. Nature and severity of concurrent diseases

Finally, to complicate the situation further, other nutritional deficiencies or diseases of a different nature may be superimposed on any of the different types and degrees of PCM, thus modifying the clinical characteristics.

These concurrent or complicating factors may also vary from region to region. For instance, vitamin A deficiencies or a certain type of anemia may be more frequently observed in children with PCM in one area than in another; or the frequency with which the syndromes are accompanied by diarrhea and dehydration may be different.

Summarizing, PCM may be manifested clinically in many different ways. The four variable, relative degrees of calorie and protein deficiencies, age of the subjects, magnitude, and duration of the deficiencies and nature and severity of concurrent diseases are, in our opinion, the main factors responsible for the clinical variation. Thus, the frequency of the different forms of PCM can vary from place to place or even in the same place as time goes on.

It has been observed, for instance, that in many parts of the world where kwashiorkor used to be the main manifestation of severe PCM, the prevalence of marasmus is becoming greater (McLaren, 1966). This change is the result of earlier weaning and improper artificial feeding of infants, often a consequence of urbanization or of a greater influence of occidental infant feeding practices in population groups who are unable to adopt them adequately because of cultural, environmental and socio-economic factors.

3. Effects of Calorie Deficiency and Protein Deficiency in the Individual

As is clear from the previous considerations, calorie and protein deficiencies induce various changes in the individual, depending on a variety of factors. The great majority of these changes are adaptative in nature and, except for the extreme deficiency states when failure of adaptation occurs, and acute, severe clinical disease supervenes, the protein and calorie deficient individual lives in an apparent healthy state except when a deeper look into his functional state is undertaken.

In the case of semi-starvation, which is primarily a process of caloric restriction, the following metabolic adaptations take place: the subject reduces his caloric expenditure by diminishing his activity and by slowing the basal metabolic processes below the decrease expected from active tissue loss. On the other hand, hormonal mechanisms are adjusted to facilitate lypolysis and lipid mobilization, and a certain degree of amino acid transport from muscle to viscera.

Protein deficiency induces adaptative mechanisms whose primary aim is protein sparing. Protein synthesis is decreased in the organism as a whole, although visceral protein synthesis is spared as compared to muscle and skin which serve as amino acid donors, thus increasing their relative catabolism. Total protein catabolism and urea synthesis are decreased and shifts in protein pools occur. As a consequence, the total protein mass is selectively decreased with sparing of specific organ proteins such as brain, kidney, liver, and heart.

Through these adaptative mechanisms the organism is able to endure mild and moderate calorie and protein deficiencies, with little impairment of its essential vital functions. Viewed in this light, calorie deficiency and protein deficiency are dynamic processes inducive of progressive adaptative changes. The more severely malnourished individual has necessarily reached a greater degree of adaptation which breaks down more easily by pathological or physiological loads, resulting in severe disease states which, if not treated adequately, can rapidly result in death.

It is important to keep the concept of adaptation in mind while interpreting functional and clinical manifestations of PCM, as well as in establishing rational bases for nutritional rehabilitation.

3.1. Characteristics

3.1.1. CHRONIC PROTEIN–CALORIE MALNUTRITION IN CHILDREN

The mild-to-moderate chronic forms of PCM are manifested primarily by a slow-down in the rate of growth. In the areas where the severe forms of PCM (kwashiorkor, marasmus) are prevalent, the large majority of children go through a period of chronic, moderate PCM. This usually starts by the fourth to the sixth month of age when, among other factors, breast feeding becomes insufficient as the only source of nutrient and the children do not receive proper supplementation or are inadequately fed when they are weaned. Their rate of growth slows down in relation to what is normal for their age, a situation which usually persists for months or years. In addition, they frequently show reduced physical activity and mental apathy, dry skin and hair, and are subject to frequent episodes of gastrointestinal disturbances (anorexia–diarrhea). Many of these children may either die from episodes of infectious diseases or they may develop an acute and severe form of malnutrition. After their second to fourth years of life, those who manage to survive usually resume a close to normal rate of growth The other signs and symptoms may disappear, but they will remain small for their age. This condition has been described as 'nutritional dwarfism' (Jelliffe, 1959). Such children, small for their age but otherwise clinically normal and growing at a normal rate, are no longer malnourished but are showing the effects of a previous period of inadequate growth as a consequence of malnutrition. Changes similar to those in physical growth are observed in bone maturation (Garn *et al.*, 1964), and at present it is of great interest to clarify whether their mental development is equally affected. Although a good correlation has been found by some investigators between the physical growth and the performance of these children in some measures of psychomotor and intellectual development (Cravioto *et al* , 1966), it has not yet been possible to demonstrate whether these last alterations are a direct result of malnutrition or of other components of the 'social deprivation syndrome'. Available information seems to indicate that malnutrition *per se* does interfere with the normal development of the central nervous system when it is severe and occurs during the first months of life (Monckeberg, 1969).

3.1.2. MARASMUS

Marasmus, which is primarily the result of severe calorie deficiency, is clinically characterized by extreme emaciation. The child, usually an infant, first stops growing and is later forced to utilize his own tissues to satisfy its basic energy requirements; initially, a large part of the adipose reserves and later a large proportion of muscle mass is utilized for energy purposes. The child with marasmus is therefore small for his age, and reduced practically to 'skin and bones' (Fig. 1). The head and the abdomen, sometimes distended, look large for the very thin arms and legs. The skin of the whole body lacks its normal turgidity and is wrinkled, thus giving the impression that it is too large for the reduced body. There is no clinical edema. If no other complications are present, the child is usually alert, cries frequently, and conserves a good appetite. Total serum proteins, albumin, and other biochemical indicators of severe protein deficiency, including the ratio of nonessential to essential free amino acids in plasma, are not significantly altered (Viteri *et al.*, 1964). The urinary excretion of hydroxyproline, a biochemical indicator of growth, is low, and in extreme cases the excretion of creatinine is also significantly lowered indicating a very reduced muscle mass (Whitehead, 1967). Similarly, although there is a marked atrophy of all the organs, no frank pathological alterations are observed. It seems, in general, that by utilizing their own tissues for surviving, these children do not develop the serious metabolic and pathological alterations observed in kwashiorkor.

3.1.3. KWASHIORKOR

Pitting edema, skin and hair lesions, gastrointestinal disturbances, and psychic changes are the most important clinical characteristics of kwashiorkor (Fig. 2). The

FIG. 1. Child 14 months old with marasmus; notice the extreme wasting and the typical facies.

edema is soft, painless, and partially localized by gravity. Although it is the sign on which, in our concept, the clinical diagnosis of kwashiorkor is based, the degree of edema varies from very mild and localized only in the feet and ankles, to cases in which it is so severe and generalized as to shut the patient's eyes from swelling of the eyelids, and to limit the person's movements. Most frequently it is present in the legs, lower abdomen, arms, and face, with little or no edema in the thorax. The degree of edema has no relationship with the severity of the protein deficiency.

The skin is almost always thin and dry and characteristic 'pellagroid' lesions are frequently observed (Fig. 3). There are areas of hyperpigmented and hyperkeratotic epidermis which peel off in large scales leaving tender, frequently exudative skin which can easily become infected. In infants, the lesions start and are more frequently observed in the perineal region; in older children, the extremities and later the face, neck, and lower trunk are the more affected areas. Hemorrhagic lesions of the skin, petechiae, and ecchymosis are observed in the very severe cases.

The hair becomes dry and brittle, straight when it has been curly, and can be pulled out easily. Frequently, it also changes color, black hair becoming reddish, yellow, or even white. These color changes may be seen over all the hair, or in stripes alternating with hair of normal color; this is known as 'flag sign' (Fig. 4). Neither the dermatosis nor the hair alterations are constant or indicative of the severity of the case.

Among the gastrointestinal disturbances, anorexia, diarrhea, and vomiting are

FIG. 2. Child 2 years old, with kwashiorkor, as observed in Central America. Notice the edema, the skin and hair lesions, the muscular wasting, and the apathy.

frequently observed. Lack of appetite during the first days of hospitalization may interfere with dietary therapy, but if the child is properly taken care of, this lasts for only a few days, to be replaced by a strong appetite. Diarrhea is frequently observed; in most cases it is associated with intestinal malabsorption and disappears with dietary treatment without any other specific measures. Even when clinical diarrhea is not present, these children often have large stool volume indicative of fat malabsorption, which persists during the first few weeks of treatment (Holemans and Lambrechts, 1955). Vomiting is frequent when the children are forced to eat large meals during the first days of hospitalization.

Psychic changes are very characteristic. Children are usually apathetic, indifferent to their environment, and even lethargic; at the same time they are irritable and cry very easily when disturbed.

As indicated previously, these children may have a variable degree of emaciation and growth retardation which reflect the condition of the child before he develops the acute severe manifestations of kwashiorkor. Different signs and symptoms due to other nutritional deficiencies or other complications such as dehydration may be superimposed on the above basic clinical syndrome. The clinical picture may also be complicated by various infectious diseases which may kill the child or interfere with recovery. These infections are not frequently detected due to reduced clinical manifestations such as fever and leukocytosis.

FIG. 3. Skin lesions characteristic of kwashiorkor.

FIG. 4. Typical hair decoloration observed in kwashiorkor and described as the 'flag sign'.

Severe anemia may be another complication. This is common in children with severe hookworm infestation, in which case the anemia is microcytic hypochromic. Cases of megaloblastosis and macrocytic anemia associated with folic acid or vitamin B_{12} deficiency have also been reported (Adams, 1954). Megaloblastosis due to folic acid deficiency, or iron deficiency with microcytic anemia, develop after the initiation of cure if insufficient quantities of these elements are provided during treatment.

Even when no specific causes of anemia are present, children with kwashiorkor usually have low blood hemoglobin concentration and reduced packed red cell volume. This mild 'normocytic anemia' seems to be only an adaptation to a reduced metabolically active tissue mass and, therefore, a lower oxygen demand; this apparent anemia is progressively corrected as protein repletion is attained (Viteri *et al.*, 1968). Among the most characteristic biochemical alterations, the following can be mentioned: low total serum protein concentration due primarily to a marked reduction in the albumin fraction (Béhar *et al.*, 1956); the ratio of nonessential to essential free amino acids in plasma (Whitehead's index) is high (Whitehead, 1964); serum lipids, vitamin A and carotene are low (Béhar *et al.*, 1956); some serum enzymes, particularly amylase and alkaline phosphatase are markedly reduced (Dean and Schwartz, 1953), and there is a low urinary excretion of urea, creatinine, and OH-proline (Arroyave, 1969). The degree of body protein deficiency can be estimated by relating the creatinine excretion (Viteri and Alvarado, 1970) or total body potassium (Alleyne *et al*, 1970) to that of a normal child of the same height.

The pathological lesions most frequently observed are: fatty infiltration of the liver, atrophy of the pancreatic acini, and other exocrine glands, as well as thinning of the gastrointestinal mucosa; the skin also shows atrophy of the epidermis and of the sebaceous glands and hair follicles (Béhar *et al*, 1956). Bronchopneumonia is a frequent necropsy finding since this condition is a common precipitating cause of death in children with kwashiorkor (Tejada Valenzuela *et al*, 1956)

4. Epidemiology

The immediately responsible etiologic factor of PCM in children is an inadequate diet, frequently acting in conjunction with the common infectious diseases of early childhood. However, in order to understand the real nature of the problem it is necessary to analyze it epidemiologically, considering the interaction of host, agent, and environmental factors. It is only from this type of analysis that the preventive measures most likely to be effective under each particular set of conditions, can be derived.

4.1. Environmental factors

The environment in which PCM in young children is most likely to occur as a public health problem is that of poverty and ignorance which characterizes large sectors of population in the underdeveloped areas of the world. In general, a low *per capita* income, low educational levels, and poor sanitary conditions are a common feature. The food supply in these communities, even when they are primarily agricultural, is quantitatively insufficient and qualitatively inadequate to satisfy the nutritional requirements of the population. This is the result of low productivity related to inefficient systems of land tenure and low economical and educational levels of the population, all of which hamper the application of modern methods of agriculture. This situation is further aggravated by the decreased working capacity of the agricultural workers due to malnutrition and frequent diseases. For these population groups, the scarcity of foods, particularly those of high nutritive value such as animal products (meat, eggs, milk), is also determined by their low purchasing power For this reason, even when such foods are produced locally, they are consumed by the well-to-do sectors of the population or used for exportation.

The poor environmental sanitary conditions, low standards of personal hygiene, and insufficient medical services favor the high incidence of infectious diseases (diarrhea,

whooping cough, measles, etc.) which precipitate or aggravate the nutritional deficiencies in children already receiving an inadequate diet.

The social, cultural, and economic isolation in which many of these communities live, frequently with the family as the only economic unit, tends to perpetuate this situation.

The process of industrialization and urbanization, with the migration of peasants to the cities, creates the shanty towns where conditions are usually even worse than in the country. Not only are living facilities less adequate from the sanitary point of view, but since these people can no longer produce any food they must obtain it in the market, a situation which they are neither culturally nor economically prepared to face; consequently, they tend to invest their limited resources in a very inefficient manner. One significant change this process is producing in relation to PCM, which has already been mentioned and will be discussed later, is the shifting of the ailment to children of a younger age, and to a greater incidence of marasmus than of kwashiorkor.

The very rapid population growth in those areas where the problem already exists is aggravating the situation and making it much more difficult to correct by applying the necessary measures.

4.2. Agent factors

In the particular case of PCM, the agents are the sources of calories and proteins which act not by their presence but by their deficit.

Breast feeding is undoubtedly the most adequate and safest way of providing the calories and nutrients required by the infant. This is particularly true for populations living under the conditions described in the previous section which are neither economically nor culturally prepared for artificial feeding of their infants. Breast milk, if used as the only food, can satisfy the nutritional requirements of infants up to the age of 4–6 months. However, from then on, supplementary feeding becomes necessary. There are two problems related to breast feeding which are of interest in relation to the epidemiology of PCM. One is early weaning and the other is prolonged breast feeding with insufficient and/or inadequate supplementary feeding. Early weaning, that is to say, the complete interruption of breast feeding before the child reaches the age of 6 months, and in some communities even later, is dangerous when the families do not have the resources, the knowledge, or the facilities to feed their children artificially, adequately, and safely. Unfortunately, the industrialization and urbanization processes and the undiscerning cultural influence of the developed areas is resulting in a tendency to earlier weaning in many areas where the population is not yet ready for such practice. What is usually done in these cases is to feed the child with overdiluted cow's milk prepared and administered under very poor sanitary conditions. The frequency of diarrheal diseases at these early ages augments the consequent increase in the incidence of marasmus. At the same time, the incidence of kwashiorkor, which results from improper feeding after late weaning, is reduced This switch from a greater frequency of the kwashiorkor to the marasmic type of malnutrition, and at earlier ages, is a phenomenon which is now being observed in different parts of the world, primarily as a consequence of the indicated factors (McLaren, 1966).

The other breast-feeding problem associated with the epidemiology of PCM, is one observed in primitive communities with many difficulties for feeding their children properly after weaning, and consists in prolonging breast feeding as much as possible. In such populations, weaning takes place during the second or third years of life. The problem resides in the very inadequate supplementary feeding, both from the quantitative and qualitative standpoints, when mother's milk no longer provides sufficient nutrients This situation frequently continues after weaning, when the children are fed mainly cereal preparations or starchy roots or fruits. Under these circumstances, the children predominantly develop the mild-to-moderate forms of PCM manifested primarily by growth retardation after 4–6 months of life, and many develop kwashiorkor after complete weaning, more frequently during the second and third years.

The problem of feeding small children with diets based mainly on starchy foods (cereal preparations, cassava, plantain, etc) that constitute the staples for these

populations and which are supplemented only with small amounts of legumes, vegetables, and fruits, and only occasionally with animal products, also merit discussion. There are two main limitations in these children's diets. One is that the protein content in relation to calorie concentration is very low, with the result that even when the calorie requirements are met, it is difficult if not impossible to satisfy the protein needs. In addition, these unbalanced diets frequently produce anorexia, thus reducing intake; consequently, not even the calorie requirements are met. The other problem is related to the biological value of the proteins of such diets which, in most instances, are deficient in one or more of the essential amino acids. This makes the possibility of satisfying the protein requirements still more difficult, particularly for infants and small children who have proportionally greater needs for both total protein and essential amino acids. The above explains why, in the same population, older children and adults who require a lower proportion of the calories provided by proteins and who can meet their total nitrogen and amino acid needs with proteins of lower biological value, are much less affected than infants and preschool children.

4.3. Host factors

Age is the most important factor related to the host in the epidemiology of PCM, and operates in the following ways. First, age is basic in determining nutritional requirements; as has already been indicated, the young child is more susceptible because of its proportionally higher requirements in calories, total protein, and essential amino acids.

The young child who has not yet developed immunity to the infectious agents of the environment is also more frequently and seriously affected by diarrheal and respiratory diseases and by the common infections of early childhood. That the role of these infectious processes, superimposed on nutritional deficiencies, is responsible for PCM, is well known (Scrimshaw *et al*, 1968).

Finally, cultural factors which influence feeding practices in relation to the age of the child, are also important. Of the foods available and consumed by the family, small children are frequently offered only those which are considered adequate and safe for them. In most cultures, the criteria for selection are based on erroneous beliefs, and usually work against the interests of the recently weaned child. The high frequency of diarrhea and other diseases worsens the situation, because during these episodes the child's usually poor diet is restricted still more and for long periods, with serious nutritional consequences.

5. Treatment

Hospitalization is recommended for treatment of severe cases of PCM (kwashiorkor and marasmus), especially when they are aggravated by other complications (dehydration, infections), as is frequently the case. A general pediatric ward presents, however, some problems for these children, particularly because they become exposed to acquiring infectious diseases which interfere with their recovery. Ideally, therefore, a special ward or an isolated unit should be considered for them. In any case, hospitalization is required for at least the initiation of cure; ambulatory treatment as outpatients is usually ineffective because such children are often anorexic and the mothers have problems in feeding them properly, even if they are provided with food. Furthermore, if not properly treated, the children may easily die as a consequence of the complications.

The following stages are recommended in the treatment of severe cases of PCM (Alvarado *et al*, 1970).

5.1. Emergency treatment

At this stage, the principal purpose is to save the life of the child. Children are not usually taken to the hospital until they are very ill and the large majority of deaths occur within the first 48 h after admission. Therefore, before the fundamental dietary treatment is instituted, it is very important to correct the conditions which can interfere

with recovery and could cause death. A very careful and complete clinical examination should be performed to indicate the need for one or more of the following measures.

5.1.1. CORRECTION OF DEHYDRATION AND ELECTROLYTE IMBALANCES

Both marasmic and kwashiorkor patients are frequently dehydrated as a consequence of diarrhea and vomiting. Even the kwashiorkor cases with severe edema may show signs of dehydration and may die in spite of the large retention of water in the extravascular space as edema.

Dehydration in the malnourished child is usually accompanied by hypo-osmolarity, a tendency to acidosis and to deficiencies of potassium and sometimes magnesium, with retention of sodium. The glomerular filtration rate is also frequently reduced. All these factors should be taken into consideration in the institution of fluid therapy directed towards their correction. Fluid administration is recommended intravenously only when clinical signs of dehydration are present. Fluids and electrolytes should be administered orally when the child does not seem clinically severely dehydrated. One-half to one-fourth normal electrolyte osmolarity solutions containing glucose are recommended to initiate diuresis. Sodium should not be given in amounts greater than 1 mEq/kg/day unless additional losses through diarrhea and/or vomiting have to be compensated. The recommended doses of potassium are 4–6 mEq/kg/day, but in the case of continuous additional losses, these can be raised to 7–11 mEq/kg/day. Potassium should be administered only after an adequate diuresis is ensured. Sometimes, when neurological manifestations of magnesium deficiency are present, the intramuscular administration of magnesium sulfate solution is indicated.

5.1.2. TREATMENT OF INFECTION

Special efforts should be made to discover any possible infection that may be complicating the case so as to institute prompt treatment with the appropriate anti-infectious drugs

Respiratory infections are common. Diarrhea is also a frequent complication, but most cases can be corrected by dietary and fluid therapy without specific treatment If amebiasis is demonstrated, specific treatment is recommended, but emetine should be avoided. For the treatment of other intestinal parasites, it is preferable to wait until the general condition of the child has improved.

Hepatic and cardiac insufficiency should be kept in mind as other possible complications during the first days of hospitalization.

5.2. Etiologic dietary treatment

While the measures indicated in previous paragraphs are instituted, the child should be started on a therapeutic diet. We recommend feeding the child progressively, starting with the administration of cow's milk preparations in amounts to provide approximately 1 g of protein/kg/day, and about 70–80 cal/kg/day during the first few days, rapidly increasing the amount in accordance with the tolerance of the child The rationale for a cautious initial feeding schedule is that the child is maximally adapted to very low protein and calorie intakes and a large load of these nutrients may cause a discompensation with complications which may precipitate death. Other foods, such as bananas, eggs, vegetables, meat, cereals, etc., may be added progressively so as to offer a varied and complete diet according to the age of the child and to provide up to 4–5 g of protein and 120–150 cal/kg/day. In marasmic children it may be necessary to increase the calorie intake up to 200 cal/kg/day, to attain an adequate recovery rate.

During the first days, when the child is frequently anorexic and has a tendency to vomit if forced to eat, small but frequent feeding administered with great care by specially trained personnel is recommended If this is not possible and the anorexia is severe, it may be necessary to resort to feeding by gastric tube until the appetite is recovered.

Although fats are not absorbed well during the acute stage, they can be given in the diet in normal amounts. An intolerance to lactose may be present and manifested by

diarrhea, but this can be corrected by reducing the amount of milk. The use of calcium caseinate or other lactose-free rich-protein foods to achieve the required protein intake, and of sucrose and vegetable oils as calorie sources in the formula, may be necessary in these cases.

When a varied and adequate diet is provided, it should satisfy the needs of all essential nutrients and no vitamin or mineral supplements are usually necessary, with the following exceptions. Vitamin A, preferably by intramuscular administration of a water-miscible preparation, and in adequate doses, is indicated as of the day of admission because of defects in absorption and transport of fatty esters of vitamin A in severe PCM. This measure assumes particular importance in areas where the deficiency of this vitamin is prevalent, and especially if the child shows ocular lesions suggestive of vitamin A deficiency. This is necessary to prevent keratomalacia which frequently complicates the severe cases of PCM.

Folic acid should be given at the initiation of therapy until a varied folate-rich-diet is instituted, particularly since milk is a poor source of folate. Iron supplementation is also needed, starting a few days later. These erythropoietic substances are necessary to satisfy the greatly increased demand of rapid hematopoiesis; otherwise, megaloblastosis may rapidly develop and hypochromic-microcytic anemia almost certainly will appear as the child recovers.

Once the clinical manifestations of severe nutritional deficiencies (edema, skin lesions, apathy and anorexia) have disappeared and the child is tolerating a varied, good quality diet and gaining weight rapidly—a situation which is usually reached in two to three weeks and sometimes even within a shorter period in the less severe cases—he may be discharged from the hospital but should be kept on a high protein, high calorie diet. Approximately 3 g of protein and about 120 cal/kg/day are recommended until complete nutritional recovery is attained, which generally requires two to three months. Convalescent homes or other appropriate services are extremely useful for this purpose.

5.3. Adaption to the home diet

Before the child is discharged from the hospital or from a convalescent home to which he may have been transferred after initiation of cure, we have found it very useful to adapt him to a diet which not only satisfies nutritional requirements, but that, as far as possible, is based on the type of foods the child will likely receive later on at home, considering the family's food availability. It is precisely this type of diet, which is adequate for the child and based on the cultural and economic characteristics of the family, in which the parents should be instructed, before the child is discharged. preferably by practical demonstrations. The purpose is to prevent a relapse, often observed in hospitals where children are cared for without any concern as to what will happen to them after discharge.

Treatment of mild and moderate cases of PCM which do not require hospitalization is based on the institution of an adequate diet. To attain this, it is often necessary to provide the families with dietary supplements, particularly high protein foods such as skim milk or vegetable mixtures of high nutritive value. Another possibility is to give the children one or more complete meals in specially organized centers. In any event whatever method is used for supplementing the home diet of the children to correct deficiencies, special emphasis should be placed on the utilization of food supplementation as a valuable tool for practical education of the mothers (Bengoa, 1967). In these cases the purpose should be not only to rehabilitate the particular malnourished child but as far as circumstances permit, to help correct the inadequate dietary practices of the family.

6. Prevention

As indicated in the epidemiological analysis, the basic responsible factors for PCM in children, when existing as a public health problem, are associated with socia

economic, and cultural limitations of societies in underdeveloped countries. A complete and permanent solution of the problem can therefore be expected only by correcting these limitations, and particularly by increasing general food availability, economic capacity, educational levels, sanitary conditions, and the availability of adequate public health services. Unfortunately, for most of the areas where the problem exists, this is a very long term proposition. Furthermore, poor health and malnutrition are among the factors contributing to maintaining these characteristics of the underdeveloped population groups. It is therefore imperative to attempt to break this vicious circle and to apply measures of more immediate action. Among these, we can distinguish between those specifically related to the problem and those only indirectly related, but equally important.

6.1. Specific measures

These include actions oriented towards the general population such as food enrichment programs or the introduction of new foods, as well as those towards the individual subjects, which would include supplementary feeding programs and person-to-person nutritional educational activities. The first, when successfully applied, have the advantage of a greater coverage although their effects are much less subject to direct evaluation. These include: supplementation of staple foods with proteins and/or with the limiting amino acids (Bressani and Elías, 1968); introduction of new and more nutritional varieties of the staple food, for instance, opaque-2 corn (Mertz *et al.*, 1965), and introduction of new foods of high nutritive value adaptable to the financial and cultural conditions of the populations, such as vegetable mixtures especially designed as weaning foods (Bressani and Béhar, 1964). Many programs of this type are being implemented in different parts of the world. Nevertheless, as indicated previously, their direct impact will be difficult to evaluate because of the impossibility of separating their effects from those derived from other changes in the general living conditions which are taking place at the same time. However, in our opinion, wherever possible these measures should be applied if their beneficial effects have been experimentally proved under controlled conditions.

Supplementary feeding programs to vulnerable groups, particularly pregnant and lactating women and weaning and post-weaning children, have been very extensively used. These consist primarily in the direct distribution, at little or no cost to the consumer, of protective foods such as skim milk or others selected with the intention of correcting the prevalent dietary deficiencies. When properly designed and applied, especially in regard to the selection and control of the beneficiaries as well as of the supplements, and when the distribution of food is accompanied by intensive nutritional educational activities, they can be extremely effective. Nevertheless, their coverage is usually very limited, and frequently the bulk of the population most in need cannot be reached by these programs.

Supplementary feeding programs for school children can be useful also if the food supplements are properly selected and used primarily as educational tools to improve the dietary habits of the children, preparing them as future adults. The need of foods as nutritional supplements is generally of less importance at this age than in late infancy and the preschool years.

Nutrition education should be regarded as a regular activity in all the health programs, as a fundamental component of supplementary feeding and should be incorporated also into the systems of formal education in primary and secondary schools. This also applies to agricultural extension, home economics, or community development programs and should always be emphasized since the educational factor is of importance in the selection, conservation, preparation, intra-familiar distribution and consumption of foods.

When possible, special advantage should be taken of mass media communication methods for nutrition education of the general population. Due to the importance of this aspect and considering that the ultimate goal of educational activities should be to improve dietary practices and not to transmit knowledge, it is fundamentally important

to test the efficiency, in regard to the capacity of modifying food habits, of the methods and of the content now being used and, if necessary, to develop new procedures. Advantage should be taken of recent advances in the sciences of communication and of the new techniques available for this purpose. The maintenance of breast feeding for at least the first 6 months of life, the proper supplementation of breast feeding and adequate weaning and post-weaning feeding practices, as well as the adequate feeding of children during disease processes, all within the local possibilities and cultural characteristics of the particular population, should be the basic messages to be transmitted.

6.2. Nonspecific measures

Because of the important epidemiological role played by infectious diseases in the development of PCM, all measures directed towards the control of these diseases are of great value in prevention.

The implementation of environmental sanitation programs such as introduction of safe water, adequate excreta and waste disposal, fly control, personal hygiene, and food quality control would be of great impact in reducing the incidence of diarrheal diseases and intestinal parasitism, and consequently, the prevalence of PCM, particularly the severe forms which they frequently precipitate. Vaccination programs against the preventable diseases of childhood, especially whooping cough and measles, could also be of great value. In areas where endemic diseases such as malaria and schistosomiasis are a problem, their control would also bring about an improvement of the overall health and financial situation of the population, thus favoring better nutrition. Doubtless, the elimination of these further burdens on small children would also help in the prevention of PCM.

Social and health programs for the working population aimed at improving food production and economic development of the area are also important. Finally, family planning programs, besides reducing the number of children to be fed and cared for in each family, also prolong birth intervals. This would be of great value because it would allow the mother to feed each child and to take proper care of them for longer periods, ideally over the second or third years of life before she is forced to concentrate her efforts and attention on another newborn It is worthwhile to bear in mind that neglect of a child because of the birth of a younger sibling, is the interpretation that has been given to the term kwashiorkor.

As the previous considerations reveal, the prevention of PCM is a complicated matter which requires organized, systematic efforts from the public health agencies and from all sectors of society. This is imperative for humanitarian reasons. In addition, it should be emphasized that malnutrition is responsible not only for the high morbidity and mortality rates of children, but also is an important contributory factor to inadequate mental and psychological development, and to low productivity of adults. Because of these deleterious effects on society, malnutrition should be considered among the important factors which are limiting the efforts for social and economic development.

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Chapter

21

*Protein-Calorie Malnutrition**

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INTRODUCTION

The body needs to ingest food in adequate amounts to obtain energy, as well as protein and the other essential nutrients to maintain normal metabolic functions at any age and physiological state. While in the case of children these amounts have to account for maintenance and growth, in adults the needs in general are for maintenance purposes only. In the adult woman; pregnancy and lactation represent periods of growth and, consequently, of increased nutritional requirements.

Large segments of the world's population live under conditions where the availability and intake of food are in deficit in relation to their needs.[1] This is the case in many developing areas where food consumption is deficient both in quantity and quality. Insufficient food intake leads to chronic caloric deficiency, and ingestion of foods with insufficient protein concentration induces protein deficiency in vulnerable groups. This is particularly true when the protein is of poor quality, as is the case with most vegetable proteins. The problem with the latter is that the bulk of the food often imposes a limit to its intake. Also, amino acid deficiencies further limit the utilization of such protein sources, so that small children cannot satisfy their naturally elevated nitrogen and specific amino acid requirements.

These dietary factors, associated with many other health problems to be described later, lead to primary chronic protein-calorie malnutrition (PCM). In conditions conducive to primary PCM, the intakes of other essential nutrients, such as vitamins and minerals, are also generally low; however, serious manifestations of their specific clinical deficiencies are less common than one would expect. This is due to the fact that, when the calorie and protein intake is the limiting factor, the requirements for other nutrients diminish. Nevertheless, in PCM, vitamin or mineral deficiencies may become overt.

Primary PCM should be differentiated from secondary PCM, which is the consequence of a primary disease that leads either to inadequate food intake or utilization or to increased nutritional requirements. Examples of secondary PCM are psychological disorders, obstructive gastrointestinal lesions, primary malabsorptive problems, diseases inducing cachexia of metabolic, infectious or neoplastic origin, as well as endocrine disorders.

This chapter deals only with primary PCM, that is, the situation where energy and protein intake are apparently the most limiting factors in malnutrition.

* Scientific articles published on this subject are much more numerous than those cited in the present Chapter. However, because of limited space, the reader is often referred to some comprehensive reviews on the subject. Publications cited at the beginning or at the end of paragraphs or sections are general references for the topic dealt with. Through these, as well as through the more recent specific articles cited, many other important references may be easily located by those interested in a deeper approach to the subject.

EPIDEMIOLOGIC AND ETIOLOGIC CONSIDERATIONS

All of the developing areas of the world have several common characteristics, among which are low weight of newborn babies, high disease prevalence, small physical size of their inhabitants, elevated mortality rates, particularly during infancy and early childhood (Table 21–1), and, as a consequence, short life expectancy. The main reasons for these characteristics are two: undernutrition and poor environmental health. These situations lead to decreased productivity and increased waste of human and economic capital, including food. This perpetuates and often aggravates underdevelopment, thus worsening nutrition and health and, therefore, establishing a vicious cycle. This general picture, associated with a large concentration of still unproductive young people, provides the background for underdevelopment.

Table 21-1. Mortality Rates of Children 0-4 Years of Age*

Age	*Guatemala (1965)*	*%*	*U.S.A. (1967)*	*%*	*Ratio Guatemala/U.S.A.*
	A. Infant mortality (deaths/1000 live births)				
0–28 days	35.9	39.1	16.6	73.8	2.2
1–11 months	55.9	60.9	5.9	26.2	9.5
1 year	91.8	100.0	22.5	100.0	4.1
	B. Mortality in children between 1 and 4 years of age (deaths/1000 children of the corresponding age)				
1 year	50.0		1.4		35.7
2 years	35.2		0.9		39.1
3 years	24.9		0.7		35.6
4 years	15 6		0.6		26.0
1–4 years	30.3		0.9		33.7

* Compounded from data published by the Pan American Health Organization: *Las Condiciones de Salud en las Américas 1965–1968.* Washington, D.C., Organización Panamericana de la Salud, septiembre, 1970 (Publicación Científica No. 207), and INCAP.[3]

Table 21-2. Children Below 5 Years of Age in Central America, 1965-1967, Presenting Growth Retardation which, by the Gómez* Classification, Could Be Catalogued as Malnourished†

Country	*Total population below 5 years of age*	*1st, 2nd, and 3rd degree malnourished*		*Malnourished*					
				1st degree		*2nd degree*		*3rd degree*	
		No. of cases	*%*	*No. of cases*	*%*	*No. of cases*	*%*	*No. of cases*	*%*
Costa Rica	294,300	153,200	52.0	117,900	40.0	31,300	10.6	4,000	1.4
El Salvador	554,400	380,000	68.5	244,600	44.1	116,900	21.1	18,500	3.3
Guatemala	833,400	611,660	73.4	380,100	45.6	197,700	23.7	33,860	4.1
Honduras	346,900	221,300	63.7	143,000	41.2	71,200	20.5	7,100	2.0
Nicaragua	287,500	148,800	51.8	112,300	39.1	32,400	11.3	4,100	1.4
Panama	207,900	104,947	50.4	84,625	40.7	18,990	9.1	1,332	0.6
Total	2,524,400	1,619,907	64.2	1,082,525	42.9	468,490	18.6	68,892	2.7

* Gómez, F., *et al.*[2]

† Numbers are extrapolations from a statistically representative sample.

The magnitude of the problem varies from area to area. As an example, we can cite the figures obtained from a survey of the Central American region, where—by projecting to the total population of the area the prevalence obtained from a statistically representative sample—of all of the 2.5 million children below 5 years of age, 1.6 million could be categorized, on the basis of their body weight, as suffering or as having had undernutrition. Nearly one-third of them had been or were moderately or severely malnourished (second and third degree undernutrition) at the time of the survey.[3] These findings are presented in Table 21–2.

Adult undernutrition is more difficult to recognize, but is also prevalent in developing areas. In Guatemala, for instance, over 8 per cent of all medical admissions to the wards of government hospitals, are due to primary PCM.

From the epidemiologic point of view, PCM can be conceived as the consequence of the interaction of the environment on the host through an agent which, in this case, is the deficient availability of calories and protein at the cell level. The environment, host and agent factors are interwoven.

Environment. This can be considered at two levels:[4] (*a*) macroenvironment, at a regional or national level, and (*b*) microenvironment, at the family and individual level.

In the developing areas, the macroenvironment is that of poverty, not only in the strict economic sense, but also in the more important concept of poverty of human resources. Both are the cause and the consequence of lack of education, unsatisfactory health of the population, poor communications, low productivity, unfavorable economic balance and inadequate utilization of natural resources; all of these factors lead to inadequate food production, conservation, distribution, and consumption.

On the other hand, the microenvironment constituted by the family, which is the biological unit in terms of nutrition, receives the impact of the macroenvironment and further limits the availability of nutrients to the host. The factors operating at this level are meager purchasing power, faulty concepts of food utilization that conduce to poor food consumption practices and inadequate distribution of available nutrients among the members of the family. The latter is particularly evident in the case of small children and when disease strikes a member of the family, whose food is very often drastically restricted.

Host and Agent. Maternal malnutrition and infectious episodes during pregnancy are frequently the cause of prematurity and small, born-at-term infants. These children, already at a nutritional disadvantage, are the victims of poor feeding practices, especially in those regions where breast-feeding is being replaced early in life by artificial formulas in the face of prevailing inadequate education, hygiene and economic resources. All of these factors must be favorable for artificial lactation to be adequate.

This inadequate feeding takes place at a time when nutritional requirements are high per unit of body weight. The consequence is the increasing number of infants who suffer from early protein-calorie malnutrition, particularly in the urban areas. The most common type of severe malnutrition at this age is that of non-edematous PCM due to a predominant caloric deficiency.[5]

Even when properly breast-fed, complementary feeding practices for the child are poor, and thus induce some degree of PCM late in infancy. When weaning occurs, most children are fed diets that provide insufficient amounts of calories and proteins. Others receive only starchy gruels or high-carbohydrate low-protein diluted cereal drinks, which accentuate protein deficiency. Table 21–3 presents the median nutrient intake of rural Central American children, expressed as per cent of the recommended allowances for each age group. It is important to realize that, in the developing areas, children are smaller in size than those of the same age in the developed areas; consequently, their actual requirements are somewhat reduced because of their smaller size. Nonetheless, a decreased food intake for age, even when it could be fairly satisfactory for size, perpetuates undernutrition. If at this time the child is forced-fed diets which are high in calories but low in protein, he becomes acutely protein-deficient, in spite of being fat. This

Table 21-3. Median Nutrient Intake as Per Cent of Recommended Allowances of Nutrients Consumed by Preschool Age Children in the Rural Area of Guatemala, 1965*†

	Age groups (years)			
Nutrients	*1* (*38*)‡	*2* (*43*)	*3* (*34*)	*4–5* (*14*)
Calories	63	66	80	48
Proteins	79	74	108	67
Calcium	72	69	101	72
Iron	56	71	103	66
Vitamin A	24	30	25	20
Thiamin	100	92	128	68
Riboflavin	50	46	50	31
Niacin	42	50	68	39
Vitamin C	40	60	56	20

* Over 90% of preschool age children consumed less calories and over 60% consumed less protein than the recommended allowances. The calories and protein consumption was lower than recommended in 80% and 40% of the families, respectively.

† Modified from: Flores, M., Menchú, M. T., Lara, M. Y., and Guzmán, M.: Arch. Latinoamer. Nutr., *20*, 41, 1970.

‡ Figures in parentheses represent the number of children.

severe protein deficiency gives rise to edematous PCM of the "sugar baby" type.[6] More often, infants become the victims of mild-to-moderate repeated infections[7] and, by the time they are weaned, develop a common diarrhea syndrome known as "weanling diarrhea."[8] After weaning, children are fed the usual family foods, with little or no milk or other animal products, and, at this time or later, may also suffer from acute severe infections. As a consequence, their nutritional condition rapidly deteriorates. These children, who prior to weaning were growing at a slower rate and very often were somewhat underweight for their height, become frankly undernourished. Those who follow this path develop also the edematous type of PCM, but at the same time are somewhat emaciated. They suffer from a predominant protein deficiency, superimposed on various degrees of caloric deficit.

The majority of children, however, do not develop a severe degree of PCM and, through a series of adaptive mechanisms, remain in a state of mild-to-moderate protein-calorie malnutrition. This condition is characterized only by growth retardation and by periods wherein they have a mild weight for height deficit, with or without traces of edema. Children who survive the critical weaning and preschool age periods continue to grow at a slower rate and, by this time, their caloric and protein requirements per unit of body mass are rapidly decreasing. Their daily diet continues to be low in both calories and protein but they usually can procure more food and often have already had most of the common childhood infectious diseases. Thus, these children can progress into adulthood without further serious risks of becoming severely undernourished. However, if a severe infection or diarrhea supervenes, they can still develop severe PCM, regardless of their age. Among the common childhood infections, measles and whooping cough are well known to precipitate severe protein-caloric malnutrition. In children and adults, repeated acute diarrheal episodes and massive parasitic infestations by hookworm, *Trichuris trichiura*, *Strongyloides*, malaria and *Schistosoma* plus other stresses, such as acute food shortage and severe physical or psychological stresses, can well induce severe PCM.

PHYSIOPATHOLOGY AND ADAPTIVE RESPONSES IN CALORIE DEFICIENCY AND IN PROTEIN DEFICIENCY

Through a series of physiological mechanisms, the body tends to maintain a dynamic equilibrium. These mechanisms are constantly in operation in a variety of aspects. A typical example is the tendency towards caloric equilibrium: after the ingestion of a meal, energy is stored mostly in the form of high energy phosphates, fat and glycogen. These are drawn upon to obtain energy during the daily regular and relatively short periods of fasting, as well as during periods of increased energy expenditure.

With longer periods of calorie and/or

protein restriction, the body progressively adapts itself in order to maintain as adequate a functional status as the limited supply of nutrients allows. Consequently, in the process leading to PCM, the body is dynamically adapting to it and continues to do so throughout, until the individual is "maximally adapted." This adaptation results in a decreased nutrient demand and in the attainment of nutritional equilibrium compatible with a lower level of cellular nutrient availability. If, at this point, the supply of nutrients becomes persistently lower than that to which the body can adapt, death supervenes. However, although in most instances the nutrient supply is low, it is not so inadequate as to cause death and the individual is thus able to live in a state adapted to the diminished intake. In this process, most functions are altered and have the following characteristics: (*a*) They are more susceptible to being overwhelmed by an overloading mechanism, whether physiological or pathological, because of diminished functional reserves. This overload brings about uncompensation or failure of adaptation, and consequently poses a threat to the life of the host. In other words, the adapted PCM individual is a labile, functionally fragile subject. (*b*) Due to their dynamic nature, the degree of functional alteration generally correlates with the degree of protein depletion. Nevertheless, this correlation is influenced by the rate at which depletion occurs, or at which repletion takes place during nutritional rehabilitation.[9]

The adaptive metabolic processes in both calorie and protein malnutrition occur by hormonal interaction, by servomechanisms at the cellular level, and by yet poorly understood generalized body reactions. Briefly, calorie deficit induces the hormonal adaptations described in Table 21–4, which lead to increased fat mobilization from adipose tissue. Moreover, during the initial phases of deficiency, the individual shows decreased physical activity, and a lower basal energy expenditure per unit of lean body mass. The body composition is progressively altered by decreasing adiposity at a fast rate and lean body mass at a slower rate. Muscle catabolism produces an increased efflux of amino acid, primarily as alanine. As the caloric deficit becomes severe, basal energy expendi-

Table 21-4. Schematic Hormonal Adaptive Mechanisms from the Nutritional Standpoint

			Hormonal activities in	
Hormone	*Stimulus*	*Result*	*Calorie deprivation*	*Protein deprivation*
Insulin	↑ Glucose ↑ amino acids	↑ Protein synthesis (muscle) ↑ Growth ↑ Lipogenesis	Decreased	Decreased
Growth hormone	↓ Glucose ↑ amino acids	↑ Protein synthesis (body) ↑ Growth ↑ Lipolysis ↓ Urea synthesis	Increased	Variable, generally increased
Glucocorticoids	↓ Glucose ↓ amino acids	↑ Protein catabolism (muscle) ↑ Protein turnover (viscera) ↑ Neoglucogenesis ↑ Lipolysis	Increased	Generally decreased
Thyroid hormones	↑ Energy metabolism	Energy homeostasis ↑ Protein turnover	Decreased	Decreased

ture may be normal or even increased per unit of lean body mass, which then decreases at a faster rate.[9–11]

Without concomitant severe caloric restrictions, protein deficit induces the hormonal changes described in Table 21–4, as well as cellular adaptation mechanisms not directly hormonally mediated, but induced by the poor availability of amino acids. The latter involve decreased protein synthesis at the ribosomal level. The results from both mechanisms of adaptation are an internal shift in protein metabolism which consists of increased muscle protein catabolism and, as a consequence, a relatively increased amino acid availability at the visceral level. The composition of the free amino acid pool is altered. There is a decrease in the synthesis and catabolism of total body proteins, the latter predominating over the former. The end result is a longer half-life of some proteins, such as albumin, and a generally decreased protein turnover. In addition, the internal body distribution of protein changes. This is the case with albumin, which diminishes more in the extravascular than in the intravascular space. Urea synthesis decreases and amino acids are more efficiently recycled. Simple nitrogen-containing compounds, such as urea, apparently are more efficiently utilized as sources of nonessential nitrogen. In terms of body composition, there occurs a progressive reduction in lean body mass, due primarily to muscle and probably also to skin protein loss. Visceral protein is initially reduced ("labile protein") but then becomes stable or may even regain some of its total mass. Adiposity should remain essentially constant. As the body protein turnover and total body protein mass decrease, basal oxygen consumption also decreases.[9,12]

These adaptations, which lead to the sparing of body protein, are easily upset by forced calorie intake, primarily in the form of carbohydrates. Hormonal adaptation mechanisms are "fooled" and, as a consequence, internal protein shifts are impaired, thus inducing visceral amino acid depletion and a breakdown of adaptation. Infections leading to disease also upset adaptation by producing fever (increased calorie waste), which is accompanied by large nitrogen losses and shifts toward amino acid utilization for energy purposes. Amino acid utilization is also diverted for increased synthesis and for the turnover of special proteins, such as gamma-globulins (antibodies).[13,14]

When the adaptive mechanisms are maintained, the impact of PCM is diminished, and the length of time that an individual takes to go from mild to severe protein-caloric malnutrition is prolonged. As mentioned before, the individual has to sacrifice certain functions and some of his nutrient reserves and, for this reason, he becomes more susceptible to injuries which a well-nourished individual can well withstand with little repercussion. Among the nutrient reserves, total body K content is reduced[15,16] so that the malnourished subject is more liable to be depleted of this cation under conditions that promote increased potassium losses. His total circulating hemoglobin is reduced *pari passu* to decreased body oxygen demands; red cell production diminishes; and hemodilution takes place.[9,10,17] From the hemodynamic point of view, cardiac work decreases[18] and central circulation predominates over the peripheral circulation. Cardiovascular reflexes are altered, conducing to postural hypotension and diminished venous return. Hemodynamic compensation in severe PCM occurs mostly from tachycardia, rather than increased stroke volume. The renal plasma flow, glomerular filtration rate and tubular function decrease. As a consequence, in the severe cases, the renal concentrating ability and acidification mechanisms are impaired.[19] Before this occurs, chronic sodium retention and increased serum and urine antidiuretic activities lead to relatively increased total and extracellular body water.[20] Intracellular water is reduced in absolute terms because of losses in lean body mass, but intracellular overhydration may be present.[15,21] Physical strength is diminished, further inducing a reduction in the physical working capacity.[22,23]

Other alterations take place which have been found not to correlate directly with the degree of protein deficit, but which are always present in advanced protein deficiency. Among these, impaired intestinal absorption, moderately decreased capacity to transport

protein-bound substances in blood, reduced gonadal function, and lowered local resistance to infection can be mentioned. Impaired intestinal absorption of lipids and disaccharides and a decreased rate of glucose absorption occur in severe protein deficiency; the greater the protein deficit, the greater the functional impairment. A decrease in gastric, pancreatic and bile production is also observed, with normal to low enzyme and conjugated bile acid concentrations. These alterations further impair the absorptive functions. Protein-deficient individuals are diarrhea-prone due to these alterations and possible also due to irregular intestinal motility and gastrointestinal bacterial overgrowth. Diarrhea *per se* aggravates the malabsorption.[24–28]

Finally, a generalized decrease in nervous system function is clearly apparent in severe PCM.[29,30] The etiology of these alterations has not been as yet elucidated. Several explanations have been proposed, among others, decreased brain potassium content and catecholamine production; reduced number of cells in the central nervous system when malnutrition occurs before 6 to 8 months of age, and small cell size when it occurs at a latter age.[31,32]

Decompensation from severe calorie deficiency occurs from inability to maintain internal energy supply, and results in hypoglycemia, hypothermia, impaired circulatory and renal functions, acidosis, coma and death. In the case of decompensation from protein deficiency, visceral functional failure also results from unavailability of amino acids. At the same time, an accelerated tissue breakdown takes place. The resulting alterations are mainly liver failure to synthesize certain proteins, such as albumin, several clotting factors, and transport proteins leading to fatty liver; increased free circulating cortisol, hemorrhagic diathesis, and jaundice in extreme cases; various degrees of renal failure with acidosis, as well as water and sodium retention; frankly decreased cardiac work, and tissue anoxia with pulmonary congestion. All of these factors lead to the development of clinical edema and, in extreme cases, skin lesions with hemorrhagic phenomena. In addition, there is fluid leakage into the gastrointestinal tract, increased susceptibility to pulmonary infections, water and electrolyte disturbances with hypokalemia and hypomagnesemia, frank central nervous system depression, and death.[33–35]

DIAGNOSTIC CHARACTERISTICS OF PROTEIN-CALORIE MALNUTRITION

The clinical and biochemical picture of PCM varies according to its severity and to the characteristics of the host, the environment and the agent.

Chronic Mild-to-Moderate PCM.[36] *Clinical.* It is obvious that the severe syndromes of edematous and non-edematous PCM, recognized as "kwashiorkor" and "marasmus," respectively, represent the critical end of a spectrum of varying degrees of deficiency.

However, before these severe stages are reached, children survive with insufficient calories, protein or both, a situation which does not allow them to grow and develop at the rate to be expected from their genetic potential. A long-standing restriction would be clearly manifested by a retardation in height and weight gain (Figs. 21–1 and 21–2). This reduced size may be a life-saving device to allow the children to survive on the restricted food available to them.

Under these chronic conditions, it is generally observed that body mass, although markedly retarded for the chronological age of the child, is adequate for its height. However, these children may be chronically affected by temporary periods of weight for height deficits. As judged by body composition studies, bone maturation and biochemical measurements, it is known that the malnourished child is not a small version of his well-nourished counterpart of equivalent chronological age. He shows an immaturity of biological development compatible with his retarded physical size. This includes deficits in lean body mass and adiposity, with relative overhydration affecting primarily the extracellular space. Without knowing the actual age of the subject, it is often difficult or even impossible to determine the presence or extent of malnutrition in these children.

Other characteristics of such cases, which are more difficult to attribute exclusively to

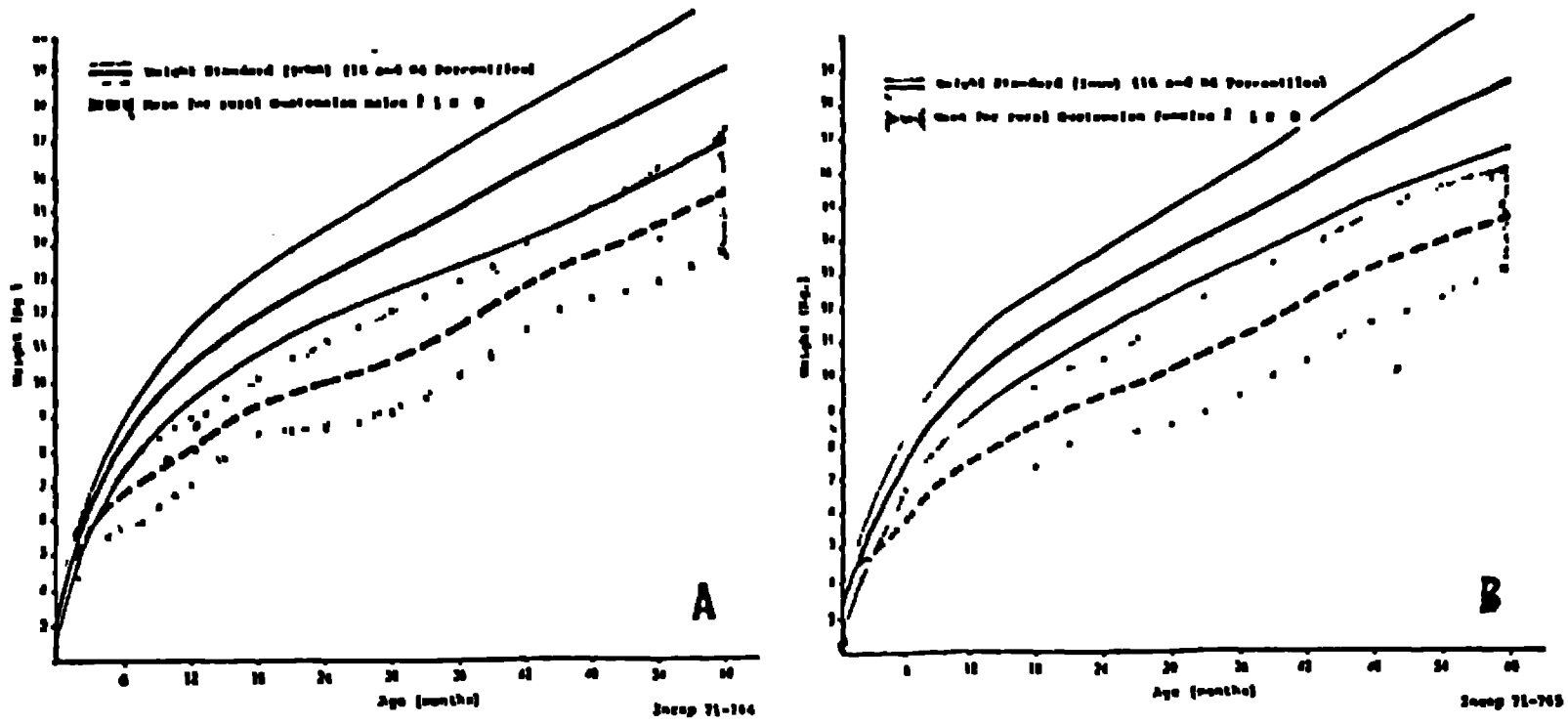

Fig. 21-1. Weight of rural Guatemalan male and female children below 5 years of age, in relation to that of U.S.A. children. Number of Guatemalan children in the sample: 431 males and 436 females.[3]

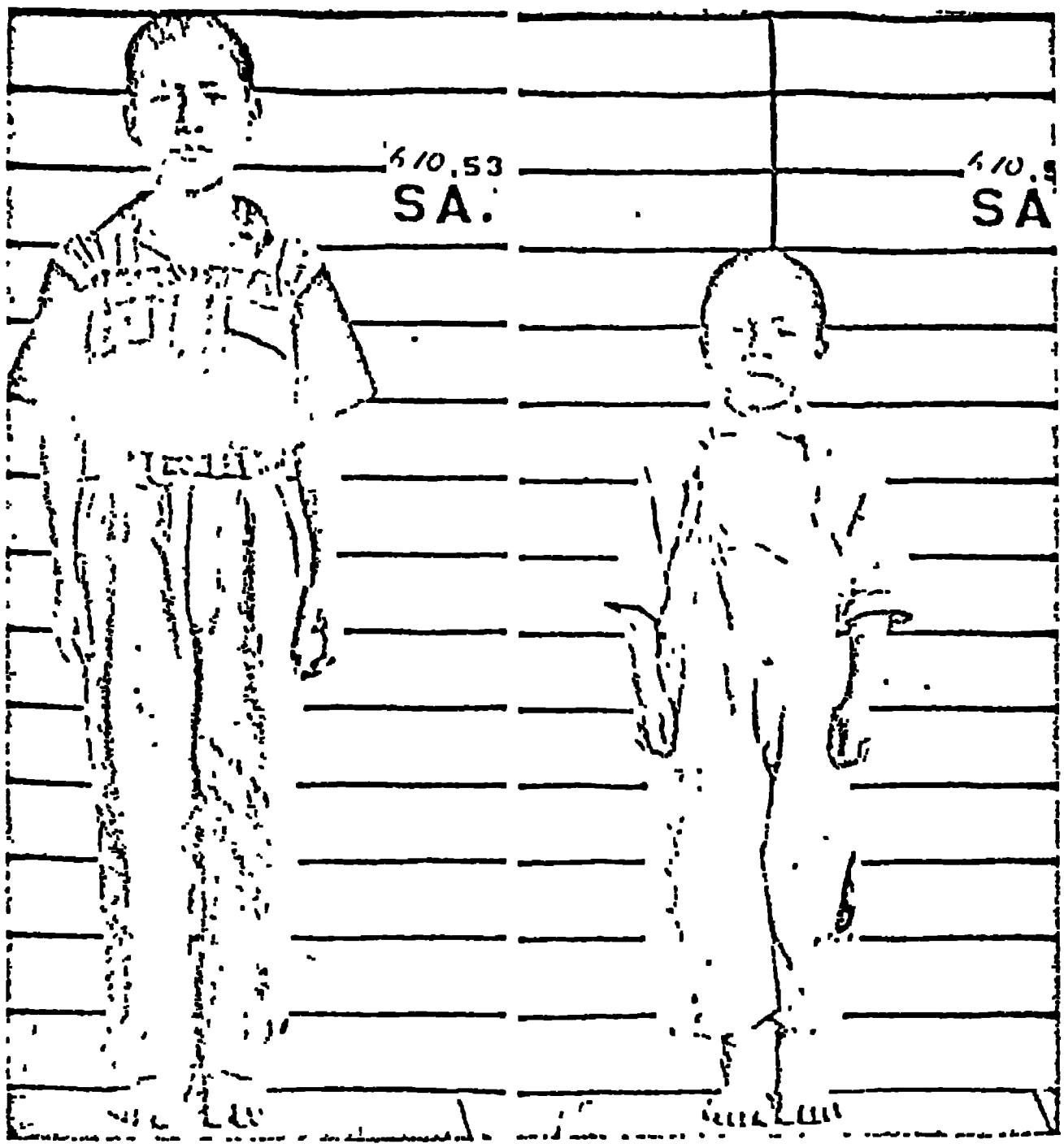

Fig. 21-2. Appearance of two 10-year-old children in the rural Central American region. The one at the left has always been well-nourished. The one at the right has been mild-to-moderately malnourished.

nutrition, are reduced physical activity, mental apathy, frequent episodes of ill-defined sickness, anorexia and diarrhea, and a higher fatality rate from common infectious diseases.

Recent studies have shown that there exists an association between retarded physical growth and development and some tests of psychomotor and mental development.[37] The isolated effect of malnutrition as a cause of this phenomenon is strongly suggested by present data derived from animal experimental work. Direct proof does not exist as yet in humans, although studies are now under way from which an answer to this question is expected. Nevertheless, it is beyond doubt that the responsible factor is the complex of social deprivation, of which nutrition is one of the most important components.[38]

Chronic PCM in adults generally results in marked leanness (Fig. 21–3), which, in severe cases, can reach a state resembling cachexia. Because their protein requirements per unit of body mass are much smaller than in children, the main manifestations are of primary caloric deficiency. Thus, physical activity and capacity for prolonged physical work are reduced, perhaps as a mechanism to keep themselves in caloric equilibrium on their low food intakes. Changes in body composition similar to those described for children can also be observed.[22,23]

Biochemical. Because of the characteristically low protein intake, subjects have a low excretion of urea N per unit of creatinine,[39] and a somewhat abnormal plasma free-amino acid pattern with a decrease of the branched essential amino acids.[40,41] It has been reported also that they excrete a lower amount of hydroxyproline in the urine, in good agreement with their slow growth rate.[42] Slight decreases in transferrin and albumin serum levels have been reported in these cases.[43,44] If lean body mass is reduced for height, this is manifested by a decreased creatinine/height index.[45]

Severe Protein-Calorie Malnutrition. *Clinical. Non-edematous PCM.* Severe caloric deficiency is clinically recognized in children by the syndrome identified as "*marasmus*" in most parts of the world, or non-edematous severe PCM (Fig. 21–4). Its main characteristics are: a child frankly small for his age who looks emaciated and, in extreme conditions, reduced to "skin and bones" because of an essentially total absence of adipose tissue. His skin is usually dry and "baggy," wrinkles easily and has lost its turgor. The hair is sparse, thin and dry, and can be pulled out easily; it loses its normal sheen and acquires a dull brown or reddish yellow color, giving it a lifeless appearance. The face resembles that of a monkey, with sunken cheeks in extreme cases, because of the disappearance of the Bichat fat-pad. The child is weak, looks hypotonic, and his pulse, blood pressure and temperature may be low. He is very sensitive to cold temperature, cries easily and is often found retracted from his

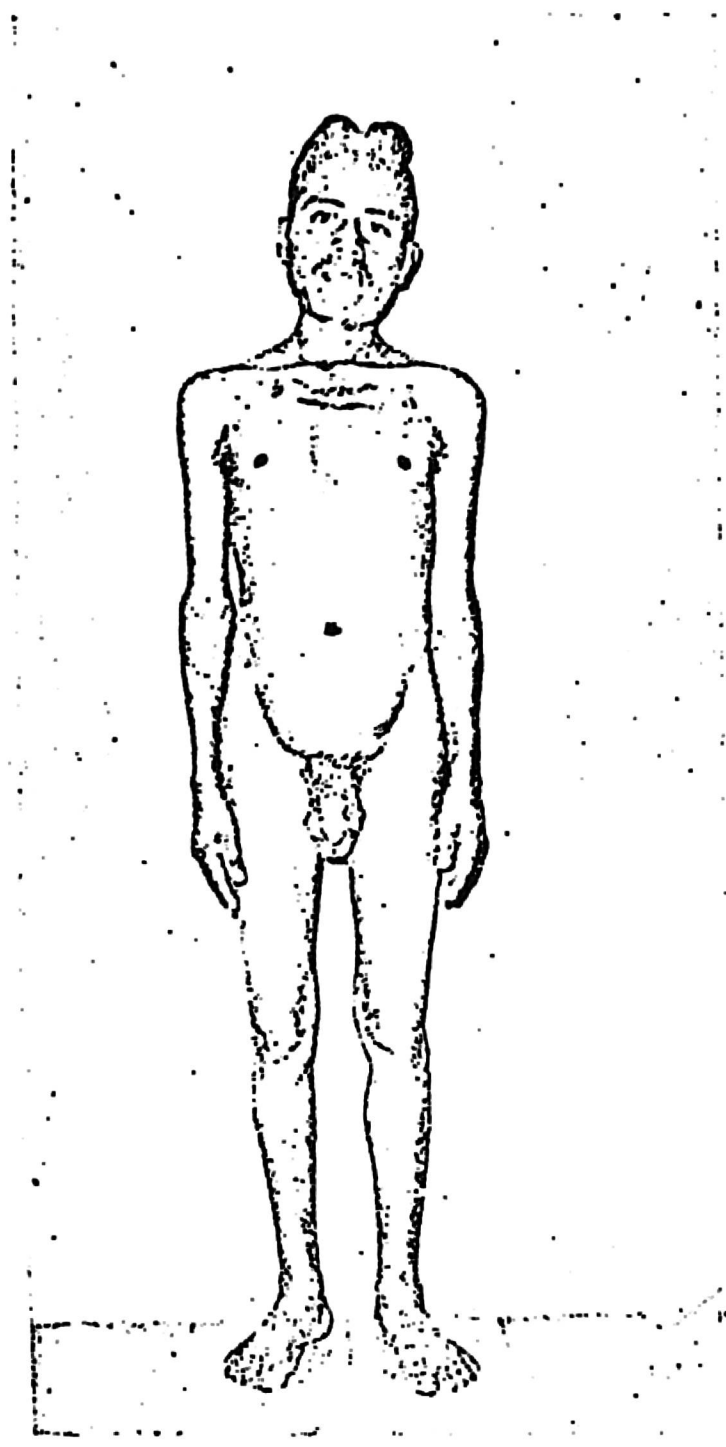

Fig. 21-3. Mild-to-moderate malnourished 36-year-old man.

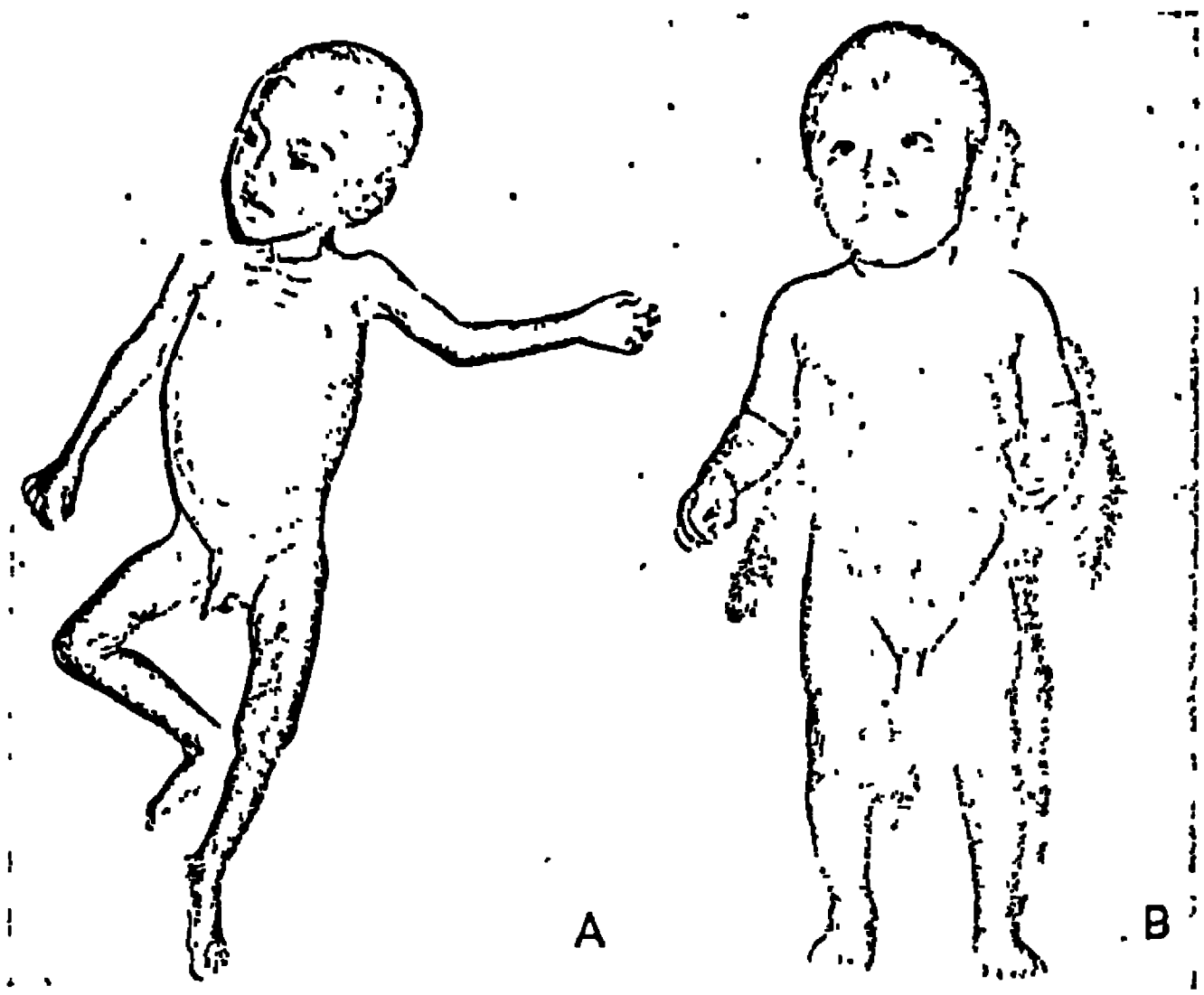

Fig. 21-4. Twenty-one-month-old child with severe non-edematous PCM (marasmus) on admission to the hospital and 4 months later, when fully recovered.

environment, sucking one or more fingers. Soon after therapy is initiated the child becomes alert and interested in his environment. His viscera are small and lymph nodes are easily felt. In adults, extreme emaciation is characteristic of calorie deficit (Fig. 21–5).

Common complicating features are eye lesions, due to hypovitaminosis A, and skin infections. The classical cases suffer from constipation and are ravenously hungry, but diarrhea, anorexia and vomiting, with dehydration, are not rare: dehydration, acidosis and electrolyte imbalances may, in fact, cause death. Postmortem examination shows only generalized atrophy, without fatty liver. Clinically, and post mortem, the child has no edema, although his total body water is increased for his size.[11,15]

Edematous PCM. The child with acute severe protein deficiency of the "*sugar baby*" type (Fig. 21–6) is usually almost normal in height for age: his body fat is normal or increased, but flabby, and he is clinically edematous. The edema may be located only in the lower segments of the body, due to action of gravity, but generally his face is swollen, his cheeks look heavy and his eyelids are swollen shut. He is pale and the skin shines in the edematous areas. In other parts of his body the skin may be dry, atrophic or have large asymmetrical confluent areas of hyperpigmentation and hyperkeratosis. A peeling type of desquamation occurs in these areas, leaving underneath a fine, atrophic pinkish skin. Hair is atrophic, dry, depigmented and has a reddish tint, falls off easily and breaks upon rolling it between the fingers. Often, zones of alopecia are noted. The nails are brittle and have horizontal grooves. The general appearance is that of a hypotonic, miserable-looking child. He is apathetic and irritable at the same time. In the severest cases his apathy is profound. Anorexia is almost universal. Hepatomegaly is frequent, as are a swollen stomach and intestinal loops. Diarrhea is almost always present. Frequent complications are eye

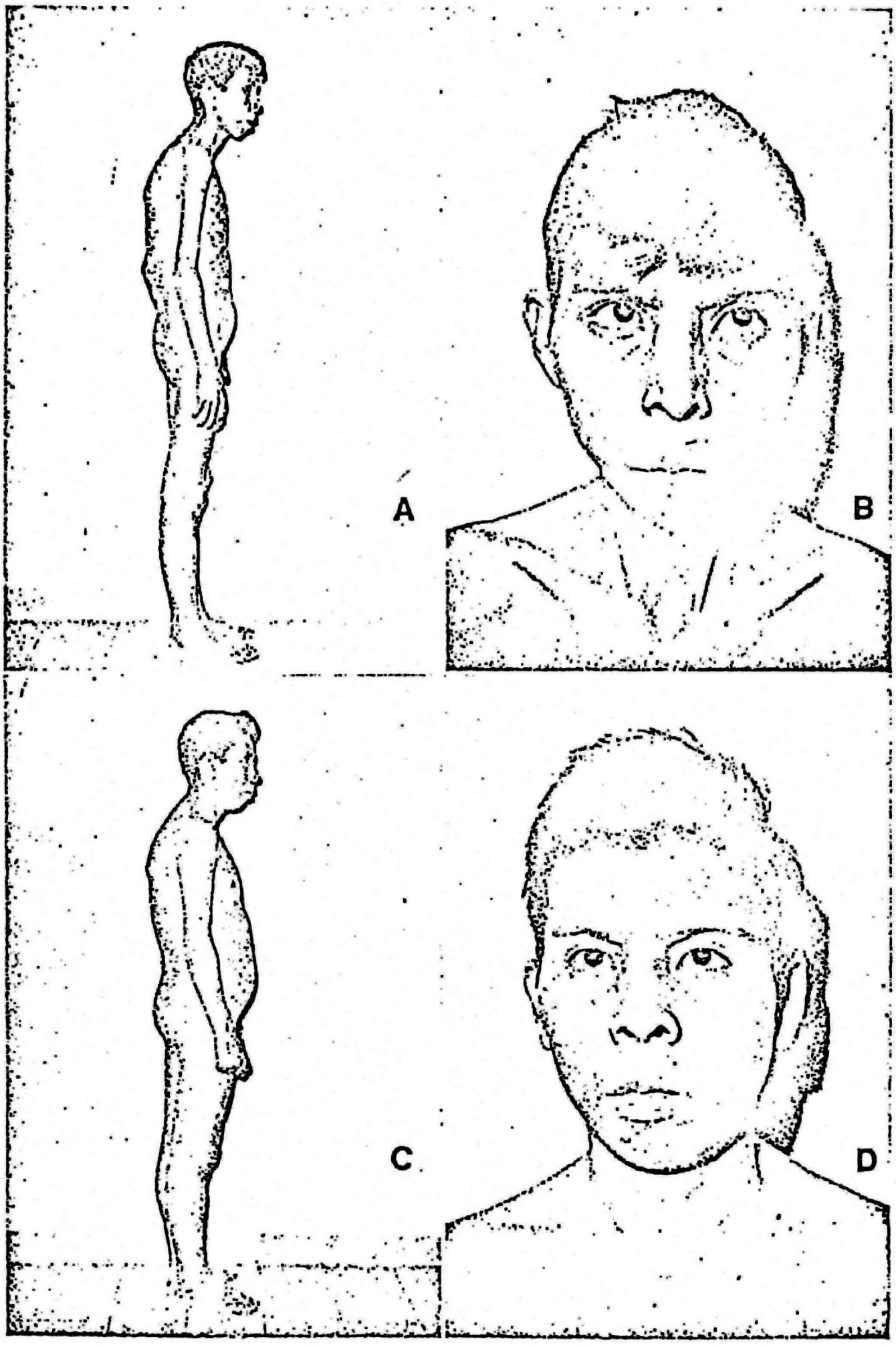

Fig. 21-5. Twenty-nine-year-old man with severe non-edematous PCM on admission to the hospital and 3 months later, when fully recovered.

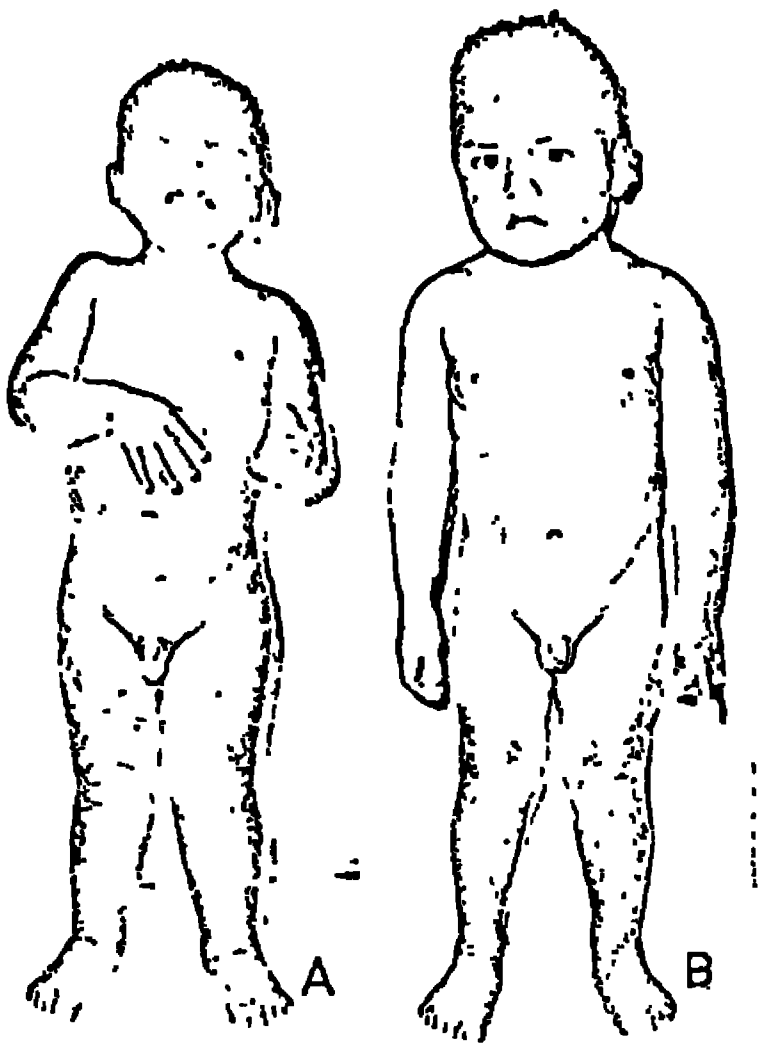

Fig. 21-6. Thirty-six-month-old child with severe edematous PCM and preservations of adiposity (kwashiorkor) on admission to the hospital and 4 months later, when fully recovered

lesions due to vitamin A deficiency, cheilitis and cheilosis, as well as other manifestations of deficiencies of the vitamin B complex. Upper respiratory infections and dehydration, even in the presence of edema, are common and often lead to death. Intestinal motility is irregular, and these children often become dehydrated before they pass a huge liquid stool. As the child begins to recover he loses his edema and remains fat and flabby. This appearance often misleads the clinician who may consider him recovered because his weight may be normal. In fact, he is still severely protein deficient in terms of lean body mass.

Pulmonary edema with bronchopneumonia, septicemia, gastroenteritis and water and electrolyte imbalances are the most commonly found causes of death. At autopsy, generalized edema, visceral and muscle atrophy and severe fatty liver are found. Red bone marrow is centripetally retracted.

The majority of cases of severe malnutrition, both in children and adults, fall between these two extremes of pure caloric and pure protein deficiency. In these cases, a moderate-to-severe protein deficit may be superimposed on a severe degree of caloric deficiency, and vice versa, a moderate-to-severe degree of caloric deficit may be superimposed on a severe degree of protein deficiency (Fig. 21–7). These subjects, suffering from severe PCM with edema, together with pure protein deficiency, have been termed "kwashiorkor" cases. Clinical edema constitutes the main characteristic for its diagnosis. The mixed PCM cases have also been identified with a variety of terms, among which are "pluricarential syndrome," in Central America, "undernutrition," in other Latin American regions, and "protein malnutrition" in certain African and Asian countries.[1,35,36] In adults, a predominant protein deficiency can also conduce to edematous PCM (Fig. 21–8).

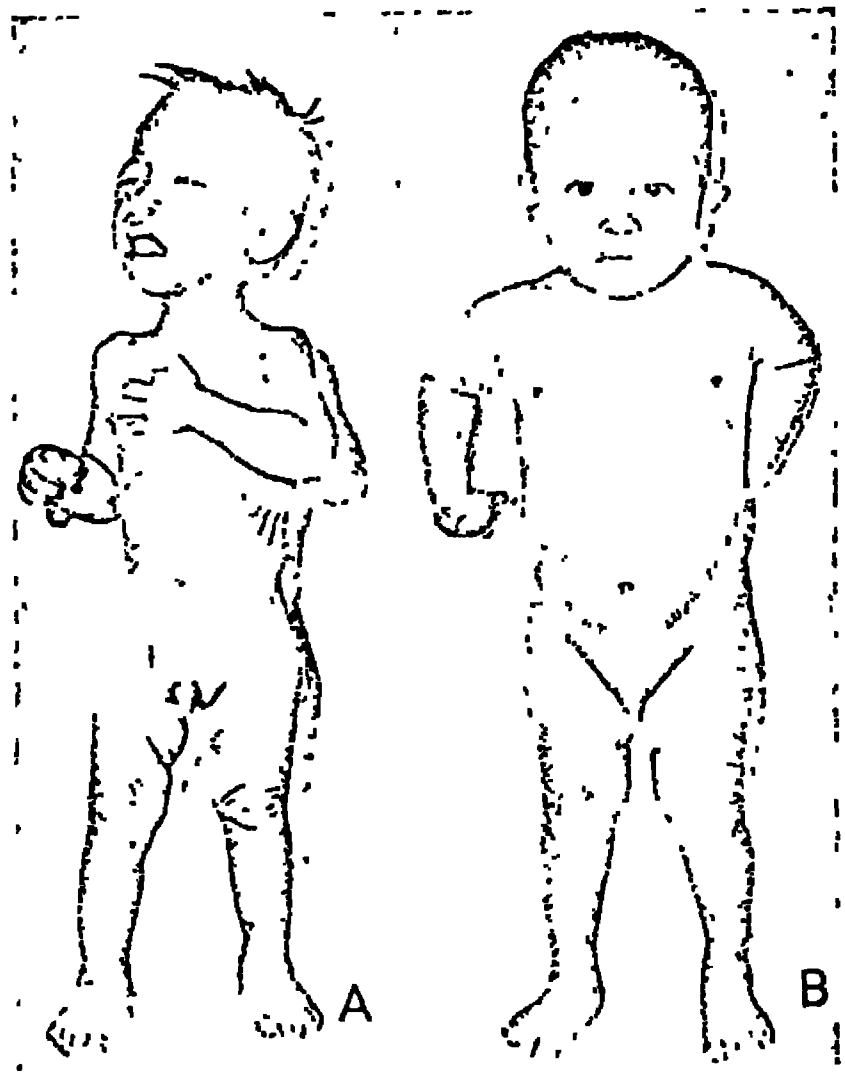

Fig. 21-7. Twenty-five-month-old child with severe edematous PCM superimposed on chronic caloric deficit. Besides being edematous, he appears wasted (marasmus-kwashiorkor). Pictures were taken on admission to the hospital and 4 months later, when fully recovered.

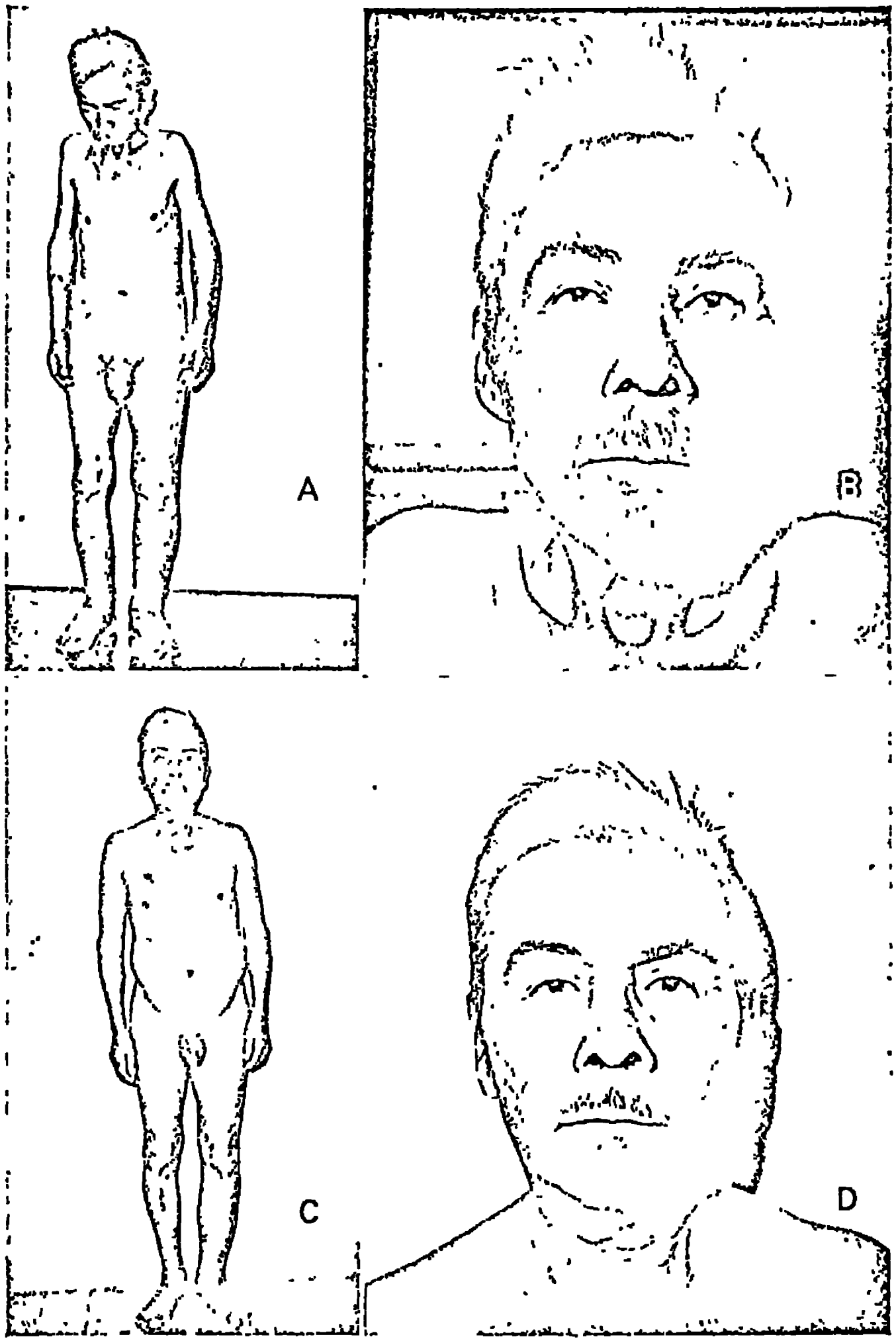

Fig. 21-8. Forty-six-year-old man with severe edematous PCM on admission to the hospital and 3 months later, when fully recovered

Biochemical. In severe protein-calorie malnutrition several biochemical alterations can be observed. Many of these are distinguishing between the *edematous* and the *non-edematous* types.

Protein and Nitrogenous Compounds. The child who has reached the severe stage of edematous PCM has been submitted to a severe negative balance of body proteins.[46] Consequently, his total body nitrogen is markedly reduced. Different organs share this protein loss to different extents.[47,48] The liver rapidly loses a fraction of proteins, while the loss of muscle protein is progressive and, because of its large mass, accounts for the major part of the protein loss. Kidney, brain and endocrine organs seem to retain their protein more efficiently. However, the importance of these different losses in terms of organ function cannot be derived from their relative magnitude. A low ratio of protein to DNA has been shown in muscle, liver, and brain, illustrating intracellular protein loss.[32,49] In the non-edematous PCM these changes are moderate, becoming severe only in the most advanced stages

The concentration of several protein fractions in the body fluids is low. The blood plasma has been studied more at depth. Although present in both types of PCM, edematous and non-edematous, the changes to be described are more pronounced in the first type. In the second one, they may be totally absent. The concentration of total proteins is reduced, and the magnitude of the reduction is explained mainly by a decreased albumin concentration. The concentration of beta-globulins is also decreased. On the other hand, the gamma-globulin fraction concentration is either normal or increased; therefore, their per cent contribution to the total plasma proteins is always high.[35] Some plasma proteins with very specific functions may also be decreased. Among them, those associated with the transport of other nutrients and hormones are particularly important, such as transferrin,[43,50] ceruloplasmin,[50] retinol-binding protein (RBP),[51] alpha- and beta-lipoproteins,[52] as well as thyroxin[53] and cortisol-binding proteins.[54] Impaired blood transport may attain significance in the development of secondary metabolic abnormalities, as has been shown in the case of lipids and vitamin A.[55] The blood concentration of urea nitrogen is found to be low, as is also its excretion in the urine. This reflects the low catabolic rate of body proteins and decreased urea synthesis, which are characteristic of primary protein deficiency.[12] When calories are the most limiting factor, urea production is increased, because body protein catabolism is elevated, as has been demonstrated in some non-edematous cases suffering mainly from marasmus.[56]

The excretion of urinary creatinine is decreased,[57,58] a consequence of the decrease in muscle tissue and lean body mass.[59]

The plasma free-amino acid pattern is abnormal in edematous PCM. A lowered concentration of valine, leucine, and isoleucine is a characteristic, as is also a very low tyrosine concentration.[60,61] The ratio of the branched essential to non-essential amino acids is low. Another finding, which is very characteristic, is a low tyrosine-phenylalanine ratio, due to a deficiency in phenylalanine hydroxylase.[62] In non-edematous PCM, plasma amino acid alterations may be absent.[40]

Hemoglobin concentration is variable, but often it is around 10 gm/100 ml because of hemodilution. Generally, the cells are normochromic and normocytic. Hypochromia can be present, if there exists a severe iron deficiency from other causes. Mild to overt megaloblastosis can occur because of folate deficiency.[63] The great majority of subjects are not anemic but physiologically adapted to the decreased oxygen demands.[10,17] Leukocytosis can occur, if infection is present: leukopenia and thrombocytopenia generally indicate the presence of gram-negative septicemia.

Although it has been observed that urinary amino acid excretion is abnormal, no consistent pattern seems to be evident. The abnormal metabolites, ethanolamine and beta-amino isobutyric acid, have been detected, suggesting a defect in transmethylation.[64] Excretion of urocanic acid has been shown to be abnormal after a histidine load.[65]

Carbohydrates. Usually blood glucose is normal. However, there is an increased tendency to hypoglycemia upon fasting.

This is compatible with the finding that liver and muscle glycogen stores are normal or low.[66] Some alterations revealed by clinical laboratory studies suggest abnormal metabolic handling of glucose. Furthermore, glucose tolerance tests give a diabetic type of curve, and insulin secretion is low.[67,68] Impaired glucose utilization, glycogenolysis and glycolysis have also been demonstrated. In addition, there are isolated pieces of evidence of impaired enzymatic steps along the glucose oxidation, the Krebs cycle and the galactose to glucose conversion paths.[66,69,70]

Lipids. Steatorrhea is a characteristic of edematous PCM, even when the diet is practically devoid of fat.[71] Lipid absorption has been found reduced.[72] Low levels of many serum lipid fractions, neutral fat, cholesterol, particularly its esters, vitamins A and E, and phospholipids have been demonstrated. These findings suggest that the changes in specific plasma proteins and physical chemical structure of the lipid-protein complexes account for impaired blood transport [65,73,74] In fact, there is direct evidence for decreased lipoproteins as well as for RBP, the specific vitamin A-binding protein.[51] A great part of the fatty liver may well be the consequence of inability to mobilize fat.[74]

Vitamins.[75] Signs of water-soluble vitamin deficiencies vary with the local dietary patterns, but, even when intakes are low, serum concentrations of thiamin, riboflavin, vitamin C, niacin metabolites and folates may well be within the normal range, and overt clinical signs of deficiency of these factors are rarely seen. Vitamin B_{12} serum levels are often found to be high All of the above findings suggest that, although the supply of these vitamins may be low, tissue demands are also decreased.

In the edematous type of PCM (kwashiorkor), serum levels of vitamins A and E are consistently lower than normal. In the case of vitamin A, poor vitamin intake and defective absorption and transport explain these alterations This explanation may well apply also to vitamin E. All levels rise rapidly with therapy.

Water and Electrolytes.[34,76,77] Hypo-osmolarity is a common finding. Serum sodium levels are from normal to low. Potassium and magnesium serum levels are not decreased, except when excessive losses of the cations occur due to diarrhea and vomiting. In such cases, hypokalemia is accompanied by a loss of potassium from specific tissues such as muscle and brain.[78] This results in a decreased cellular potassium-to-nitrogen ratio. Mild acidosis is also common, on account of a decrease in the renal acidification mechanisms. Total serum calcium is somewhat low, primarily due to the protein-bound fraction.

Enzymes. The activity of several serum enzymes such as amylase, pseudocholinesterase and alkaline phosphatase is reduced. Their drop is consistent and quite parallel to that of albumin, so that they may be normal in non-edematous PCM.[35,79] Serum transaminases are elevated and reflect increased tissue transaminase activity and leakage from the cells.[80] Around 15 hepatic enzymes have been studied,[81,82] including dehydrogenases, oxidases and esterases; of these, 4 are clearly decreased in the edematous type of PCM: xanthine oxidase, glycolic acid oxidase, d-amino acid oxidase and cholinesterase. It has been pointed out that these enzymes are not involved in fundamental physiological functions and seem to be of relatively little importance. On the other hand, cytochrome C reductase, a key enzyme in electron transport, is well preserved.

More complex systems, which depend on the integrity of the mitochondria, have been studied. Oxidative phosphorylation is somewhat reduced, and phosphate uptake into phosphatides is about half the value seen in recovered children.[46]

Enzymatic changes in liver and PMN leukocytes have been studied comparatively.[83] It has been found that not only are changes in both tissues very similar, but that they are characteristically different in the edematous and non-edematous types. In summary, these changes are: increased activity of fumarase and aconitase, and decreased activity of isocitric dehydrogenase, glutamic dehydrogenase and aldolase in the edematous malnourished child. The reverse is true in the non-edematous patients Muscle creatine phosphokinase activity has been found to be consistently low in children with

the edematous type, while, in those suffering from the marasmic type, low or normal values can be observed.[84]

It is impossible to separate the effects of protein-deficiency *per se* on enzymes from changes in activity which may reflect changes in functional pattern in response to adaptation. In general, the latter interpretation seems more plausible. Furthermore, the measurements done *in vitro* with reconstructed systems tell nothing about subcellular structure changes, which may alter linking of enzymes with their substrates and co-factors. These could well involve alterations in membrane structure at the cellular and subcellular level.

TREATMENT

Chronic Mild-to-Moderate Protein-Calorie Malnutrition. Children suffering from chronic protein-calorie malnutrition are, as mentioned before, smaller in height and lighter in weight than their counterparts of equivalent chronological age. Because these children are not only physically retarded but also proportionally immature, their protein and caloric intake should be calculated on the basis of their height, that is, as if the child were well-fed but younger, of an age for which his height would correspond to the 50th percentile. This means a higher caloric and protein intake per kg of body weight than that of children of the same chronological age. These intakes, therefore, will promote a retention of energy and protein to permit catch-up in growth and development. Of course, they should contain the appropriate concentrations of all the other essential nutrients. Even more, when marked deficiencies of other nutrients are also prevalent, administration of specific supplements is called for.

Severe Protein-Calorie Malnutrition. The severe, uncompensated forms of PCM require medical guidance during the initial phases of treatment.[85,86] In these cases, even when hospitalized, mortality is high, ranging from 11 to 50 per cent, depending on the centers where they are treated and on certain characteristics of the patients. Table 21–5 lists those characteristics which carry a poor prognosis.

The treatment of severe PCM may be divided into two phases:

(*a*) That oriented towards saving the patient's life by bringing him back to his adapted stage, and

(*b*) The rehabilitation or "consolidation of cure" phase. At this stage, body protein and energy repletion for the patient's height should be achieved.

The main objectives of the initial treatment are: therapy of infection and correction of water and electrolyte imbalances, as well as of other factors which lead to decompensation. It is during this phase that a cautious handling of the nutrition aspect is essential. This demands patience, and the personnel must be conscious of the fact that the most common causes of death are one or more complications and not malnutrition *per se*. Drastic therapeutic nutritional measures, such as high protein or calorie load from the start, may precipitate death by posing an "iatrogenic" overload on enzymatic and various physiologic functions which have reached "maximal adaptation" in several weeks or even months in the process of progressive malnutrition.

Table 21-5. Characteristics of Severely Protein-Calorie Malnourished Children Which Carry a Poor Prognosis

1. Stupor or coma.
2. Age less than 6 months
3. Weight-for-height deficit greater than 40%.
4. Severe, protracted diarrhea.
5. Infection, primarily bronchopneumonia or measles.
6. Hemorrhagic tendency. Purpura is usually associated with septicemia.
7. Severe eye lesions
8. Extensive exudative or exfoliative dermal lesions.
9. Extensive and deep decubitus ulcers.
10. Dehydration and electrolyte disturbances, particularly hyponatremia, hypokalemia, and probably hypomagnesemia.
11. Clinical jaundice or increased serum bilirubin and/or frankly elevated serum glutamic-oxalacetic and glutamic-pyruvic transaminases.
12. Hypoglycemia and/or hypothermia.
13. Total serum proteins below 3 gm/100 ml.

Maintenance of adequate urinary output is of primary importance. This is preferably accomplished by oral therapy, keeping in mind the fact that the severely PCM individual is hypo-osmolar. Therefore, solutions of around 280 mOs/liter are preferred. These should provide from 6 to 8 mEq/kg/day of K and, if needed, the potassium concentration can be raised to 10 mEq/kg/day so as to replace actual K losses which are usually 40 mEq/liter from diarrhea or vomiting. Sodium intake should replace losses (about 35 mEq/liter from diarrhea, and 12 mEq/liter from emesis), but, otherwise, it should be low (1 mEq/kg/day) because PCM patients have an excess of body sodium. An excess of sodium and osmolar overloads can easily induce cardiac failure. Magnesium should also be administered, particularly when diarrhea and vomiting occur. Usually 1 cc of Mg $SO_4.7H_2O$, 50 per cent solution, I.M. every 12 to 24 hours is adequate. This therapy is important if tetany, oculogyric crises, tremor and bizarre neurologic signs occur in the initial phases of realimentation. Unless severe, acidosis should not be treated. Usually, renal function will handle acid-base balance efficiently.

If needed, intravenous therapy can and should be used, following the general outline described for oral rehydration, except that K therapy should not exceed 6 mEq/kg/day; osmolarity should be kept at around 280 mOs/liter, and sodium must be kept low. Administration of plasma or other "protein-rich" fluids is contraindicated.

Shock, due to severe dehydration or gram-negative septicemia, should be treated as if the individual were not malnourished. In some of these cases blood transfusions are indicated, but hemoglobin concentrations should be brought only to about 10 gm/100 ml which is commonly the hemoglobin level these children achieve from adaptation. Transfusions of packed red cells are indicated only when severe anemia is present and cardiorespiratory failure is imminent. Again, hemoglobin concentration should be brought only to around 10 gm/100 ml.

Infection should be treated vigorously and, if possible, with the help of a laboratory, so that the infective organisms can be isolated and their sensitivity to antibacterial agents determined.

A free airway with adequate lung ventilation is essential. When pneumonia is present, tracheostomy should be undertaken, because it often happens that these subjects are weak and cannot clear their airways satisfactorily.

When severe hepatic failure occurs, it should be treated accordingly, as is done when cardiac failure supervenes. Diarrhea is treated mainly by diet. No anti-cholinergic drugs are used. Another general rule that must be followed is to guard the PCM patient from exposure to cold and hypothermia, as well as from hypoglycemia. During this initial phase of therapy a diet based on high-quality protein, such as milk-casein mixtures (to reduce lactose loads), casein alone, egg or fish protein, is recommended. In children this should provide, during 3 to 4 days, around 1 gm/kg/day of protein and 80 to 100 calories/kg/day, 20 per cent of the calories derived from vegetable fat. From then on, and based on the same ingredients, dietary therapy should be progressively increased to reach, in a 4- to 6-day period, from 3 to 4 gm of protein and from 120 to 180 calories/kg/day, 20 to 30 per cent from a fat source. In adults, calorie intakes at the start may be 50 calories/kg/day to reach, later on, 80 to 100 calories/kg/day.

Vitamins, including folate, should be administered from the beginning, to meet recommended allowances. On admission, the routine administration of a single high dose (20,000 mcg) of water-dispersible vitamin A is recommended to avoid acute eye lesions due to vitamin A deficiency when high calorie and protein diets are initiated. This is followed by a daily dose of 1500 mcg P.O

The diet should also provide from 4 to 5 mEq/kg/day of K, 1 mEq/kg/day of Na, and adequate amounts of magnesium, calcium and phosphorus. Iron, in amounts from 16 to 32 mg, as $FeSO_4$, is routinely administered by mouth as soon as increased protein-calorie intakes are begun, in order to supply the excess requirements of this mineral produced by the rapid increase in total circulating hemoglobin.

With this initial regimen, the severely malnourished subjects begin a smooth recovery: they start to lose edema and to gain in body mass; their general state shows the first signs of improvement and anorexia is replaced by a frankly increased appetite. Then the patient may begin to eat a more varied diet; serum and urine values also start a trend towards normal and the hematological status initiates recovery. All of these changes are accompanied by a clear rise in nitrogen and energy retention. Except for sodium, mineral retention also increases. Rapid changes in weight should be avoided, particularly a rapid loss of edema. Usually, within 2 to 3 weeks of therapy, serum composition returns to normal limits, and consolidation of cure begins.

This second phase of therapy is accomplished only by dietary means. The patients should by then be receiving a complete mixed diet providing the protein and calorie levels reached in the later phase of the initiation of therapy. Progressive physical activity should be encouraged. Complete calorie and protein repletion generally is accomplished in a 6- to 12-week period, depending on the deficits at the start of treatment. Caloric repletion is judged by weight-for-height, and is considered achieved when this index is 0.90 or more. Generally, in non-edematous PCM, normalization of weight-for-height is reached later than normalization of the creatinine/height index. In edematous PCM the opposite occurs. These changes are illustrated in Figures 21–9 and 10.

PREVENTION

Two are the aspects from which prevention can be approached: (1) measures to decrease the risk of individuals reaching severe PCM, and (2) improvement of the general nutritional status of the population, so that even chronic mild-to-moderate PCM cases become rare.

The first aspect of prevention is amenable to some direct actions. These include: (*a*) fostering of maternal lactation and adequate supplementation practices during infancy; (*b*) food supplementation programs of vulnerable groups, such as pregnant and lactat-

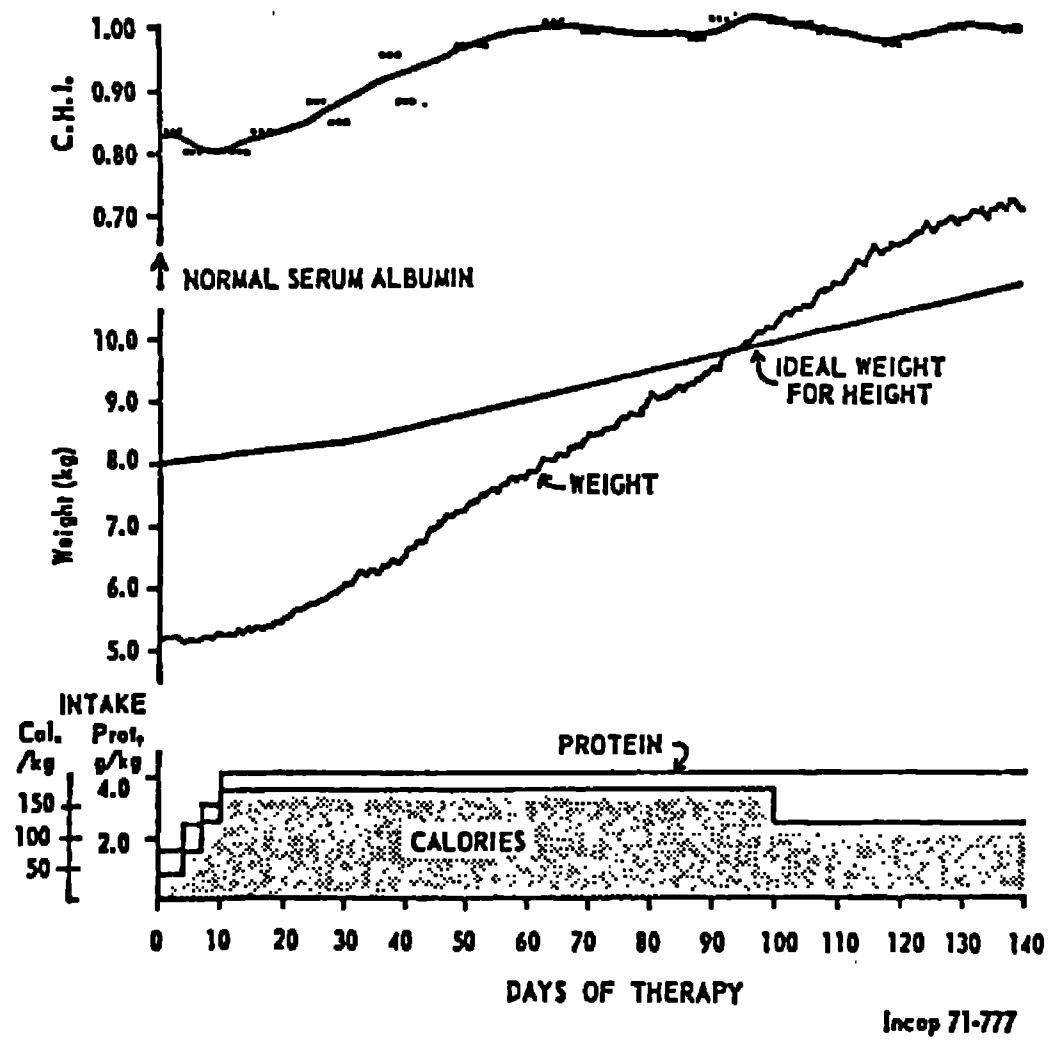

Fig. 21-9. Clinical record of a 16-month-old child during recovery from non-edematous PCM. His lean body mass (CHI) reached normal levels before his weight-for-height was normal.

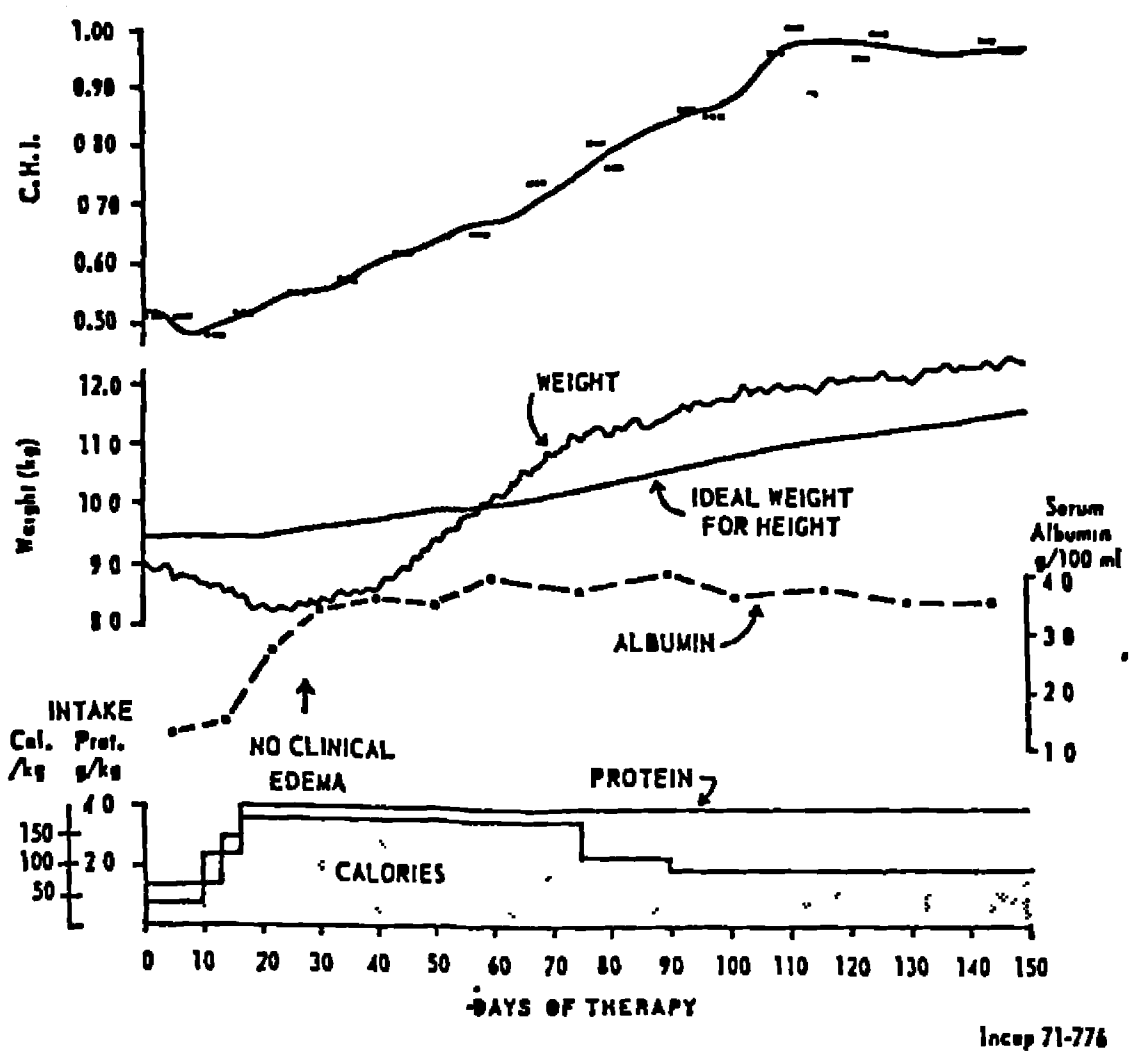

Fig. 21-10. Clinical record of a 20-month-old child during recovery from edematous PCM. His lean body mass (CHI) reached normal levels after his weight-for-height was normal

ing women, children up to school age and above, if possible, and physically hard-working men; (*c*) improvement of sanitary conditions, and (*d*) specific nutrition education. For this last objective, nutrition education and recuperation centers[87] have been instituted in several countries Their main objective is to educate the parents of chronic mild-to-moderate PCM children by having them participate actively in the nutrition rehabilitation of their own children. These centers must be (*a*) located in the community and adapted to the local environment; (*b*) supported by each community; (*c*) children must be rehabilitated by the proper feeding of locally available foods, and (*d*) the mothers must rotate in the care of the children, so as to have direct experience of the benefits that adequate nutrition brings to their children. Experience is accumulating on the effects of these specific preventive measures, indicating that they appear to fulfill their goals

Improvement of the general nutritional status of the population, so that malnutrition is eradicated, requires a complex approach. This is inseparable from the acceleration of socioeconomic development; the actions to bring this about are beyond the scope of this chapter.

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The Etiology of Malnutrition among Preschool Children in Rural Costa Rica*

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Introduction

The major purpose of this research was to define the risk factors for malnutrition in a rural community, utilizing a holistic anthropological approach The functional reason for seeking to define risk factors for malnutrition or any other disease is pragmatic Once the major factors which are associated with the disease are identified, it is then possible to identify that portion of the population which is at greatest risk for contracting the disease With a determination of the population which is at risk, planners may design intervention programs which are targeted specifically at this group Scarce resources, of both material and manpower, may be conserved through directed involvement in programs which will provide the greatest return on invested labor

In the specific case of malnutrition the definition of risk factors serves to identify, on a predictive basis, those children who probably are, or will be, malnourished Paraprofessional personnel may then concentrate their efforts on the families of children determined to be at risk As the definition of risk factors also properly includes an explanatory aspect, the intervention team thus receives some guidance concerning appropriate avenues for intervention Appropriate diet adjustments may be recommended in the light of local deficiencies and available resources, counseling on health care problems, which affect the child's nutritional status, may be conducted where determined to be appropriate, and preventive educational programs may be conducted with those mothers whose children are determined to be at risk for future nutritional distress

The identification of risk factors in a country may be conducted at any one of several levels, national, regional or local It is the basic contention of this approach that the local definition of risk factors may be conducted on a community basis, and then, with proper adjustments, extrapolated to apply to a wider area In this case, the information from the subject community provides an analysis in depth of the sources of nutritional problems, and their range of variation in the community

The research project was an integral part of the pilot program of community medicine in San Ramón, an innovative program which pioneered the involvement of paraprofessional personnel in rural public health programs in Costa Rica The program maintains health posts in each of the rural districts of three cantons San Ramón, Zarcero, and Naranjo with a total population of over 60,000 These are staffed by auxiliary nurses daily and are visited weekly by pediatric residents and general practice doctors; prenatal and family planning clinics are held monthly The direct services are supported by an active health education program, and the overall program coordinates with other governmental ministries, semi-autonomous agencies and volunteer groups to provide an integrated program of health services and general community development

The research was conducted in Concepción de San Ramón, one of the rural districts in the program's area, selected to be as representative as possible in terms of land use, land tenure, and access to services within the range of variation present on the Central Plateau, where most of Costa Rica's population is located The community had a population of 849 in March 1974, 250 of which were children below six years of age The research took the form of a general ethnographic survey which covered a full agricultural year and which focused on agricultural production, food consumption, domestic economics, child-rearing, and the cultural components of diet and nutrition

Material and Methods

All preschool children in the community were weighed and measured in their homes every three months and compared with INCAP standards Utilizing the 24-hour recall method, diet surveys were carried out on a sample of 20 children These were done in January and September, to control for seasonal variations A detailed morbidity survey was conducted during six months of the research period controlling for seasonal variation Two coproparasitological surveys of the children were conducted in January and July 1974

Risk factors related with malnutrition were

* The research described in this report was supported by a grant from the Research Corporation

identified on the basis of their relationship with the nutritional status of specific children based on weight for age data, and on their relationship with households considered to be either "normal" or "deficient". Households classified as normal had all children, or all but one child in normal weight category Deficient households contained children and II and III degree of malnutrition, all below normal, or more than one child below normal Statistical correlations were calculated for a range of elements hypothetically related to nutritional deficiencies Statistical relationships were also confirmed through directed interviewing and participant observation, at the same time establishing the path of relationship through intervening variables.

Results and discussion

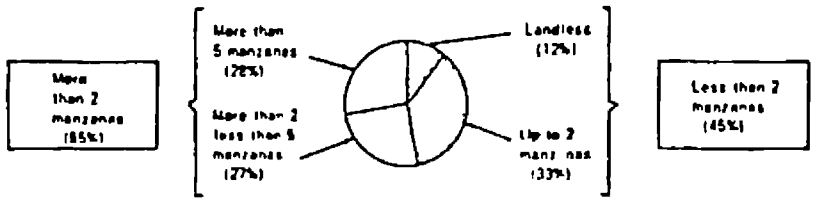
A. Description of the Study Community

The community, composed of descendants of European settlers, is distributed in 157 households, located on or near the unpaved roads which follow the ridgelines running through the district. Almost all households are composed of complete nuclear families, although many of these are clustered in regional concentrations of extended family units Near the middle of the district, the major community services are grouped on either side of the road. these include the church, a health post, and two general store/bars *(pulperias)*, one of which has a dance salon Two schools, providing classes through the sixth grade, are located at opposite ends of the main road through the district

Almost all male residents of the district are farmers, involved in a combination of subsistence and commercial production The major categories of land use are coffee, sugar cane, cattle, and basic staples Very few farmers are dedicated exclusively to one form of use or the other, but rather attempt to have diversified holdings within the limits of available land

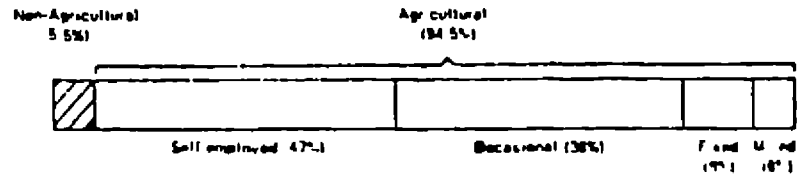
As shown in Figure 1, land holdings are small, with 45% of the farmers having access to less than 2 manzanas of land (1 manzana = 7 hectares)

Figure 1
Land Access by Household,
Concepcion de San Ramon, 1974



Almost all household heads are agriculturalists Of these, less than half have enough land and other resources to be completely self sufficient, and the others must seek income through agricultural labor either on a part time or full time basis Figure 2 presents the occupational activities of household heads

Figure 2
Occupation of Household Heads in
Concepción de San Ramón, 1974



Labor opportunities are rare, with seasonal variations, and wages are low Only 19 men in the district have year round fixed employment, and the others who seek employment are able to obtain it only occasionally. Women contribute to the household economy through participation in the coffee harvest or by making and selling small hand-rolled cigars *(puros)*.

B. Nutritional Status of Children

The anthropometric data indicate that the nutritional deficiencies of the children are moderate, but chronic The children of the community showed the following distribution according to Gomez's classification

Table 1

Nutritional Status of Pre-school Children Using Gomez Weight-for-age-categories in Concepción de San Ramón, 1974

	Normal	First Degree	Second and Third Degrees	Total
Number of Cases	62	79	16	157
Percent	40%	50%	10%	100%

Only two children were in the III° category, and 10% of them appear below 75% of standard weight However, almost half of the children are midly deficient in weight for age

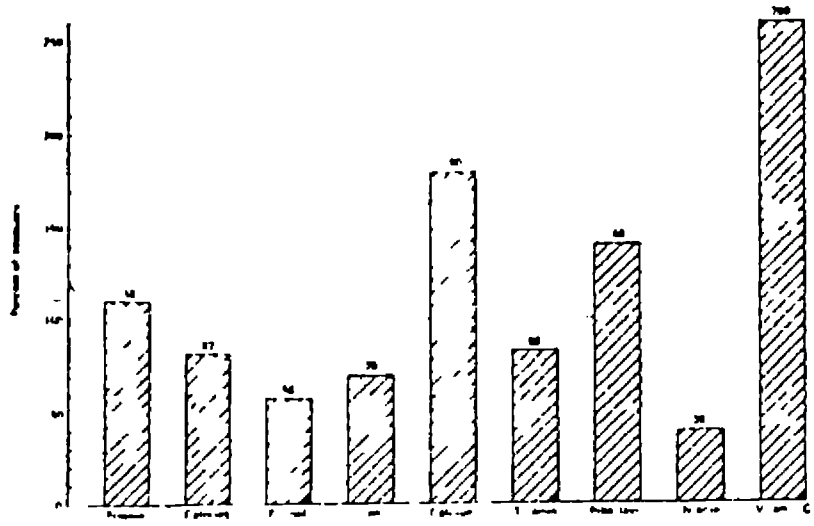
Weight deficiencies show a secular tendency to increase with age Most of the children in II° and III° are in their fourth or fifth year of life, and the deficiency is mild but cumulative Most of these children, viewed in terms of weight for height, have normal proportions, with both anthropometric parameters reduced equally This stunting is not considered to be susceptible to clinical intervention in the later preschool years

A detailed analysis of the anthropometric data from a sample of children in the rural areas and the urban center of San Ramón confirms the indications from the subject community, with the added perception that rural children are measurably more nutritionally deficient than their urban peers (Valverde and Rawson, 1975) These data indicate that while the nutritional deficiencies of rural Costa Rican children are moderate, they fulfil far less of their physiological potential than do urban children

C. Children's Diets

The results indicate that the major dietary deficiency is caloric, with other nutrients deficient as well

Figure 3
Percent of Adequacy of Diet Nutrients in Children 0-6 Years
Concepción de San Ramon, August 1974



The adequacy of children's diets in protein intake is due primarily to general access to local sources of fresh cow's milk, eggs, and vegetable protein (beans/rice, beans/corn mixes) The source of caloric inadequacy appears in many cases to be a quantitative deficiency in the diets, or an over dependence upon milk as a dietary staple among younger children (1-4 years) The comparative study cited above (Valverde and Rawson, 1975) also indicates a contrast in diet adequacy between rural and urban children, with urban children generally receiving adequate amounts of both proteins and calories

D Morbidity

The morbidity information indicates that upper respiratory and gastrointestinal infections are very common among children in this area The average child reported 47 sick-days of upper respiratory infections and 40 days of gastrointestinal illnesses per year

In January 1974, 83% of the children were infected with some sort of intestinal parasite, and in July the rate was 72% This is despite the presence of running water and latrines in all households in the district The most common parasites encountered were Ascaris and Tricocephalus, followed by Giardia Lamblia Three children had hookworm

E. Factors Associated with Malnutrition

Forty households and forty one were classified as normal and deficient respectively Nutritional status was associated with land tenure, number of siblings 0 6 years of age, occupation and education of parents, level of living code ownership of house and house plot, type of family unit, intergestational period, age at weaning, sex of child, and salary income Certain of these showed a positive association and others showed none A summary is presented in Table 2

As noted in Figure 1, almost half of the households have access to less than 2 manzanas of land This extension is frequently cited by residents as being the minimum required to guarantee self sufficiency *(para defenderse)*, but probably not sufficient to fulfil

Table II

Factors Statistically Related to Nutritional Status in Concepcion de San Ramón

Factors Associated with Nutritional Status	X^2	Significant at less than*
Access to land (0-1 9 manzanas/2 or - more manzanas)	5 20	025
Number of Siblings 0 6 years (0-1/2 4)	20 89	.005
Occupation — Father (self employed/other)	17 88	005
Occupation — Mother (in home/out)	7 82	005
House Code (to 2 5/2 6 or higher)	6 09	025
Type of Stove (good/poor)	19 38	005
Ownership of House (owned/not)	15 59	005
Access to Fresh Milk– (yes/no)	19 97	005

Factors Found Not to be Associated with Nutritional Status	Significant at:
Education — Mother (0 3/4 or more years)	10
Education — Father (0 3/4 or more years)	10
House Ownership (owned/not)	NS
Type of Family Unit (unclear/other)	NS
Sex of Child (male/female)	NS
Intergestational Period (less than 18 mo /18 mo or more)	NS
Age at Weaning (less than 6 mo /6 mo or more)	10
Salary Income	NS

suggested adequate living conditions of living (Schatan, 1974) This narrative information is supported by statistical analysis, children in households with less than 2 manzanas of land have a greater tendency to be below normal in weight for age ($P < 025$) A direct causal chain probably does not exist between land tenure and nutritional status However, the former affects intervening variables which in turn affect the nutritional status of children.

1 Intervening Variables

(a) Labor — Father

A household head with access to less than 2 manzanas has insufficient resources with which to support his family, he must work as a day laborer outside the household In this area, permanent labor opportunities are rare (9% of household heads are so employed) Labor opportunities are also irregular, and must be confirmed weekly or daily The salaries are low, approximately $200 colones per month ($23 dollars) This income barely supports a family of five, the mean family size in the community. From a study

on income and cost of minimum cost diets in Costa Rica (Valverde, 1975) it is estimated that a family income of ₡372 per month ($43 dollars) at 1972 prices is necessary to fulfil only food needs for a family of five It does not take into account other expenses such as housing, clothing etc

(b) Labor — mother

Most mothers in households with less than two manzanas must work outside the home also Most commonly, this means picking coffee (42% of the mothers who work do this), or rolling cigars Pay for picking coffee is good, and despite the long hours, is not unusually physically demanding However, the local coffee season lasts only four months Major purchases are put off until coffee season, and thus few families are able to save from that period to insure cash resources in other seasons In the rainy season, many mothers and other family members roll cigars The pay for this is low ($1 50 — $2 00 per week), but the work may be done at home, and combined with other domestic activities A relationship is shown between mother's labor and the nutritional status of her children, as well as with land access In a household with access to less than two manzanas, the mother is more apt to seek labor opportunities outside the home such as picking coffee, and mothers who do so tend to have children with below-normal weights

(c) Ownership of House Plot

Out of all the houses in the district, 35% of them are placed on land which is borrowed or rented Most of these houses are of simple frame construction, and may be taken down and moved As the house owner does not have the title to the lot, the insecurity of his tenure discourages investment in maintenance and improvements Such houses also tend to have dirt floors and other elements which qualify the residence as being substandard A level of living code, developed to evaluate the quality of housing in terms of construction and maintenance, indicates a lower rating for houses which are on borrowed or rented land than for houses which are on land which is owned by the resident

2 *Subsequent Effects of Intervening Variables*

(a) A father who works as a day laborer does not have either the time or the resources to maintain a source of subsistence foods (the major requirements being land, labor time and fertilizers and sprays) As a result, his family subsists on a cash economy, purchasing foodstuffs with scarce economic resources

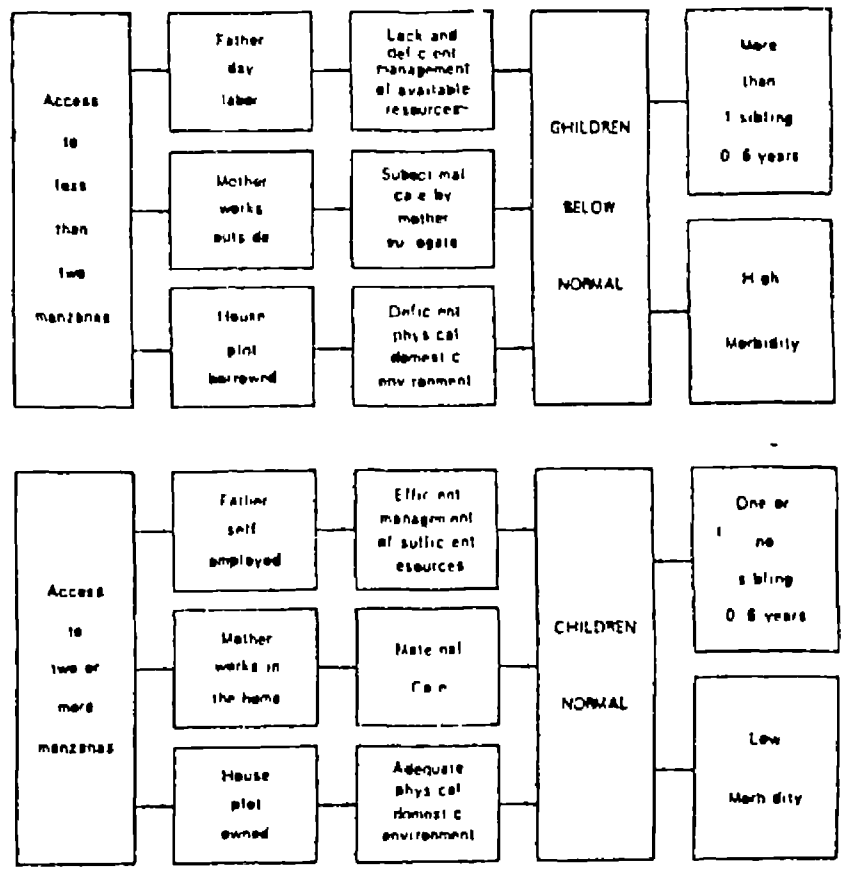
(b) Mothers who work outside the home must leave their preschool children in the care of an older sibling During coffee season for instance, children in such households receive suboptimal care from their mother surrogates who lack proper training or motivation to fulfil their role for as long as four months The problem of stimulus deficiency, both aural or visual, which is general in this area, is heightened in these households, contributing another negative element to the microenvironment of growth and development of the children

(c) The level of living code indicated that a poorly built and badly maintained house logically provides more sources of infection, which affect the physiological balance of resident children As a methodological footnote, a useful device emerged from the use of the house code the type of stove in the house served as a significant predictor of nutritional status, and as an indicator of the house code A final, statistically firm, relationship is shown between the stove type and nutritional status Therefore, a short cut may be used in predicting nutritional status of children by evaluating the stove type, obviating the need for the full house survey

The effects of these variables, and their interrelationships may be seen more clearly in graphic representation in Figure 4.

Figure 4

Identified Risk Factors for Malnutrition and Their Interrelationships in Concepción de San Ramon, 1974



3 *Anomolous Cases*

Land tenure may be seen to be a primary variable which affects, through other related factors, the nutritional status of children The statistical association between land tenure and nutritional status ($P < .025$) may be seen to be strengthened when the anomolous situations are analyzed, i e , the cases seen to be "deficient" in households with more than 2 manzanas, and those termed "normal" with less than 2 manzanas

(a) "Deficient", with Sufficient Land

There was a total of eleven cases In five of them, the domestic environment of the children is visibly deficient, the houses are dirty, and the children

themselves are usually unclean and not cared for In one of these five the house was inherited, and although it is well built it is poorly maintained, and a worse environment than that of others which are less well constructed Other factors contribute to a deficient microenvironment in several of these houses In one the mother is frequently absent, leaving the children to be cared for by an older sister, who is poorly motivated to care for the children In another, domestic problems generated by a husband who is open about his extra marital alliances, contribute to deficient care In a third home, the mother is frank in admitting that caring for four preschool and four school aged children makes excessive demands on her time and resources

In two cases, the deficient children are four or five years old and are in I° weight category, probably the result of a moderate but cumulative nutritional insult. One of the other children is reported in II°, but was in the process of recovering from a low birth weight At the end of this study the child had attained a normal weight

It is probable that the problems of the remaining two cases may be traced to maternal care In one instance, the mother fusses over her late born son, bringing him often to the health post because he is not eating well The other child has frank psychological problems, diagnosed by the psychiatric resident at the San Ramón hospital The mother reports that she suffered a "susto" (she was frightened by a white horse) while pregnant with the child and that the child was born abnormal The psychiatrist feels that the mother rejected the child in infancy, and he is now withdrawn, spending as much time as possible with his father He may be rejecting food an an indirect form of revenge against his mother who prepares it

(b) "Normal" but with Less Than 2 Manzanas

Of the 19 households in this category, three are represented by three-generation households, in which unmarried mothers live with their parents, they themselves have no land resources, but are supported by their natal households

Ten of these cases are relatively young couples who are living on land lent to them by the parents of one spouse usually the husband They are at a semi-independent stage of the development cycle, in which they have no direct access to land, but probably will inherit at least 2 manzanas Meanwhile they are permitted to work land owned by their parents and keep most of the profits from this These households perhaps might be classified in the category of access to 2 manzanas or more but their right of access is unclear, as is the extent of land to which they have rights Three other families are more dependent upon the parents of the husband or wife, living in houses set up in the same *patio* These share in the labor and production of family lands either on a wage basis or on the basis of proportion of work contributed While they have no direct access to land, their indirect access appears to be sufficient to provide an adequate diet for their children

Of the other three cases, one owns a pulperia, which provides adequate income for his family's needs In the other two, the household heads have fixed agricultural employment, guaranteeing a year-round income, the men are well respected as laborers, and are relatively well paid

In eight of the households mentioned above, the wives work during coffee season, picking coffee for others However, in all but one case, this involves harvesting coffee which belongs either to their parents or to those of their spouse This, therefore, indicates either wage income, or possibly sharing in the income from harvest production

4 Other Factors Related to Nutritional Status

(a) If a child has more than one sibling of preschool age, the child has a statistically greater chance of being below normal in weight for age The same relationship does not exist between nutritional status and intergestational period to the next youngest child The latter factor is related to nutritional status in other places, notably Haiti, where short intergestational periods are associated with precipitate weaning (Webb, Ballweg & Fougere, 1973) Breast feeding is neither common nor extended in rural Costa Rica, and the availability of fresh milk provides a protective element A mother with more than two preschool children to care for does not have the time nor the resources to properly care for them all This may be noted both by observation and through the observation of the mother herself As a result, either sub-optimal care is general for all children, or one child receives, by maternal preference, deficient care and stimulus Both of these patterns were noted in the study

(b) Many mothers, particularly those with many demands on their time, prepare bottles of milk for their children For many children, even up to the ages of three and four years, these bottles of milk provide the major portion of the volume of their diet In addition to the risk of infection from poor sanitary habits from prolonged contact with the nipple, the use of the bottle is frequently related to a lack of interest on the child's part in solid foods, heightening the protein/calorie imbalance noted earlier

(c) 37% of the households in the community have at least one cow Most who do, have only one or two cows, which produce milk for domestic consumption Some families sell bottles of milk on a contract basis to neighbors or family members During the dry months, production of milk is reduced, and families with neither a cow nor a contract have no access to fresh milk Ownership of a cow involves an initial investment and sufficient land for pastures, contract purchases require a year round cash availability, neither of which is generally available to households with limited access to land

(d) The acquisition of foodstuffs involves a

combination of production and purchase, all nuclear families purchase at least part of their food, especially prepared foods Foods may be purchased in the community's general stores where selection is limited and prices are high, or they may be purchased in San Ramón, where the advantages of selection and price are offset by the difficulty of access due to distance (5 kilometres) and limited means of transportation

Families with limited land resources must purchase more of their food needs than do families who have sufficient land to produce annual food requirements These families usually also have limited cash availability The problem of insufficient home-produced food is compounded by the lack of cash for food purchases and the problems, through distance and transportation costs, of access to less expensive food sources Credit for food purchases is available only at the local general stores, so those who must buy on credit are restricted to those sources with higher prices and limited variety Thus the quality of food available to land-poor families is restricted directly through limited production of staples, and indirectly through limited labor opportunities, reduced cash income and problems of food purchasing

(e) Infection Disease and Nutrition

The average preschool child reported 47 days of upper respiratory infections and 40 days of gastrointestinal illnesses per year, a feedback loop was identified in the comparison of weight gain or loss and morbidity during specific periods A high rate of parasitic infection was noted among preschool children

F. Some Factors Not Associated With Nutritional Status

1 Type of Family

Nutritional status does not seem to be related to the type of family of the subject child, most families are complete nuclear units, and those which are not do not seem to generate nutritional deficiencies For example, four mothers in the community are unmarried, all live in three-generation households, and all have children who are of normal weight

2 Parents' Schooling

Even though 75% of the fathers and 60% of the mothers in the community did not go beyond the third grade in school, most are functionally literate In addition, a high level of awareness of the nutrient qualities of specific foodstuffs is noted among mothers The educational level of neither parent is significantly related to nutritional status

3 Age at Weaning

Few mothers breast feed their children for more than two or three weeks The length of time children receive breast milk is not related to their nutritional status A weak ($P \leq .10$) relationship is seen, but this may not be reflecting the direct nutritional benefits of breast milk as much as the level of attention and care given by the mother to the child

4 Sex of the Child

The sex of the child is not a strong indicator of nutritional status, both boys and girls have an equal opportunity of being either well or poorly nourished These data provide an interesting contrast to indications in other countries, where cultural preferences result in the generally better nutritional status of male children

5 Salary Income

Salary income has been related to nutritional status in other etiological studies, specifically in India and Barbados (PAHO 1972, Grewal *et al*, 1973) In the agricultural regions of Costa Rica, where almost half of the farmers are self-employed, an estimated conversion from agricultural production to salary income is difficult to perform accurately For those who are employed, salaries are low, and the mere fact that they must work as day laborers is related to both land tenure and to the nutritional status of their children, as noted earlier Within the salaried group, the range of variation is so limited that a division of the group for analytical purpose is not possible.

Summary

In the present study, access to land appears to be the primary variable affecting nutritional status, although it operates indirectly in this relationship Households with access to less than two manzanas of land usually have fathers who work as day laborers, working mothers, and an identifiably deficient physical domestic environment All of these factors affect negatively the nutritional status of children in households, through inadequate resource availability and management, suboptimal domestic care, and a heightened risk for infection and disease Additionally, children with more than one preschool sibling were found to be at greater risk for nutritional deficiency, although access to land was not related to the number of children 0-6 years of age in the household

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Chapter 24

PROTEIN-CALORIE MALNUTRITION*

Fernando E. Viteri
and
Benjamin Torún

Large segments of the world's population live under conditions where the availability and intake of food are inadequate for their needs.[1] This is the case in many developing areas where food consumption is deficient both in quantity and quality. Insufficient food intake leads to chronic caloric deficiency, and ingestion of foods with insufficient protein concentration induces protein deficiency in vulnerable groups. This is particularly true when the protein is of poor quality, as is the case with most vegetable proteins. The problem with the latter is that the bulk of the food often imposes a limit to its intake. Also, amino acid deficiencies further limit the utilization of such protein sources, so that small children cannot satisfy their naturally elevated nitrogen and specific amino acid requirements.

These dietary factors, associated with many other health problems to be described later, lead to primary chronic protein-calorie malnutrition (PCM). In conditions conducive to primary PCM, the intakes of other essential nutrients, such as vitamins and minerals, are also generally low; however, serious manifestations of their specific clinical deficiencies are less common than might be expected because, when the calorie and protein intake is the limiting factor, the requirements for other nutrients diminish. Nevertheless, in PCM, vitamin or mineral deficiencies may become overt.

Primary PCM should be differentiated from secondary PCM, which is the consequence of a primary disease that leads either to inadequate food intake or utilization or to increased nutritional requirements. Examples of secondary PCM are psychologic disorders, obstructive gastrointestinal lesions, primary malabsorptive problems, diseases inducing cachexia of metabolic, infectious or neoplastic origin and endocrine disorders.

This chapter deals only with primary PCM, that is, the situation where energy and protein intake are apparently the most limiting factors in malnutrition.

EPIDEMIOLOGIC AND ETIOLOGIC CONSIDERATIONS

All developing areas of the world have several common characteristics, among which are low weight of newborn babies, high disease prevalence, small physical size of inhabitants, elevated mortality rates,

*Scientific articles published on this subject are much more numerous than those cited in the present chapter. However, because of limited space, the reader is often referred to some comprehensive reviews on the subject. Publications cited at the beginning or at the end of paragraphs or sections are general references for the topic dealt with. Through these, as well as through the more recent specific articles cited, many other important references may be easily located by those interested in a deeper approach to the subject.

Table 24–1. Mortality Rates of Children 0-4 Years of Age*

Age	*Guatemala (1965)*	*%*	*U S A (1967)*	*%*	*Ratio Guatemala/U S A*
	A Infant mortality (deaths/1000 live births)				
0–28 days	35 9	39 1	16 6	73 8	2 2
1–11 months	55 9	60 9	5 9	26 2	9 5
1 year	91 8	100 0	22 5	100 0	4 1
	B Mortality in children between 1 and 4 years of age (deaths/1000 children of the corresponding age)				
1 year	50 0		1 4		35 7
2 years	35 2		0 9		39 1
3 years	24 9		0 7		35 6
4 years	15 6		0 6		26 0
1–4 years	30 3		0 9		33 7

* Compounded from data published by the Pan American Health Organization *Las Condiciones de Salud en las Américas 1965–1968* Washington, Organización Panamericana de la Salud, Septiembre 1970 (Publicación Científica No 207), and INCAP [3]

particularly during infancy and early childhood (Table 24–1) and, as a consequence, short life expectancy The main reasons for these characteristics are undernutrition and poor environmental health These situations lead to decreased productivity and increased waste of human and economic capital, including food This perpetuates and often aggravates underdevelopment, thus worsening nutrition and health and, therefore, establishing a vicious cycle This general picture, associated with a large concentration of still unproductive young people, provides the background for underdevelopment

The magnitude of the problem varies from area to area As an example, we cite the figures obtained from a survey of the Central American region where, by projecting to the total population of the area the prevalence obtained from a statistically representative sample of all of the 2 5 million children below 5 years of age, 1.6 million could be categorized, on the basis of body weight, as suffering from or as having had undernutrition Nearly one-third of them had been or were moderately or severely malnourished (second- and third-degree undernutrition) at the time of the survey.[3] These findings are presented in Table 24–2.

Mild and moderate forms of adult undernutrition are more difficult to recognize but are also prevalent in developing areas The manifestations of chronic PCM in this age group are more evident in terms of performance than in symptoms or clinical signs.

In adult males engaged in agricultural practices requiring intensive physical effort, caloric intake is often insufficient and leads to chronically limited energy expenditure in order to maintain a delicate energy balance. This results in suboptimal work performance, inadequate interactions with other family members or poor participation in community programs after working hours In adult women, chronic undernutrition results in inadequate reproductive performance, which includes little weight gain during pregnancy, delivery of small-for-date babies and inadequate milk production in terms of both quantity and quality.[5,6]

A high proportion of newbc with low weight at birth is associated with a higher incidence of infant mortality [7] Inadequate quantity and quality of woman's milk in groups of low socioeconomic condition are important factors in infant malnutrition

Protein-calorie malnutrition should then be considered a social disease affecting

Table 24–2. Children Below 5 Years of Age in Central America, 1965–67, Presenting Growth Retardation which, by the Gómez* Classification, Could be Cataloged as Malnourished†

Country	Total Population below 5 Years of Age	1st, 2nd, and 3rd Degree Malnourished		Malnourished					
				1st Degree		2nd Degree		3rd Degree	
		No of Cases	%	No of Cases	%	No of Cases	%	No of Cases	%
Costa Rica	294,300	153,200	52 0	117,900	40 0	31,300	10 6	4,000	1 4
El Salvador	554,400	380,000	68 5	244,600	44 1	116,900	21 1	18,500	3 3
Guatemala	833,400	611,660	73 4	380,100	45 6	197,700	23 7	33,860	4 1
Honduras	346,900	221,300	63 7	143,000	41 2	71,200	20 5	7,100	2 0
Nicaragua	287,500	148,800	51 8	112,300	39 1	32,400	11 3	4,100	1 4
Panama	207,900	104,947	50 4	84,625	40 7	18,990	9 1	1,332	0 6
Total	2,524,400	1,619,907	64 2	1,082,525	42 9	468,490	18 6	68,892	2 7

* Gómez, et al [2]

† Numbers are extrapolations from a statistically representative sample

families, communities and geographic areas because of the negative effects that mild-to-moderate PCM of adults has on the well-being of the children and the development of the community.

In these settings, the few subjects who develop severe PCM with clinical manifestations must be interpreted as index cases which point at a widespread underlying nutritional problem Thus, the fact that over 8 per cent of all adults admitted to public hospitals in countries such as Guatemala have moderate-to-severe primary PCM strengthens the concept that the poor functional performance of underprivileged populations is closely related to underlying mild-to-moderate PCM

From the epidemiologic point of view, PCM can be conceived as the consequence of the interaction of the environment on the host through an agent which, in this case, is the deficient availability of calories and protein at the cell level The environment, host and agent factors are interwoven

Environment

This can be considered at two levels (1) macroenvironment, at a regional or national level and (2) microenvironment, at the family and individual level

In the developing areas, the macroenvironment is that of poverty, not only in the strict economic sense but also in the more important concept of human resources Both are the cause and the consequence of lack of education, unsatisfactory health of the population, poor communications, low productivity, unfavorable economic balance and inadequate utilization of natural resources; all of these factors lead to inadequate food production, conservation, distribution and consumption

The microenvironment constituted by the family, which is the biologic unit in terms of nutrition, receives the impact of the macroenvironment and further limits the availability of nutrients to the host The factors operating at this level are meager purchasing power, faulty concepts of food utilization that lead to poor food consumption practices and inadequate distribution of available nutrients among the members of the family. The latter is particularly evident in the case of small children and when disease strikes a member of the family whose food intake is very often thereby drastically restricted

Host and Agent

Maternal malnutrition and infectious episodes during pregnancy are frequently the cause of prematurity and small born-at-term infants, as well as of poor nursing performance Children already at a nutritional disadvantage are the victims of poor feeding practices, especially in those regions where breast-feeding is being replaced early in life by artificial formulas in the face of prevailing inadequate education, hygiene and economic resources. All of these factors must be adequate to allow successful artificial feeding

Inadequate feeding takes place at a time when nutritional requirements are high per unit of body weight The consequence is an increasing number of infants who suffer from early protein-calorie malnutrition, particularly in urban areas The most common type of severe malnutrition at this age is that of nonedematous PCM, due to a predominant caloric deficiency [9]

Even when properly breast-fed, complementary feeding practices for the child are poor, and induce some degree of PCM after the first 3 or 4 months of life When weaning occurs, most children are fed diets that provide insufficient amounts of calories and proteins Others receive only starchy gruels or high-carbohydrate low-protein diluted cereal drinks, which accentuate protein deficiency Table 24–3 presents the median nutrient intake of rural Central American children, expressed as per cent of the recommended allowances for each age group

It is important to realize that, in the developing areas, children are smaller in size than those of the same age in the developed areas, consequently, their actual requirements are somewhat reduced Nonetheless, a decreased food intake for age, even when it could be fairly satisfactory for size, perpetuates undernutrition If, at this time, the child is forced-fed diets high in calories but low in protein, he becomes acutely protein-deficient in spite of being fat This severe protein deficiency gives rise to edematous PCM of the "sugar-baby" type [10] More often, infants become the victims of mild-to-moderate repeated infections[11] and, by the time they are weaned, develop a common diarrhea syndrome known as "weanling diarrhea "[12]

After weaning, children eat little or no milk and other animal products and they are fed the usual family foods, frequently in insufficient amounts, because of poor availability of food and incorrect cultural practices in child feeding Also, after weaning, children living in these environments frequently suffer from acute infections As a consequence, their nutritional condition rapidly deteriorates Those children who prior to weaning were growing at a slower rate and very often were somewhat underweight for their height become frankly

Table 24–3. Median Nutrient Intake as Per Cent of Recommended Allowances of Nutrients Consumed by Preschool Children in the Rural Area of Guatemala*†

	Age Groups (years)			
Nutrients	*1 (38)‡*	*2 (43)*	*3 (34)*	*4–5 (14)*
Calories	63	66	80	48
Proteins	79	74	108	67
Calcium	72	69	101	72
Iron	56	71	103	66
Vitamin A¶	24	30	25	20
Thiamin	100	92	128	68
Riboflavin	50	46	50	31
Niacin	42	50	68	39
Vitamin C	40	60	56	20

* Over 90 per cent of preschool children consumed less calories and over 60 per cent consumed less protein than the recommended allowances The calories and protein consumption was lower than recommended in 80 per cent and 40 per cent of the families, respectively

† Modified from Flores, Menchú, Lara, and Guzmán Arch Latinoam Nutr , *20*, 41, 1970

‡ Figures in parentheses represent the number of children

¶ Vitamin A intake has improved, especially in the older preschoolers, since sugar fortification with this vitamin was begun in 1976

undernourished. Those who follow this path develop the edematous type of PCM, but at the same time are somewhat emaciated. They suffer from a predominant protein deficiency, superimposed on various degrees of caloric deficit.

The majority of children, however, do not develop a severe degree of PCM and, through a series of adaptive mechanisms, remain in a state of mild-to-moderate protein-calorie malnutrition. This condition is characterized only by growth retardation and by periods wherein they have a mild weight-for-height deficit, with or without traces of edema. Children who survive the critical weaning and preschool periods continue to grow at a slower rate and their calorie and protein requirements per unit of body mass rapidly decrease. Their daily diets continue to be low in both calories and protein, but they usually can procure more food and often have already had most of the common childhood infectious diseases. Thus, these children can progress into adulthood without further serious risks of becoming severely undernourished. However, if a severe infection or diarrhea supervenes, they can still develop severe PCM, regardless of age. Among the common childhood infections, measles and whooping cough are well known to precipitate severe protein-calorie malnutrition. In children and adults, repeated acute diarrheal episodes, chronic malaria, schistosomiasis and massive infestations by hookworm, Trichiuris trichiura or Strongyloides, plus other stresses such as acute food shortage and severe physical or psychologic stresses, can induce severe PCM.

PHYSIOPATHOLOGY AND ADAPTIVE RESPONSES IN CALORIE AND IN PROTEIN DEFICIENCY

Through a series of physiologic mechanisms, the body tends to maintain a dynamic equilibrium. A typical example is the tendency toward caloric equilibrium: After the ingestion of a meal energy is stored, mostly in the form of high-energy phosphates, fat and glycogen, which are drawn upon to obtain energy during the daily regular and relatively short periods of fasting and during periods of increased energy expenditure.

With longer periods of calorie and/or protein restriction, the body progressively adapts itself in order to maintain as adequate a functional status as the limited supply of nutrients allows. Consequently, in the process leading to PCM, the body is dynamically adapting to it and continues to do so throughout, until the individual is "maximally adapted." This adaptation results in a decreased nutrient demand and in the attainment of nutritional equilibrium compatible with a lower level of cellular nutrient availability. If, at this point, the supply of nutrients becomes persistently lower than that to which the body can adapt, death supervenes. However, although in most instances the nutrient supply is low, it is not so inadequate as to cause death and the individual is thus able to live in a state adapted to the diminished intake. In this process, most functions are altered and have the following characteristics: (1) They are more susceptible to being overwhelmed by an overloading mechanism, which brings about decompensation or failure of adaptation and consequently poses a threat to the life of the host. In other words, the adapted PCM individual is a labile, functionally fragile subject. (2) Because of their dynamic nature, the degree of functional alteration generally correlates with the degree of protein depletion. This correlation is also influenced by the rate at which depletion occurs, or at which repletion takes place during nutritional rehabilitation.[13]

The adaptive metabolic processes in both calorie and protein malnutrition occur by hormonal interaction, by servomechanisms at the cellular level and by as yet poorly understood generalized body reactions. Briefly, calorie deficit induces the hormonal adaptations described in

Table 24–4. Schematic Hormonal Adaptive Mechanisms in Malnutrition

			Hormonal Activities in	
Hormone	*Stimulus*	*Result*	*Calorie Deprivation*	*Protein-calorie Deprivation*
Insulin	↑ Glucose ↑ amino acids	↑ Protein synthesis (muscle) ↑ Growth ↑ Lipogenesis	Decreased	Decreased
Growth hormone	↓ Glucose ↑ amino acids	↑ Protein synthesis (body) ↑ Growth ↑ Lipolysis ↓ Urea synthesis	Variable, generally normal	Increased
Glucocorticoids	↓ Glucose ↓ amino acids	↑ Protein catabolism (muscle) ↑ Protein turnover (viscera) ↑ Neoglucogenesis ↑ Lipolysis	Increased	Variable, generally normal
Thyroid hormones	↑ Energy metabolism	Energy homeostasis ↑ Protein turnover	Decreased	Decreased

Table 24–4, which lead to increased fat mobilization from adipose tissue

During the initial phases of deficiency, the individual shows decreased physical activity and a lower basal energy expenditure per unit of lean body mass The body composition is progressively altered by decreasing adiposity at a fast rate and lean body mass at a slower rate Muscle catabolism produces an increased efflux of amino acids, primarily as alanine. As the caloric deficit becomes severe, basal energy expenditure may be normal or even increased per unit of lean body mass, which then decreases at a faster rate [13–15]

Protein deficit usually occurs together with caloric inadequacy and the hormonal changes are generally similar to those observed in caloric deprivation; often, fasting circulating growth hormone levels are higher in protein deprivation than in caloric deficit[16,17] and glucocorticoids are not increased in the former, although free cortisol is higher than normal, resulting in functional hypercorticism[18] (Table 24–4) Somatomedin levels are low in PCM, especially in cases with severe protein deficiency [19] In protein deficit there are also cellular adaptation mechanisms not directly hormonally mediated but induced by the poor availability of amino acids, causing decreased protein synthesis at the ribosomal level The result of both mechanisms of adaptation are an internal shift in protein metabolism to an increase in muscle protein catabolism and, therefore, a relative increase in amino acid availability at the visceral level The composition of the free amino acid pool is altered. There is a decrease in both the synthesis and the catabolism of total body proteins, the latter predominating over the former

The most significant change in protein metabolism is a marked recycling of amino acids The end-result is a longer half-life of some proteins, such as albumin, and a generally decreased protein and amino acid turnover In addition, the internal body distribution of protein changes This is the case with albumin, which diminishes more in the extravascular than in the intravascular space Urea synthesis de-

creases and simple nitrogen-containing compounds, such as urea, apparently are more efficiently utilized as sources of nitrogen. In terms of body composition, a progressive reduction in lean body mass occurs, resulting primarily from muscle, and probably also from skin, protein loss Visceral protein is initially reduced ("labile protein") but then becomes stable or may even regain some of its total mass As the body protein turnover and total body protein mass decrease, basal oxygen consumption also decreases [13,20,21]

These adaptations, which lead to the sparing of body protein, are easily upset by forced calorie intake, primarily in the form of carbohydrates such as starch gruels Hormonal adaptation mechanisms are "fooled" and, as a consequence, internal amino acid and protein shifts are impaired, thus inducing visceral amino acid depletion and a breakdown of adaptation Infections leading to disease and other stresses also upset adaptation by causing anorexia and markedly reduced food intake in the face of increased energy and protein needs. Fever increases energy waste and is accompanied by large nitrogen losses and shifts toward amino acid utilization for energy purposes Amino acid utilization is also diverted for increased synthesis of special proteins, such as gamma globulins (antibodies).[22,23] This probably also reflects a breakdown of the amino acid-sparing adaptive mechanisms described

An important finding in most investigations of the hormonal status in PCM is that hypophyseal functional capacity is unimpaired Another important concept must be kept in mind in explaining metabolic adaptations: Hormonal effects may not be wholly explained by circulating levels of hormones and metabolites Cellular responses to hormonal stimulation, as well as hormonal metabolism, may be markedly altered in PCM

When the adaptive mechanisms are maintained, the impact of PCM is diminished and the length of time that an individual takes to go from mild to severe protein-calorie malnutrition is prolonged Of course, the individual has to sacrifice certain functions and some nutrient reserves and, for this reason, becomes more susceptible to injuries which a well-nourished individual can withstand with little repercussion Total body K content is reduced [24–26] Total circulating hemoglobin is reduced pari passu with decreased body oxygen demands Red cell production is diminished and hemodilution takes place.[13,14,27] Cardiac work decreases, as does functional reserve,[28] and central circulation takes precedence over peripheral circulation Cardiovascular reflexes are altered, leading to postural hypotension and diminished venous return Hemodynamic compensation in severe PCM occurs primarily from tachycardia rather than from increased stroke volume The renal plasma flow, glomerular filtration rate and tubular function decrease As a consequence, in severe cases, the renal concentrating ability and acidification mechanisms are impaired [29] Before this occurs, chronic sodium retention and increased serum and urine antidiuretic activities lead to relatively increased total and extracellular body water [30] Intracellular water is reduced in absolute terms because of losses in lean body mass, but intracellular overhydration may be present [24,26,31] Physical strength is diminished, further inducing a reduction in the physical working capacity [32,33]

Other alterations not directly correlated with the degree of protein deficit, but always present in advanced protein deficiency, include impaired intestinal absorption, moderately decreased capacity to transport protein-bound substances in blood, reduced gonadal function and lowered resistance to infection The immune systems affected in severe PCM include those mediated by cells antibodies, phagocytes, complement and other nonspecific factors including lysozyme.[34] Moderate

PCM and fetal malnutrition, as well as other specific nutrient deficiencies, appear to have profound effects on cell-mediated immunity

Impaired intestinal absorption of lipids and disaccharides and a decreased rate of glucose absorption occur in severe protein deficiency, the greater the protein deficit, the greater the functional impairment. A decrease in gastric, pancreatic and bile production is also observed, with normal to low enzyme and conjugated bile acid concentrations These alterations further impair the absorptive functions Protein-deficient individuals are diarrhea-prone because of these alterations and possibly also because of irregular intestinal motility and gastrointestinal bacterial overgrowth Diarrhea per se aggravates the malabsorption [35–40]

Finally, a generalized decrease in nervous system function is clearly apparent in severe PCM [41,42] The etiology of these alterations has not been elucidated Several explanations have been proposed, among others decreased brain potassium content and catecholamine production, reduced number of cells in the central nervous system when malnutrition occurs before 6 to 8 months of age and small cell size when it occurs at a later age.[41–43]

Decompensation from severe calorie deficiency occurs from inability to maintain internal energy supply and results in hypoglycemia, hypothermia, impaired circulatory and renal functions, acidosis, coma and death In the case of decompensation from protein deficiency, visceral functional failure also results from unavailability of amino acids. At the same time, an accelerated tissue breakdown takes place. The resulting alterations are failure of the liver to synthesize certain proteins such as albumin, several clotting factors and transport proteins, leading to fatty liver, increased free circulating cortisol, hemorrhagic diathesis, and jaundice in extreme cases, various degrees of renal failure with acidosis, as well as water and sodium retention, frankly decreased cardiac work and tissue anoxia with pulmonary congestion occur All of these factors lead to the development of clinical edema and, in extreme cases, skin lesions with hemorrhagic phenomena In addition, fluid leakage into the gastrointestinal tract,

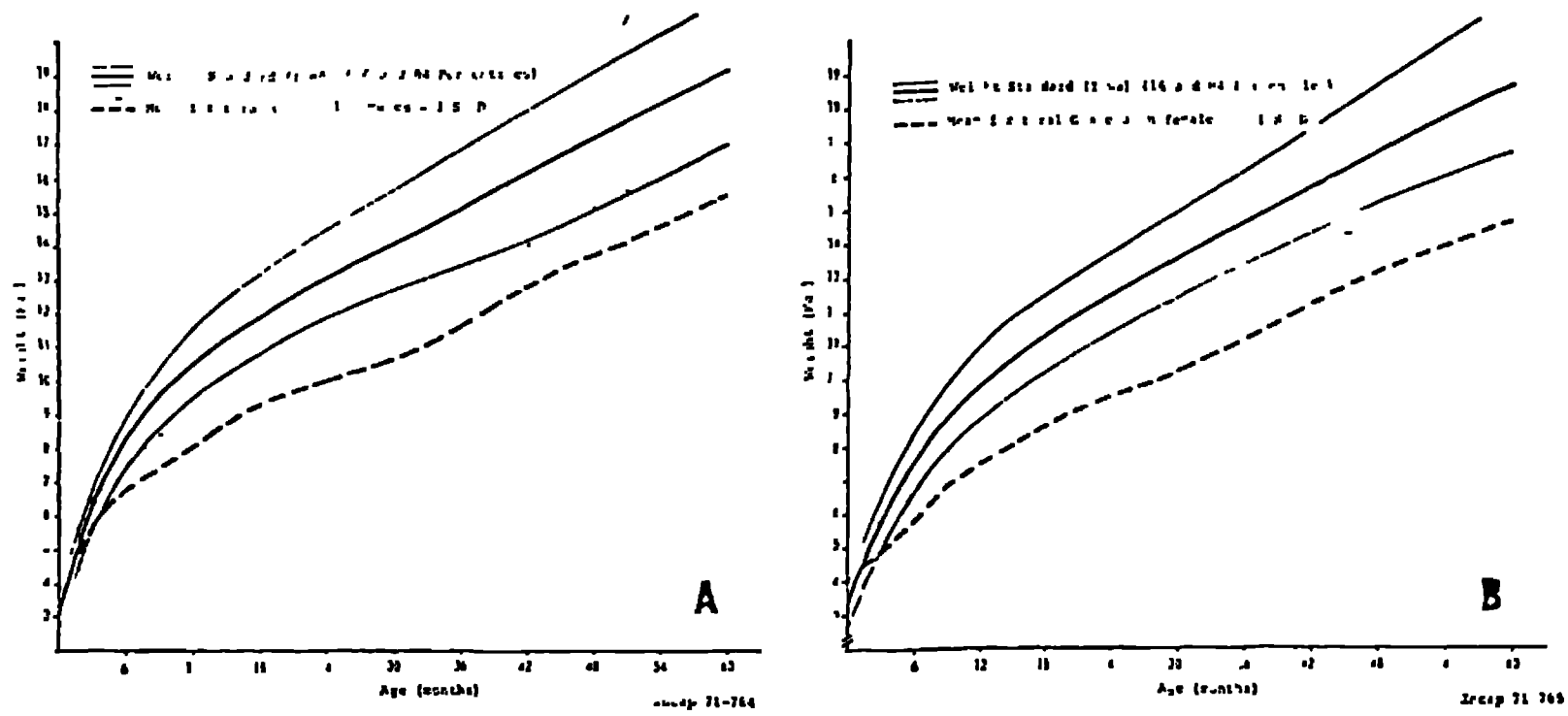

Fig 24–1 Weight of rural Guatemalan male and female children below 5 years of age, in relation to that of U S A children Number of Guatemalan children in the sample 431 males and 436 females (From INCAP [3])

increased susceptibility to pulmonary infections, water and electrolyte disturbances with hypokalemia and hypomagnesemia, frank central nervous system depression and death can result.[46–48]

DIAGNOSTIC CHARACTERISTICS OF PROTEIN-CALORIE MALNUTRITION

The clinical and biochemical picture of PCM varies according to its severity and to the characteristics of the host, the environment and the agent.

Chronic Mild-to-moderate PCM[49]

Clinical. It is obvious that the severe syndromes of edematous and nonedematous PCM, recognized as kwashiorkor and marasmus, respectively, represent the critical end of a spectrum of varying degrees of deficiency.

However, before these severe stages are reached, children survive with insufficient calories, protein or both, a situation which does not allow them to grow and develop at the rate to be expected from their genetic potential. A long-standing restriction would be clearly manifested by a retardation in height and weight gain (Figs. 24–1 and 24–2). This reduced size may be a life-saving device to allow the children to survive on the restricted food available to them.

Fig. 24–2. Appearance of two 10-year-old children in the rural Central American region. The one at the left has always been well nourished. The one at the right has been mild-to-moderately malnourished.

Under these chronic conditions, it is generally observed that body mass, although markedly retarded for the chronologic age of the child, is adequate for its height. However, these children may be chronically affected by temporary periods of weight-for-height deficits. As judged by body composition studies, bone maturation and biochemical measurements, the malnourished child is not a small version of his well-nourished counterpart of equivalent chronologic age. He shows an immaturity in biologic development compatible with his retarded physical size. This includes deficits in lean body mass and adiposity, with relative overhydration affecting primarily the extracellular space. Without knowing the actual age of the subject, it is often difficult or even impossible to determine the presence or extent of malnutrition.

Other characteristics of such cases, which are more difficult to attribute exclusively to nutrition, are reduced physical activity, mental apathy, frequent episodes of ill-defined sickness, anorexia and diarrhea and a higher fatality rate from common infectious diseases.

It has been shown that an association exists between retarded physical growth and development and some tests of psychomotor and mental development.[50–52] The isolated effect of malnutrition as a cause of this phenomenon is strongly suggested by data derived from animal experimental work. Direct proof does not exist in humans, although studies are now under way from which an answer to this question is expected. Nevertheless, it is beyond doubt that the responsible factor is the complex of social deprivation, of which nutrition is one of the most important components.[53]

Chronic PCM in adults generally results in marked leanness (Fig. 24–3), which, in severe cases, can reach a state resembling cachexia. Because their protein requirements per unit of body mass are much smaller than those of children, the main

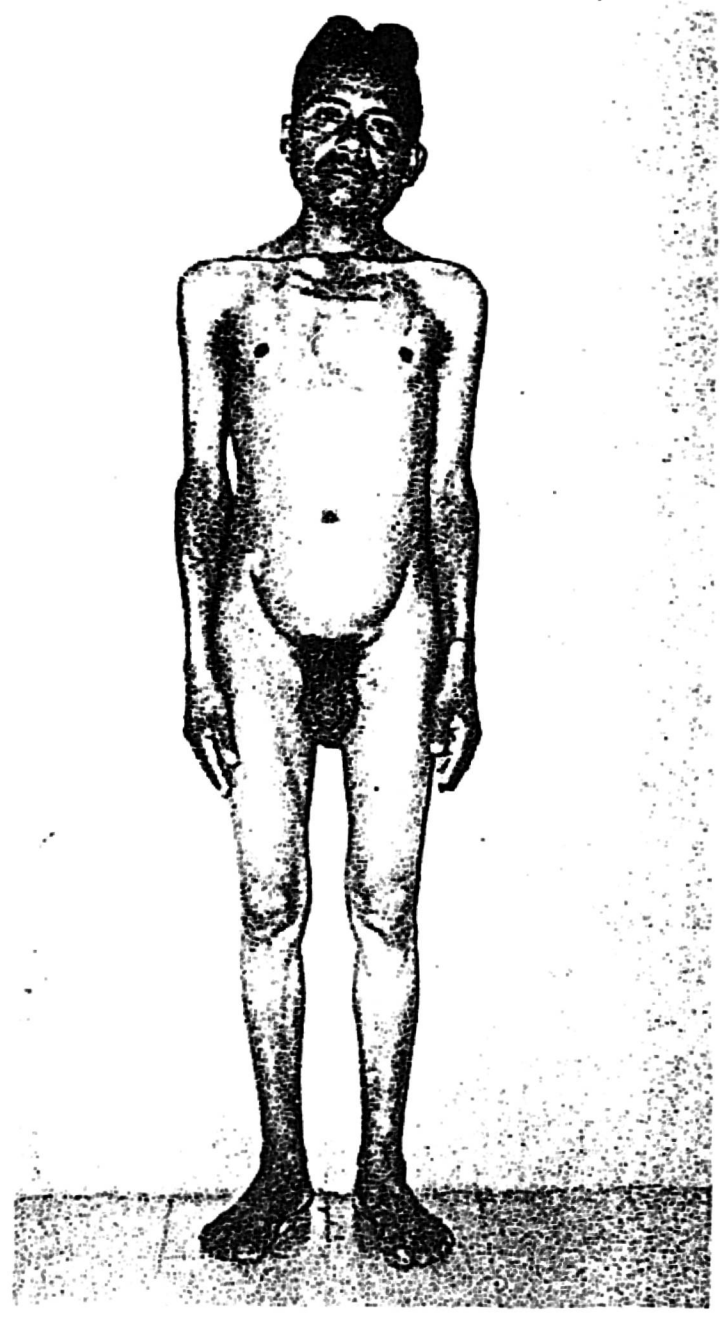

Fig. 24–3. Mild-to-moderate malnourished 36-year-old man.

manifestations are of primary calorie deficiency. Thus, physical activity and capacity for prolonged physical work are reduced, perhaps as a mechanism to maintain caloric equilibrium on low food intake. Changes in body composition similar to those described for children can also be observed.[32,33]

Biochemical. Because of the characteristically low protein intake, subjects have a low excretion of urea N per unit of creatinine[54] and a somewhat abnormal plasma free amino acid pattern with a decrease of the branched essential amino acids.[55,56] It has been reported also that

they excrete a lower amount of hydroxyproline in the urine, in good agreement with the slow growth rate.[57] Slight decreases in transferrin and albumin serum levels have been reported.[58,59] If lean body mass is reduced for height, this is manifested by a decreased creatinine/height index.[60]

Severe Protein-calorie Malnutrition

Clinical. ***Nonedematous PCM.*** Severe calorie deficiency is clinically recognized in children by the syndrome identified as marasmus in most parts of the world, or nonedematous severe PCM (Fig. 24–4). The child is frankly small for his age, looks emaciated and, in extreme conditions, reduced to "skin and bones" because of an essentially total absence of adipose tissue. His skin is usually dry and "baggy," wrinkles easily and has lost its turgor. The hair is sparse, thin and dry, and can be pulled out easily; it loses its normal sheen and acquires a dull brown or reddish yellow color, giving it a lifeless appearance. The face resembles that of a monkey, with sunken cheeks in extreme cases, because of the disappearance of the Bichat fat-pad. The child is weak and looks hypotonic, and his pulse, blood pressure and temperature may be low. He is sensitive to cold temperature, cries easily and is often found retracted from his environment, sucking one or more fingers. His viscera are small and lymph nodes are easily felt. Soon after therapy is initiated the child becomes alert and interested in his environment. In adults, extreme emaciation is characteristic of calorie deficit (Fig. 24–5).

Common complicating features are eye lesions, due to hypovitaminosis A, and skin infections. The classical cases suffer from constipation and are ravenously hungry, but diarrhea, anorexia and vomiting, with

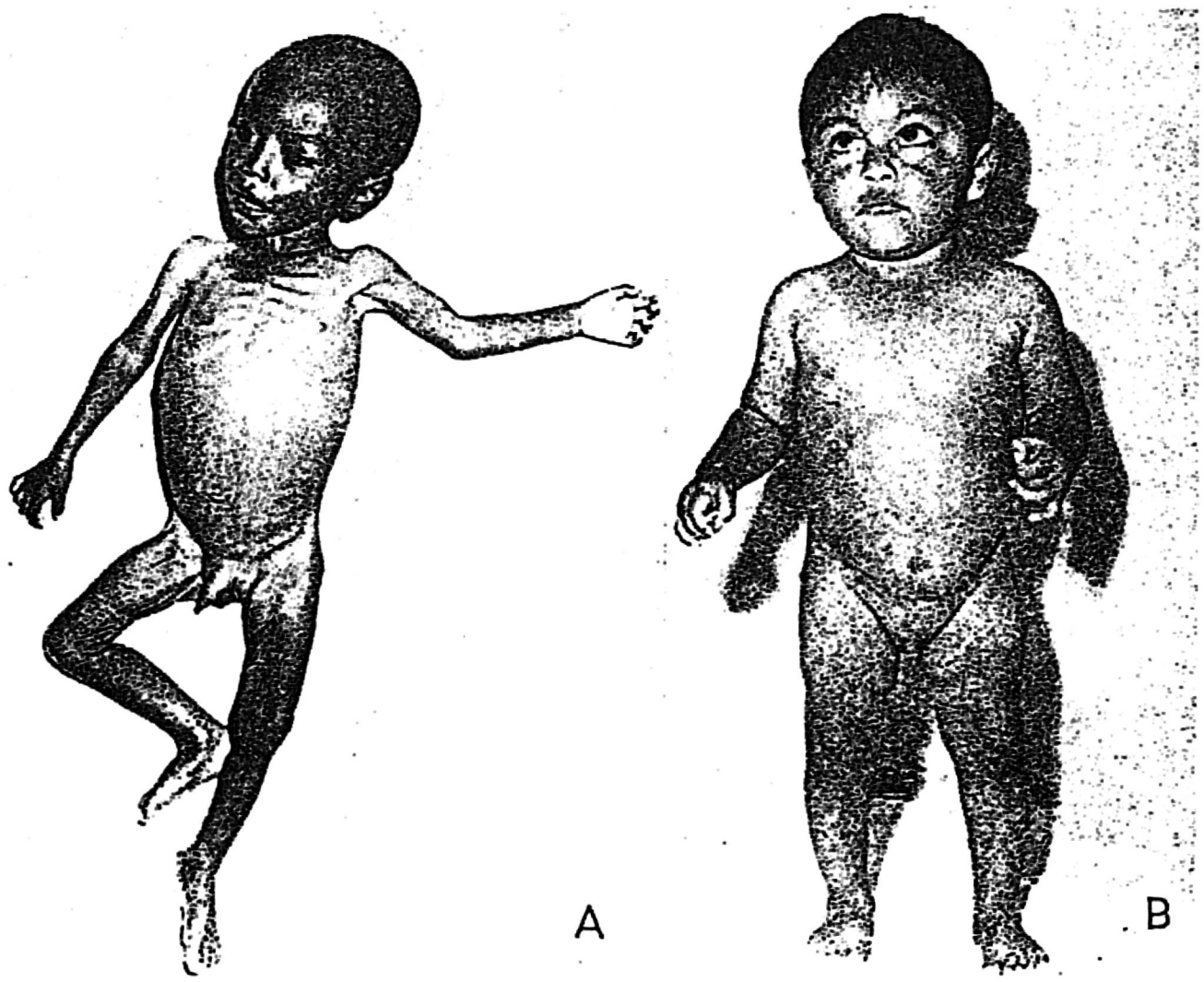

Fig. 24–4. Twenty-one-month-old child with severe nonedematous PCM (marasmus) on admission to the hospital and 4 months later, when fully recovered.

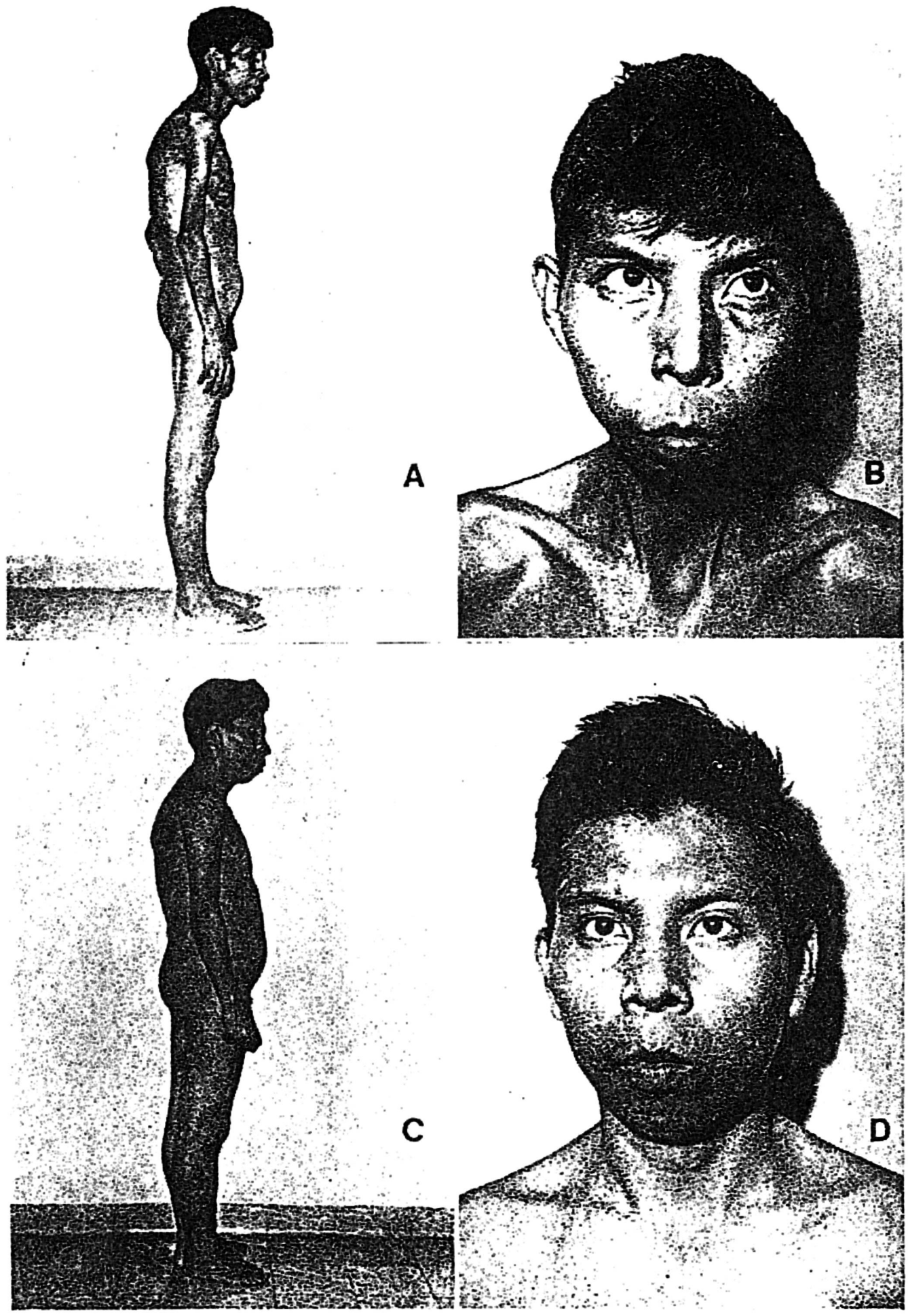

Fig. 24–5. Twenty-nine-year-old man with severe nonedematous PCM on admission to the hospital and 3 months later, when fully recovered.

dehydration, are not rare; dehydration, acidosis and electrolyte imbalances may, in fact, cause death. Postmortem examination shows only generalized atrophy, without fatty liver. Clinically and post mortem, the child has no edema, although his total body water is increased for his size.[15,24]

Edematous PCM. The child with acute severe protein deficiency of the sugar-baby type (Fig. 24–6) is usually almost normal in height for age; his body fat is normal or increased, but flabby, and he is clinically edematous. The edema may be located only in the lower segments of the body, through the action of gravity, but generally his face is swollen, his cheeks look heavy and his eyelids are swollen shut. He is pale and the skin shines in the edematous areas. In other parts of his body the skin may be dry and atrophic or have large asymmetric confluent areas of hyperpigmentation and hyperkeratosis. A peeling type of desquamation occurs in these areas, leaving underneath a fine, atrophic pinkish skin. Hair is atrophic, dry, depigmented and has a reddish tint, falls off easily and breaks upon rolling between the fingers. Often, zones of alopecia are noted. The nails are brittle and have horizontal grooves. The general appearance is that of a hypotonic, miserable-looking child. He is apathetic and irritable at the same time. In the severest cases his apathy is profound. Anorexia is almost universal. Hepatomegaly is frequent, as are a swollen stomach and intestinal loops. Diarrhea is almost always present. Frequent complications are eye lesions due to vitamin A deficiency, cheilitis and cheilosis, as well as other manifestations of deficiencies of the vitamin B complex. Upper respiratory infections and dehydration, even in the presence of edema, are common and often lead to death. Intestinal motility is irregular, and these children often become dehydrated before they pass a huge liquid stool. As the child begins to recover he loses his edema and remains fat and flabby. This appearance often misleads the clinician who may consider him recovered because his weight may be normal. In fact, he is still severely protein deficient in terms of lean body mass.

Fig. 24–6. Thirty-six-month-old child with severe edematous PCM and preservations of adiposity (kwashiorkor) on admission to the hospital and 4 months later, when fully recovered.

Pulmonary edema with bronchopneumonia, septicemia, gastroenteritis and water and electrolyte imbalances are the most common causes of death. At autopsy, generalized edema, visceral and muscle atrophy and severe fatty liver are found. Red bone marrow is centripetally retracted.

Most cases of severe malnutrition, both in children and adults, fall between these two extremes of pure caloric and pure protein deficiency. In these cases, a moderate-to-severe protein deficit may be superimposed on a severe degree of calorie deficiency, and vice versa (Fig. 24–7). These subjects, suffering from severe PCM with edema, together with pure

Fig. 24–7. Twenty-five-month-old child with severe edematous PCM superimposed on chronic caloric deficit. In addition to being edematous, he appears wasted (marasmus-kwashiorkor). Pictures were taken on admission to the hospital and 4 months later, when fully recovered.

protein deficiency, have been identified with kwashiorkor. Clinical edema constitutes the main characteristic for diagnosis. The mixed PCM cases have also been identified with a variety of terms, among which are pluricarential syndrome in Central America, undernutrition in other Latin American regions, and protein malnutrition in certain African and Asian countries.[1,48,49] In adults, a predominant protein deficiency can also lead to edematous PCM (Fig. 24–8).

Biochemical. In severe protein-calorie malnutrition several biochemical alterations can be observed. Many of these distinguish between the *edematous* and the *nonedematous* types.

Proteins and Nitrogenous Compounds. The child who has reached the severe stage of edematous PCM has been submitted to a severe negative protein balance.[61,62] Consequently, his total body nitrogen is markedly reduced. Different organs share this protein loss to different extents.[63–65] The liver rapidly loses a fraction of proteins, while the loss of muscle protein is progressive and, because of the large muscle mass, accounts for the major protein loss. Kidney, brain and endocrine organs seem to retain their protein more efficiently. However, the importance of these different losses in terms of organ function cannot be derived from their relative magnitudes. A low ratio of protein to DNA is found in muscle, liver and brain, indicative of intracellular protein loss.[44,66] In nonedematous PCM these changes are moderate, becoming severe only in the most advanced stages.

The concentration of several protein fractions in the body fluids is low. (Although present in both types of PCM, edematous and nonedematous, the changes to be described are more pronounced in the first type. In the second, they may be totally absent.) The concentration of total proteins is reduced, mainly due to a decreased albumin concentration. The concentration of beta-globulins is also decreased. The gamma-globulin fraction concentration is either normal or increased; therefore, the per cent contribution to the total plasma proteins is always high.[48] Some plasma proteins with very specific functions may also be decreased. Among them, those associated with the transport of other nutrients and hormones are particularly important: transferrin,[58,67] ceruloplasmin,[67] retinol-binding protein (RBP),[68] alpha- and beta-lipoproteins,[69] thyroxin,[70,71] and cortisol-[72,73] and aldosterone-binding proteins.[74] Impaired blood transport may attain significance in the development of secondary metabolic abnormalities, as has been shown in the case of lipids and vitamin A.[75] The blood concentration of urea nitrogen is low, as is its excretion in the urine. This reflects the

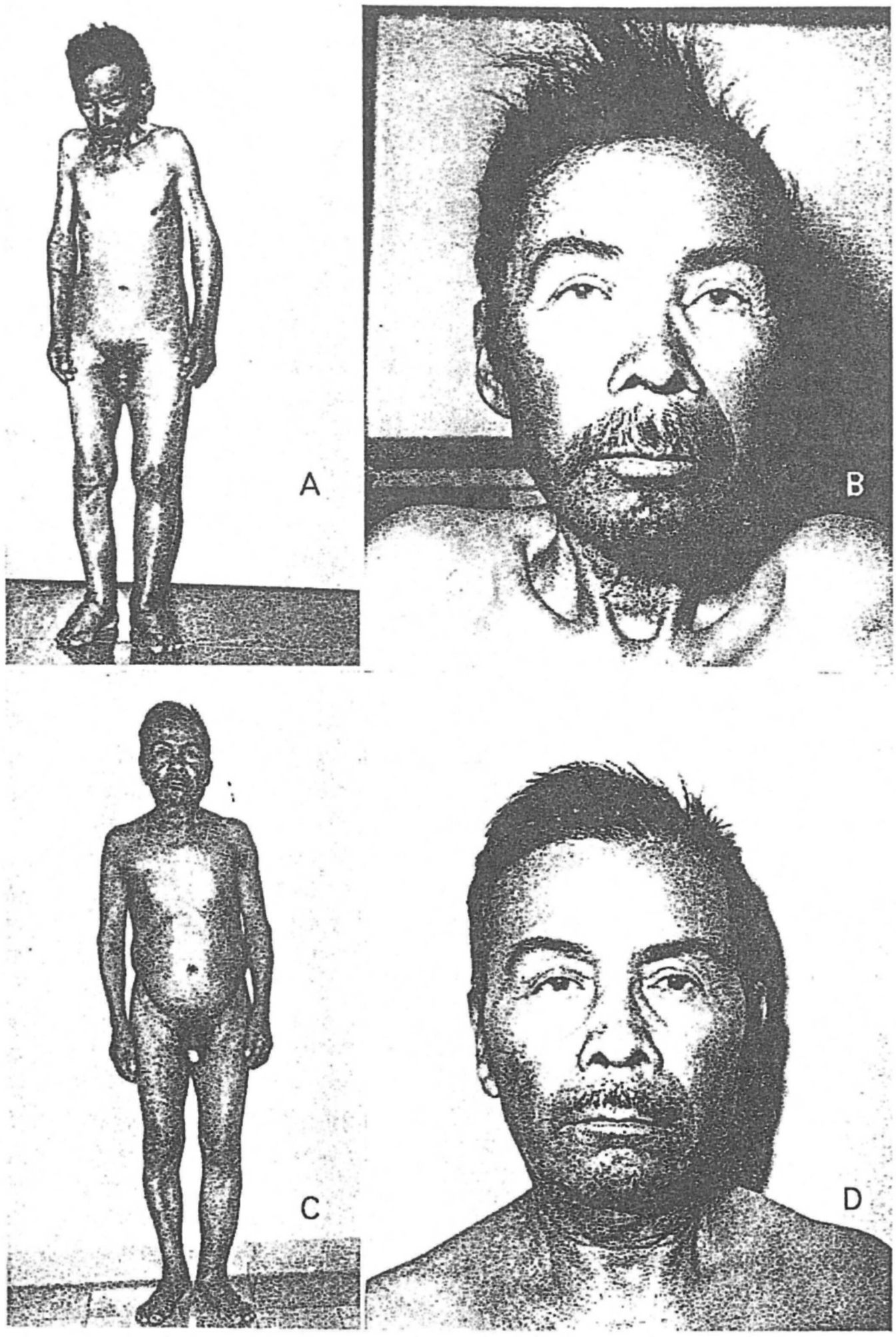

Fig. 24–8. Forty-six-year-old man with severe edematous PCM on admission to the hospital and 3 months later, when fully recovered.

low catabolic rate of body proteins and decreased urea synthesis, which are characteristic of primary protein deficiency.[20,76,77] When calories are the most limiting factor, urea production is increased because body protein catabolism is elevated.[78]

The excretion of urinary creatinine is decreased,[79,80] a consequence of the decrease in muscle tissue and lean body mass.[81,82]

The plasma free-amino acid pattern is abnormal in edematous PCM. A lowered concentration of valine, leucine, and isoleucine is characteristic, as is also a very low tyrosine concentration.[83,84] The ratio of the branched essential to nonessential amino acids is low. Another finding, which is very characteristic, is a low tyrosine/phenylalanine ratio, as a result of a deficiency in phenylalanine hydroxylase.[85] In nonedematous PCM, plasma amino acid alterations may be absent.[55]

Hemoglobin concentration is variable, but often it is around 8 to 10 gm per 100 ml because of hemodilution. Generally, the cells are normochromic and normocytic. Hypochromia can be present if a severe iron deficiency exists from other causes. Mild to overt megaloblastosis can occur because of folate deficiency.[86] The great majority of subjects are not anemic but physiologically adapted to the decreased oxygen demands.[14,27] Leukocytosis can occur if infection is present. Leukopenia and thrombocytopenia generally indicate the presence of gram-negative septicemia.

Although it has been observed that urinary amino acid excretion is abnormal, no consistent pattern seems to be evident. The abnormal metabolites ethanolamine and beta-aminoisobutyric acid have been detected, suggesting a defect in transmethylation.[87] Excretion of urocanic acid has been shown to be abnormal after a histidine load.[88]

Carbohydrates. Usually blood glucose is normal. However, there is an increased tendency to hypoglycemia upon fasting. This is compatible with the finding that liver and muscle glycogen stores are normal or low.[89] Some alterations revealed by clinical laboratory studies suggest abnormal metabolic handling of glucose. Glucose tolerance tests give a diabetic type of curve, and insulin secretion is low.[90,91] Impaired glucose utilization, glycogenolysis and glycolysis have also been demonstrated. In addition, there are isolated pieces of evidence of impaired enzymatic steps along the glucose oxidation, the Krebs cycle and the galactose-to-glucose conversion paths.[89,92,93]

Lipids. Steatorrhea is a characteristic of edematous PCM, even when the diet is practically devoid of fat.[94] Lipid absorption is reduced.[95] Low levels of many serum lipid fractions, neutral fat, cholesterol, particularly its esters, vitamins A and E and phospholipids have been demonstrated. These findings suggest that the changes in specific plasma proteins and physical chemical structure of the lipid-protein complexes account for impaired blood transport.[75,96,97] In fact, there is direct evidence for decreased lipoproteins as well as for decreased RBP, the specific vitamin A-binding protein.[68] A great part of the fatty liver may well be the consequence of inability to mobilize fat.[97]

Vitamins.[98] Signs of water-soluble vitamin deficiencies vary with the local dietary patterns, but, even when intakes are low, serum concentrations of thiamin, riboflavin, vitamin C, niacin metabolites and folates may well be within the normal range, and overt clinical signs of deficiency of these factors are rarely seen. Vitamin B_{12} serum levels are often found to be high. All of the above findings suggest that, although the supply of these vitamins may be low, tissue demands are also decreased.

In the edematous type of PCM (kwashiorkor), serum levels of vitamins A and E are consistently lower than normal. In the case of vitamin A, poor vitamin intake and defective absorption and transport explain these alterations. This expla-

nation may well apply also to vitamin E All levels rise rapidly with therapy

Water and Electrolytes.[47,98–101] Hypoosmolarity is a common finding Serum sodium levels are from normal to low Potassium and magnesium serum levels are not decreased, except when excessive losses of the cations occur through diarrhea and vomiting In such cases, hypokalemia is accompanied by a loss of potassium from specific tissues such as muscle and brain [26,102] This results in a decreased cellular potassium/nitrogen ratio Mild acidosis is also common, on account of a decrease in the renal acidification mechanisms Total serum calcium is somewhat low, primarily because of the protein-bound fraction

Enzymes The activity of several serum enzymes such as amylase, pseudocholinesterase and alkaline phosphatase is reduced Their drop is consistent with and quite parallel to that of albumin, so that they may be normal in nonedematous PCM [48,103] Serum transaminases are elevated and reflect increased tissue transaminase activity and leakage from the cells [104] Around 15 hepatic enzymes have been studied,[105,106] including dehydrogenases, oxidases and esterases Of these, 4 are clearly decreased in the edematous type of PCM—xanthine oxidase, glycolic acid oxidase, d-amino acid oxidase and cholinesterase It has been pointed out that these enzymes are not involved in fundamental physiologic functions and seem to be of relatively little importance On the other hand, cytochrome c reductase, a key enzyme in electron transport, is well preserved

More complex systems, which depend on the integrity of the mitochondria, have been studied Oxidative phosphorylation is somewhat reduced, and phosphate uptake into phosphatides is about half the value seen in recovered children [61]

Enzymatic changes in liver and PMN leukocytes have been studied comparatively [107] It has been found that not only are changes in both tissues similar but that they are characteristically different in the edematous and nonedematous types In summary, these changes are increased activity of fumarase and aconitase, decreased activity of isocitric dehydrogenase, glutamic dehydrogenase and aldolase in the edematous malnourished child with the reverse being true of the nonedematous patients. Muscle creatine phosphokinase activity has been found to be consistently low in children with the edematous type, while in those suffering from the marasmic type low or normal values can be observed [108]

It is impossible to separate the effects of protein deficiency per se on enzymes from changes in activity, which may reflect changes in functional pattern in response to adaptation In general, the latter interpretation seems more plausible Measurements done in vitro with reconstructed systems tell nothing about subcellular structure changes, which may alter linking of enzymes with their substrates and cofactors These could well involve alterations in membrane structure at the cellular and subcellular level

TREATMENT

Chronic Mild-to-moderate Protein-calorie Malnutrition in Children

Because the children are not only physically retarded but also proportionally immature, their protein and calorie intake should be calculated on the basis of their height, that is, as if the child were well-fed but younger, of an age for which his height would correspond to the 50th percentile This means a higher calorie and protein intake per kg of body weight than that of children of the same chronologic age These intakes, therefore, will promote a retention of energy and protein to permit catch-up in growth and development Of course, they should contain the appropriate concentrations of all the other essential nutrients When marked deficiencies of

other nutrients are also prevalent, administration of specific supplements is called for

Severe Protein-calorie Malnutrition

The severe, uncompensated forms of PCM require medical guidance during the initial phases of treatment [109,110] Whenever possible, children with noncomplicated PCM should be treated on an outpatient basis,[111,112] Hospitalization in pediatric wards increases the risk of cross-infections The presence of the mother or another close relative in the hospital is highly desirable

Mortality in severe, uncompensated PCM is high even with hospitalization, ranging from 11 to 50 per cent depending on the center where treated and on certain characteristics of the patients, such as those listed on Table 24–5 In most cases the cause of death is a complication rather than PCM per se, but such complications do not have such high mortality in well-nourished patients

Table 24–5. Characteristics of Severely Protein-calorie Malnourished Children which Carry a Poor Prognosis

Stupor or coma
Age less than 6 months
Weight-for-height deficit greater than 40 per cent
Severe, protracted diarrhea
Infection, primarily bronchopneumonia or measles
Hemorrhagic tendency Purpura is usually associated with septicemia
Severe eye lesions
Extensive exudative or exfoliative dermal lesions
Extensive and deep decubitus ulcers
Dehydration and electrolyte disturbances, particularly hyponatremia, hypokalemia and probably hypomagnesemia
Clinical jaundice or increased serum bilirubin and/or frankly elevated serum glutamic-oxaloacetic and glutamic-pyruvic transaminases
Hypoglycemia and/or hypothermia
Total serum proteins below 3 gm per 100 ml
Severe anemia with clinical signs of hypoxia
Severe tachycardia, signs of heart failure and/or respiratory distress

The treatment of severe PCM may be divided into two phases

1 That oriented toward saving the patient's life by bringing him back to his adapted stage
2 The rehabilitation or 'consolidation of cure phase At this stage, body protein and energy repletion for the patient's height should be achieved

The main objectives of the initial treatment are therapy of infection and correction of water and electrolyte imbalances as well as of other factors which lead to decompensation

Maintenance of adequate urinary output is of primary importance Preferably this is accomplished by oral therapy, keeping in mind the fact that the severely PCM individual is hypo-osmolar [99] In addition to hypo-osmolarity, other peculiarities of the severely malnourished patient that must be taken into account to correct and/or maintain his electrolyte balance are (1) total body potassium depletion, frequently without hypokalemia, because of intracellular potassium depletion, (2) mild-to-moderate metabolic acidosis, which tends to disappear when electrolyte balance is reestablished and the patient receives dietary or parenteral energy and (3) increased tolerance to hypocalcemia, partly because of the acidosis, which produces a relative increment in ionized Ca^{++}, and partly because of hypoproteinemia (when present), which makes less protein available to bind Ca^{++}

As plasma proteins increase, hypocalcemia and even tetany may appear if calcium intake is inadequate

If there is adequate diuresis, the diet should also provide from 6 to 8 mEq per kg body weight per day of K If needed, the potassium concentration can be increased to supply 10 mEq per kg per day body weight to replace actual K losses from diarrhea or vomiting, which are usually 40 mEq per liter Sodium intake should be sufficient to replace losses (about 35 mEq/L from diarrhea and 12 mEq/L from emesis),

but otherwise it should be relatively low (3 to 5 mEq per kg per day) because PCM patients have an excess of body sodium Diets very low in sodium, however, hamper both renal function and normalization of intracellular electrolyte composition [113] An excess of sodium and osmolar overloads can easily induce cardiac failure Magnesium should also be administered, particularly when diarrhea and vomiting occur Usually 1 ml of Mg SO_4 $7H_2O$, 50 per cent solution IM every 12 to 24 hours, is adequate This therapy is important if tetany, oculogyric crises, tremor and bizarre neurologic signs occur in the initial phases of realimentation In patients with tetany, calcium gluconate should also be administered intravenously, 0 5 to 1 gm slowly in 1 hour Unless severe, acidosis should not be treated Usually, renal function will handle acid-base balance efficiently

If needed, intravenous therapy can and should be used, following the general outline described for oral rehydration, except that K therapy should not exceed 6 mEq per kg per day Osmolarity should be kept at around 280 mOs per liter, and sodium must be kept low Administration of plasma or other "protein-rich" fluids is contraindicated, except when severe intravascular dehydration (hypovolemia) with shock is present Shock due to severe dehydration or gram-negative septicemia should be treated as if the individual were not malnourished In some of these cases blood transfusions are indicated, but hemoglobin concentrations should be brought only to 10 gm per 100 ml or less, which are commonly the hemoglobin levels these children achieve from adaptation Transfusions of packed red cells are indicated only when severe anemia is present and cardiorespiratory failure is imminent Again, hemoglobin concentrations should be brought only to about 10 gm per 100 ml

Infection should be treated vigorously and, if possible, with the help of a laboratory, so that the infective organisms can be isolated and their sensitivity to antibacterial agents determined When there is a choice, the use of antibiotics that inhibit protein synthesis should be avoided

A free airway with adequate lung ventilation is essential When pneumonia is present, oxygen therapy and even tracheostomy may have to be undertaken, because it often happens that these patients are weak and cannot clear their airways satisfactorily

When severe hepatic failure occurs it should be treated accordingly, as is done when cardiac failure supervenes Diarrhea is treated mainly by diet No anticholinergic drugs are used Another general rule is to protect the PCM patient from exposure to cold and hypothermia, and from hypoglycemia Hypoglycemia is prevented by avoiding prolonged periods of fasting If a patient cannot be fed by mouth, intravenous infusions should provide 20 to 30 kcal per kg per day body weight as glucose

During this initial phase of therapy a diet based on high-quality protein, such as milk-casein mixtures (to reduce lactose loads), casein alone, egg or fish protein, is recommended During this phase a cautious handling of the nutrition aspect is essential This demands patience, and personnel must be conscious of the fact that the most common causes of death are the complications and not malnutrition per se Drastic therapeutic nutritional measures, such as high protein or calorie load from the start, may precipitate death by posing an "iatrogenic" overload on enzymatic and various physiologic functions which had reached maximal adaptation in several weeks or even months in the process of progressive malnutrition This cautious dietary approach should provide initially, in children, around 1 gm protein and 80 to 100 kcal per kg per day 20 per cent of the calories should be derived from fat After 2 to 4 days, the protein and energy contents of the diet should increase gradually, as shown in Table 24–6, until they provide

Table 24–6. Example of a Dietary Therapeutic Regimen for Children Based on Dry Skim Milk, Sugar and Vegetable Oil*

Days from Beginning of Treatment	*Protein (gm)*	*Energy (kcal)*	*Milk (gm)*	*Sugar (gm)*	*Oil (ml)*	*Water (ml)*
1	0 8–1	80–100	3	17	2	100
3	1 5–2 5	110–120	6	20	2	130
5	2 5–3 5	140–150	9	20	4	150
7	3 5–4 5	150–160	12	20	4	160
12 (marasmus‡)		175‡			6‡	
17		195			8	
22		215			11	
	3 5–4 5	‡	12	20	‡	160

* All amounts per kg body weight per day The liquid formula must be supplemented with adequate levels of vitamins, minerals and electrolytes

‡ Marasmic patients may require more than 150 to 160 kcal per kg per day Vegetable oil 2 to 3 ml per kg per day at 5-day intervals should be added until the rate of weight gain becomes adequate

3 to 4 gm protein and 120 to 160 kcal per kg per day Twenty to 40 per cent of the energy then should come from fat, preferably of vegetable origin with a high content of polyunsaturated fatty acids (e g corn or cottonseed oils) Marasmic patients may need a higher energy intake to recover In these cases, 20 to 25 kcal per kg per day should be added to the diet as vegetable oil at 5-day intervals, until weight gain becomes adequate In a few instances this may require 200 or more kcal per kg per day and, even though a mild steatorrhea may develop, this regimen should be maintained The example shown in Table 24–6 is based on a liquid diet Children who can eat solids should receive a varied diet, aiming at the same levels of protein and energy intakes

In the adult, the therapeutic scheme is the same but the diet should initially provide around 0 6 gm protein and 50 kcal per kg per day and eventually reach 3 to 4 gm protein and 80 to 100 kcal

Vitamins, including folate, should be administered from the beginning, to meet recommended allowances On admission, the routine administration of a single high dose (20,000 μg) of water-dispersible vitamin A is recommended to avoid acute eye lesions resulting from vitamin A deficiency when high calorie and protein diets are initiated and there is greater physiologic demand for the vitamin This is followed by a daily oral dose of 1500 μg

The diet should also provide from 4 to 5 mEq per kg body weight per day of K, 3 to 5 mEq per kg per day of Na and adequate amounts of magnesium, calcium and phosphorus Iron, in amounts from 16 to 32 mg, as $FeSO_4$, is routinely administered by mouth as soon as increased protein-calorie intakes are begun, in order to supply the excess requirements for this mineral produced by the rapid increase in total circulating hemoglobin

With this regimen, the severely malnourished subjects begin a smooth recovery They start to lose edema and to gain body mass, their general state shows the first signs of improvement and anorexia is replaced by an increased appetite, then the patient may begin to eat a more varied diet Serum and urine values also start a trend toward normal and the hematologic status initiates recovery All of these changes are accompanied by a rise in nitrogen and energy retention Except for sodium, mineral retention also increases Rapid changes in weight should be avoided, particularly a rapid loss of edema Usually within 2 to 3 weeks of therapy

serum composition returns to normal limits, and consolidation of cure begins

The second phase of therapy is accomplished only by dietary means The patients should by then be receiving a complete mixed diet, providing the protein and calorie levels reached in the later phase of the initiation of therapy A systematic program of psychosocial stimulation and progressive physical activity should be undertaken [114 115] In children this can be accomplished through games that require frequent walking, preferably uphill, running, jumping and climbing In adults it can be accomplished through exercise that imposes a gradual increment in cardiorespiratory work load Complete calorie and protein repletion generally is accomplished in a 6- to 12-week period, depending on the deficits at the start of treatment Calorie repletion is judged by weight for height, and is considered achieved when this index is 0 90 or more, based on the 50th percentile of normal well-nourished populations It is a mistake to use weight for age as an indicator of nutritional recovery A child who is stunted in height would have to become obese in order to reach a normal weight for age Generally, in nonedematous PCM, normalization of weight for height is reached later than normalization of the creatinine/height index an indicator of protein repletion [60] In edematous PCM the opposite occurs These changes are illustrated in Figures 24–9 and 24–10 Some children, however, stabilize at a creatinine/height index lower than 0 9, though fully recovered from PCM according to other indicators

PREVENTION

Prevention can be approached by (1) measures to decrease the risk of individuals reaching severe PCM and (2) improvement of the general nutritional status of

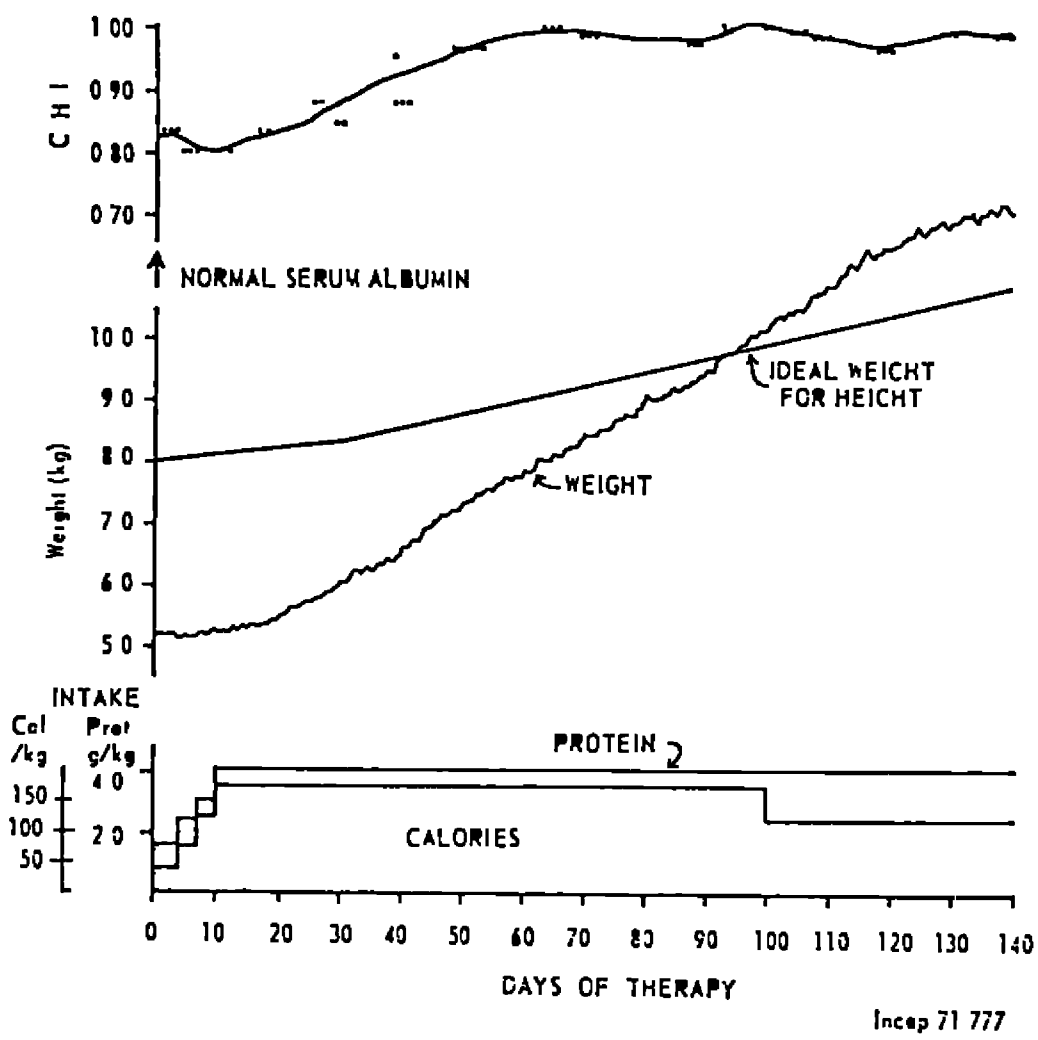

Fig 24–9 Clinical record of a 16-month-old child during recovery from nonedematous PCM His lean body mass (CHI) reached normal levels before his weight for height was normal

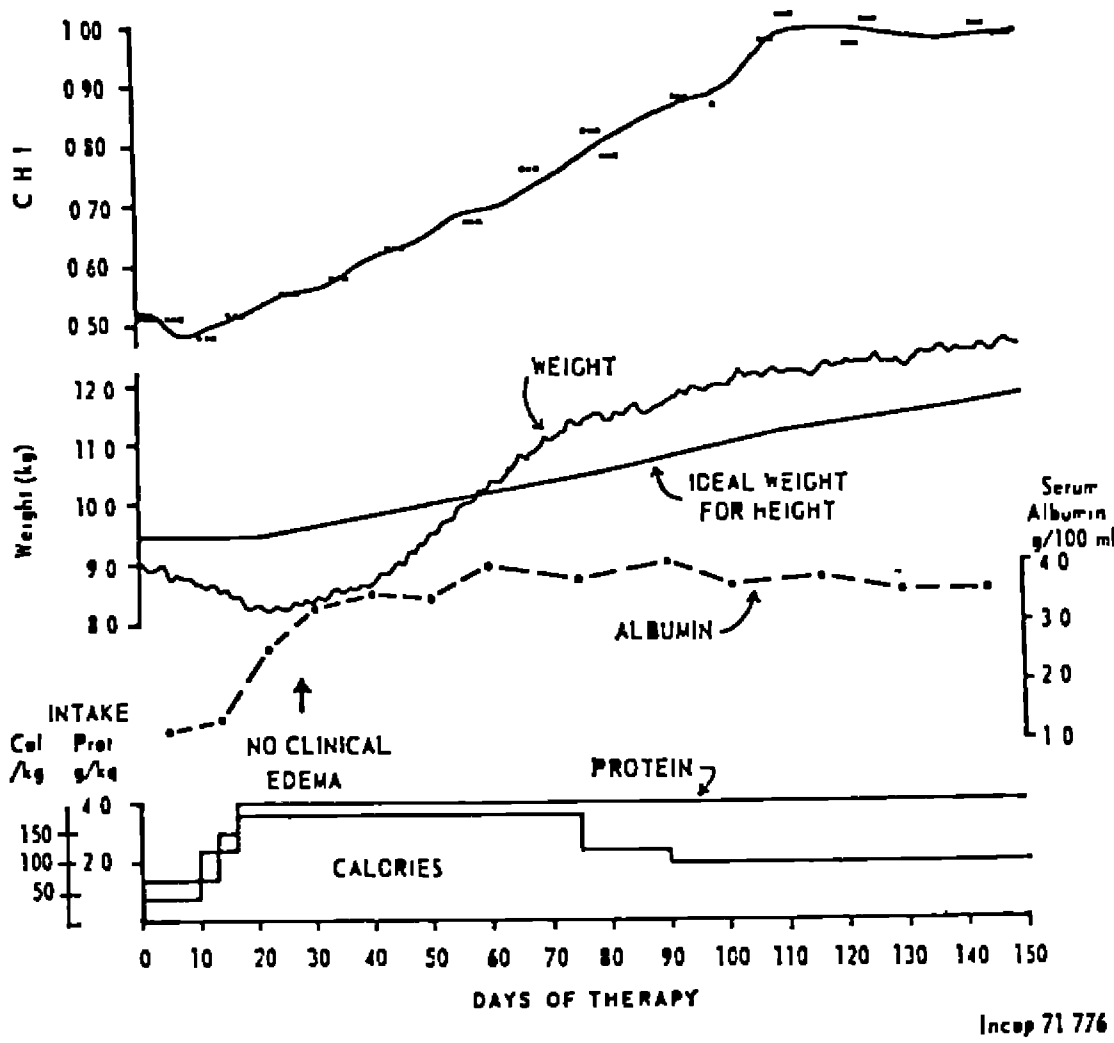

Fig. 24–10. Clinical record of a 20-month-old child during recovery from edematous PCM His lean body mass (CHI) reached normal levels after his weight for height was normal

the population, so that even chronic mild-to-moderate PCM cases become rare

The first is amenable to some direct actions (1) fostering of maternal lactation and adequate supplementation practices during infancy, (2) food supplementation programs of vulnerable groups, such as pregnant and lactating women, children up to school age and above, if possible, and physically hard-working men, (3) improvement of sanitary conditions and (4) specific nutrition education For this last objective, nutrition education and recuperation centers have been instituted in several countries [116] Their main objective is to educate the parents of chronic mild-to-moderate PCM children by having them participate actively in the nutrition rehabilitation of their own children These centers must (1) be located in the community and be adapted to the local environment, (2) be supported by each community, (3) see that children are rehabilitated by the proper feeding of locally available foods and (4) see that mothers are rotated in the care of the children, so as to have direct experience of the benefits that adequate nutrition brings to their children Experience is accumulating on the effects of these specific preventive measures, indicating that they appear to fulfill their goals [117]

Improvement of the general nutritional status of the population, so that malnutrition is eradicated, requires a complex approach [118] This is inseparable from the acceleration of socioeconomic development, the actions to bring it about are beyond the scope of this chapter

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Infantile Malnutrition in the Tropics

By NOEL W. SOLOMONS, M.D and BENJAMIN TORUN, M D., Ph.D

INTRODUCTION

Severe protein-energy malnutrition of the edematous type, or kwashiorkor, was first described by Cecily Williams in 1935[1] It focused medical attention on infantile malnutrition in the tropics. Although the war and the period of political change in Africa diverted some of this attention to other issues, the interest was rekindled and by 1954 Trowell and his colleagues published a book entitled *Kwashiorkor.*[2] Classical descriptions of the various forms of protein-energy malnutrition syndromes followed 1) the pure protein-deficient "sugar-baby" type in Jamaica, 2) the wasted, protein and energy depleted marasmic child, and 3) a spectrum of mixed types with intermediary characteristics[3] In 1955, Gomez et al[4] proposed a classification of protein-energy malnutrition (PEM) that related deficits in weight-for-age to risk of mortality in severely malnourished children

ETIOLOGY OF PROTEIN-ENERGY MALNUTRITION: ECOLOGICAL CONSIDERATIONS

Access to food is not the only determinant of nutritional status of children in developing countries[5] One of the major factors in the development of severe PEM is infection Studies from such diverse locations as Guatemala, Uganda and the Gambia implicated the number and duration of diarrheal episodes as causal or contributory factors in growth failure and malnutrition[6,7] Upper respiratory infections[6] and malaria[7] can also cause deterioration in nutritional status Questions about the impact of subclinical infections with intestinal parasites, specifically *A lumbricoides,* hookworm, *E. histolytica* and *G lamblia,* on growth and nutrition have been raised, but there is no convincing evidence of a major negative effect.

Several studies have pointed to social and environmental factors associated with poor nutritional status in children Family size, access to land, occupation of parents and similar factors all influence nutriuon of children[1,9] Although ecological risk factors are always important, the specific ones that predominate vary with geography and culture.

Infantile malnutrition also develops in societies perturbed by change, the so-called transitional societies As pointed out by Mata, "Increased exposure of persons living in traditional societies to the way of life of urban centers results in a measurable increase in the complexity of diets . In modern times, there has been unparalleled exodus from the rural areas throughout the world, accompanied by the mushrooming of slums in both developing countries and industrial worlds"[10] Decline in breast feeding is yet another major cause of nutritional deficiency at an early age

FEEDING PRACTICES IN RELATION TO MALNUTRITION

Breast Milk vs. Artificial Formula In Infant Feeding

Breast milk is considered the best nutrition for infants under six months of age.[11] In addition to its nutritive value, breast milk apparently also plays a role in prevention of infections This role may be based on the presence in milk of some immunological factors, such as antibodies and macrophages[12,13] (Table 1), which may protect the breast fed infant from infection An additional

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TABLE 1

IMMUNOLOGICAL FACTORS IN COLOSTRUM AND BREAST MILK

Factors	Presumed Function
Soluble Components	
Immunoglobulins (s-IgA, IgM, IgG)	Act against bacterial, viral and protozoal pathogens
Complement	Promotes opsonization of bacteria
"Anti-Staphylococcus factor"	Inhibits staphylococcal proliferation
Immunoregulatory mediators	Direct the function of T and B lymphocytes
Chemotactic factors	Guide the movement of phagocytes to pathogens
Lactoperoxide	Bactericidal against enteric bacteria
Lactoferrin	Competes for iron; prevents proliferation of iron-dependent bacteria
Lysozyme	Lyses bacteria
Interferon	Inhibits viral replication
"Ribonuclease-like factor"	Acts against RNA viruses
"Bifidus factor"	Promotes colonic colonization with Bifidobacteria
Cellular Components	
Macrophages and neutrophils	Phagocytize bacterial pathogens, produce various soluble factors
B lymphocytes and plasma cells	Synthesize immunoglobulins
T lymphocyte	Regulate other cellular components
Transplantation antigens	? Govern the recognition of self and non-self

Modified from Mata L: Am J Clin Nutr 1978, 31 2058-2065, and Dayton D, Orga PL (eds) Immunology of Breast Milk, New York Raven Press, 1979, pp 185-193

protective value of breast feeding may simply be the absence of microbial contamination, which is so difficult to avoid in the unhygienic environments that prevail in the developing countries

Association between feeding of human breast milk and a reduction in infections was demonstrated in a study in New Delhi Study of in-hospital mortality and infectious morbidity among low birth weight infants fed expressed maternal milk showed a dramatic reduction in rates of infection and death compared with a cohort fed a carefully prepared sterile formula [14]

Although it is possible to mimic the composition of human milk in the artificial preparations, bioavailability of some of the micronutrients in the human milk, eg. zinc and iron, cannot always be duplicated in the formulas

The great majority of women are capable of successful lactation, however, exclusive breast feeding beyond six months may not always provide adequate nutrition Whitehead and Paul[15] have demonstrated normal growth patterns in exclusively breast fed babies of well nourished, British mothers This is not true of mothers who are not well nourished Many women of low-income groups in tropical countries have milk outputs of only 600 to 750 ml daily and have a reduced fat concentration in their milk [16] A decline in growth velocity of infants solely breast fed beyond three months of age by these women is a rule

Nevertheless, the high rate of bacterial contamination of artificial feedings available in the tropics especially liquid formulas or the watery, starchy beverages improvised in many regions, and the consequent high risk of diarrhea,[17] would still make extended lactation the better alternative.

Weaning Foods

Supplementation of breast feeding after six months of age is desirable In the tropical countries, supplementation of protein is very important, but its sources and means for its incorporation into the diet vary with the locale

Satisfaction of Protein and Energy Needs in Preschool Children

Foods commonly consumed by low-income families in the tropics do not fulfill the energy and protein needs (including the quantities of essential amino acids) of growing infants and toddlers [18-20] The traditional dishes available to many weaned children in most developing countries are based on bulky vegetable foods, difficult to digest and low in energy and protein Moreover, inadequate nutritional education, cultural constraints and misconceptions about the properties of some foods

TABLE 2

SOME MANIFESTATIONS IN PATIENTS WITH PROTEIN-ENERGY MALNUTRITION THAT GENERALLY SIGNIFY A POOR PROGNOSIS

1 Age less than six months
2. Deficit in weight-for-height of greater than 30% or in weight-for-age of greater than 40%.
3 Extensive exfoliative or exudative cutaneous lesions or deep decubitus ulceration.
4 Dehydration and electrolyte imbalances specifically hypokalemia and possibly hypomagnesemia.
5. Clinical jaundice or elevated serum bilirubin concentrations with or without elevations in the transaminases
6 Hypoglycemia or hypothermia
7 Total serum protein concentrations less than 3 0 g/dl
8 Severe anemia with hypoxia
9 Generalized hemorrhagic tendencies (purpura is usually a sign of septicemia or a viral infection)
10 Intercurrent infections, particularly measles and bronchopneumonia
11. Severe ocular lesions
12. Persistent tachycardia and/or respiratory difficulty.
13 Coma, stupor or other alterations in mental status and consciousness

Modified from Torun B, Viteri FE Rev Col Med *(Guat) 1976, 27 43-62*

prevent the inclusion of some good protein sources in the diets of children.

ASSESSMENT OF NUTRITIONAL STATUS AND RISK OF MORTALITY

Marasmus and Kwashiorkor

Marasmus is characterized by wasting of muscles, absence of subcutaneous fat, wrinkled skin, thin and sparse hair, and weakness Protein concentration in the serum is usually above 5 5 g 'dl, excretion of creatinine is reduced, and concentration of hemoglobin decreased to below 10 g/dl

In kwashiorkor, the predominant feature is edema, which may reach the proportions of anasarca, wasting of muscles is slight and subcutaneous fat deposits may be normal, the skin glistens in the edematous regions and has dry, atrophic, hyperpigmented areas, the hair is dry, brittle, easily pluckable and is often depigmented showing a reddish tint The liver is enlarged Serum protein concentration is usually below 5 g dl, creatinine excretion is as low as or even lower than that in marasmus, and hemoglobin concentration is low The affected child is apathetic and irritable

The term "marasmic-kwashiorkor" describes the edematous patient with muscle wasting and decreased subcutaneous fat

Within this picture of intense PEM, there are relative degrees of severity, usually associated with a substantial risk of mortality Table 2 lists the main clinical and biochemical characteristics that normally indicate a poor prognosis Anthropometric characteristics of severely malnourished children have been evaluated in relationship to the risk of mortality, on the basis of the Gomez classification [4] Other studies have also considered the association between childhood mortality and anthropometric measurements [21-23]

Mild and Moderate PEM

The assessment or classification of the less severe forms of PEM is based primarily on anthropometric measurements Ideally, these should be simple to obtain, independent of age, and provide reliable information on the prevalence, severity and nature of malnutrition when used in surveys or surveillance of populations [24-26] The Gomez classification[4] relates weight to chronological age. A deficit in weight-for-age, however, may occur in a child who is truly underweight, or in one who is short in stature with a proportionate reduction in body mass Waterlow[26] proposed a classification system that differentiates these two situations. He suggested the term "stunted" to describe a child too short for age, who may also be underweight, and "wasted" for the one truly underweight Wasting is evidence of current malnutrition, whereas stunting is a reflection of past malnutrition chronic malnutrition, or both The degree of wasting can only be determined in reference to some standard of body mass for a given stature (weight-for-height) and stunting is assessed with reference to the height appropriate for a given age (height-for-age)

The World Health Organization currently recommends the use of the data from the U S National Center for

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Health Statistics as reference.[27] Any problems arising from the use of so-called "foreign" standards, with the possibility of genetic differences in stature, must be resolved in the interpretation of the data. The line that separates "normal" from "deficient" anthropometric measurements is a matter of value judgment, as are the further subdivisions into "mild," "moderate" and "severe" forms.[23,26,28]

Other anthropometric indices have been used, based mainly on weight, height, and mid-arm circumference. Chen et al[21] recently examined the value of such indices in predicting the risk of death among rural Bangladeshi children, 13 to 23 months old. Severely malnourished children had a higher risk of death than normal, mildly malnourished, and moderately malnourished children whose risk of death was identical. The discriminating power of anthropometric classification was enhanced when maternal weight and height and size of the household were factored into the evaluation of mortality risk.[21] Other findings in Bangladesh[22] and in the Punjab[23] correlated infant mortality rates with moderate and severe deficits in arm circumference-for-height and weight-for-age.

THERAPY AND REHABILITATION

The basic treatment of malnutrition is dietary. It provides the necessary nutrients to cure the lesions of deficiency, restore normal metabolic functions, replenish body stores, permit catch-up growth and allow the continuation of adequate growth. Attention must be paid to treatment of associated deficiencies, infections and other complications that frequently accompany malnutrition.

Severe Malnutrition

Kwashiorkor and marasmus are life-threatening conditions with case fatality rates as high as 40%.[29] Hospitalization — although essential in severe cases — may contribute to mortality rate, because of the high risk of nosocomial infections. Whenever conditions in the home allow it, the less severely malnourished patients may be treated more adequately in an ambulatory setting.

Treatment is divided into three stages: 1) attending to acute problems, 2) restoring nutritional balance, and 3) ensuring nutritional rehabilitation. The first stage consists of treating potentially life-threatening complications or metabolic disorders, such as infections, fluid and electrolyte disturbances, heart failure and severe anemia. The second stage provides nutritional replacement therapy designed to correct metabolic functions and to maintain homeostasis. There is general agreement on the principle of providing protein and energy in foods that are easily digested and, at least during the first few da therapy in a liquid form administered orally nasogastric tube if necessary. Parenteral nutrition rarely indicated. As the child's nutritional condition improves, the second stage gives way to the third stage. It may begin in the hospital, but must continue on an outpatient basis. In this phase other foods must be reintroduced into the diet, especially those available at home, but in combination with the energy- and protein-rich and highly digestible foods used in the hospital. Care must be taken to ensure a minimum daily intake of 3 to 4 g of protein and 120 to 150 Kcal of energy per kg. To achieve this, the patient must be fed a diet of solid foods whose energy density and protein density and quality are high. The energy density can be increased by supplementation with oil or fat, protein quality can be improved by mixtures of animal and vegetable proteins.

Deficiency of Micronutrients In Severe PEM

It is important to realize that PEM also includes deficiencies of many micronutrients. Deficiencies of vitamin A and E, potassium and magnesium, and of the trace minerals — iron, zinc, chromium, and selenium — usually accompany PEM.

It is well known that vitamin A replacement is an early priority in the therapy of PEM, failure to replete the exhausted vitamin A stores prior to protein and energy rehabilitation often precipitates the severe ocular manifestations of hypovitaminosis A, xerophthalmia and keratomalacia. It has recently been shown, moreover, that some of the reduction in circulating retinol levels is due to deficiency of zinc. Zinc plays an important role in the release of retinol-binding protein from the liver. In Hyderabad, Shingwekar et al[30] showed that zinc therapy — exclusive of protein, energy or vitamin A

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TABLE 3

EXAMPLE OF A DIETARY THERAPEUTIC REGIMEN FOR CHILDREN BASED ON DRY SKIM MILK, SUGAR AND VEGETABLE OIL*

Days from Beginning of Treatment	Protein (g)	Energy (kcal)	Milk (g)	Sugar (g)	Oil (ml)	Water (ml)
1	0 8 - 1.0	80-100	3	17	2	100
3	1.5 - 2 5	100-120	6	20	2	130
5	2 5 - 3 5	140-150	9	20	4	150
7	3 5 - 4 5	150-160	12	20	4	160
12 (marasmust)		175†			6†	
17		195			8	
22		215			11	
etc	3 5 - 4 5	†	12	20	†	160

All amounts per kg body weight per day The liquid formula must be supplemented with adequate levels of vitamins, minerals and electrolytes

†Marasmic patients may require more than 150 to 160 kcal per kg per day Vegetable oil to 3 ml per kg per day at five-day intervals should be added until the rate of weight gain becomes adequate [35]

supplementation — raised circulating vitamin A levels in children with edematous PEM.

Repletion of potassium and magnesium stores is an important facet of therapy because the deficiency of these two nutrients can retard clinical recovery Golden and Golden[31] have recently demonstrated that zinc may also be a limiting nutrient in recovery. Malnourished children achieved a greater velocity of weight gain during the period of rapid catch-up growth when zinc was added to their rations, these children also deposited a greater proportion of recovered weight as lean tissue

Iron is one nutrient that can be conserved during periods of dietary restriction of protein and energy Nonetheless, low hemoglobin levels are characteristic of kwashiorkor and marasmus Viteri et al[32] determined that this was most often a "physiological" anemia due to the decreased demand for oxygen by a depleted lean-body mass, and a consequently reduced demand for oxygen transport The low efficiency of absorption of iron seen in some children with severe PEM appears to be due to nutritional damage to the intestinal mucosa [33] Recent studies in our laboratories suggest that this reduced absorption is the result of a functioning regulatory system for iron uptake and that it may be related to the relative adequacy of the body stores to support the decreased demand for circulating red cells (B Caballero, N W Solomons B Torun, unpublished data, 1982)

Severe PEM as an Adapted State

A key to the treatment of children with severe malnutrition is the realization that the organism adapts metabolically to the loss of lean mass and energy reserves. On the premise that the patient has adapted fully or partially to the malnourished state, it seems reasonable to begin nutritional treatment slowly and to increase nutrients gradually, especially in the cases of edematous malnutrition [34] In fact, a premature introduction of high-energy and high-protein formulas may be fatal [35] Various initial regimens have been advocated [36,37] Table 3 shows one such regimen followed by the authors, which has led to excellent results and relatively low (5% to 15%) case fatality rates [37] The milk diet is supplemented to provide daily 6 to 8 mEq of potassium, 3 to 4 mEq of sodium, 1 to 2 mEq of magnesium per kg, 60 mg of elemental iron, 0 3 mg of folic acid, 5000 I U. of vitamin A and other vitamins and minerals The total daily volume of formula is divided equally into six to 12 feedings per day, depending on the patient's age and general condition This frequent feeding of small volumes prevents vomiting and the development of hypoglycemia

If the progressive advancement of the protein and energy content of the diet is moderate, as previously described, one can expect a gradual loss of, weight, corresponding to the diuresis of interstitial edema, followed by a phase of compensatory or "rapid catch-up growth" in which the child replaces the lean-body and adipose tissue appropriate to stature (Figure 1) This velocity of weight gain is often 15 times that in a healthy child of the same age Finally the growth velocity

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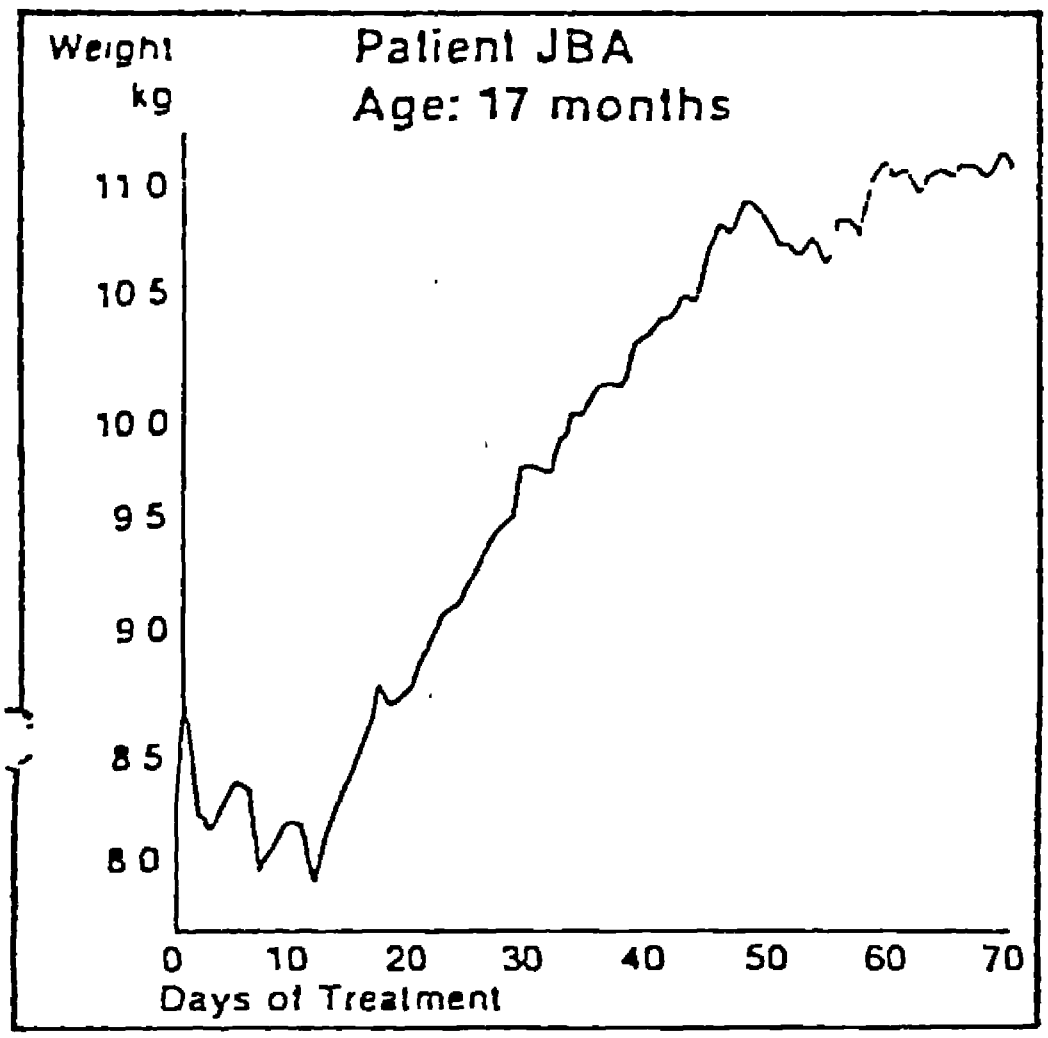

Figure The graphic record of the daily weights of a preschool child admitted to the Clinical Research Center of INCAP with severe PEM of the edematous type During the first ten days there was a diuresis of the edema, this was followed over the next 27 days by a phase of rapid catch-up growth during which time the child gained 7 6 g/kg daily finally the growth velocity moderated to assume that expected for a child of this height

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moderates to assume the pattern characteristic of a normal child of the same height.

Choice of Protein Source In Recovery Diets

Severe PEM is associated with changes in gastrointestinal ecology and function In part, these alterations are due to nutritional injury and adaptation to the semistarved condition, they are also attributable to infectious enteritides that commonly accompany clinical malnutrition [38,39] Therefore the patient may not be able to tolerate a normal diet.

Many clinical reports have made note of the reduction of mucosal disaccharidases and consequent impairment of the absorption of lactose in children with severe PEM We recently reviewed the literature related to the use of milk in malnourished children[40] and performed a retrospective survey of records from 24 children receiving a diet based on milk, delivering 3 to 4 g/kg of protein from milk and >120 Kcal of energy for from 20 to 49 days (Table 4) Our analysis has cast substantial doubt on the reported difficulties with diets containing cow's milk.[40] We conclude that, for routine treatment of severe PEM, it is not necessary to remove lactose from the diet

Other animal protein sources, such as meat and meat extracts or powdered eggs are generally well accepted and have excellent nutritional characteristics They a not as widely available however, as milk and their cos a limiting factor. Fish protein concentrates are relative inexpensive, but they are not usually accepted in non-f eating societie. Combinations of animal foods and oth proteins, eg, K-mix (a mixture of calcium caseinate, sk milk powder, sucrose and vegetable oil), are qu adequate to treat severe PEM.[41] However, such produc are generally less available and more costly than milk other single animal proteins

Soy protein is of particular interest because of its hi biological value in man,[42] but there is concern abo possible interference with the biological availability minerals that the high phytic acid content of the soybea might impose. Marasmic Jamaican children fed a so protein formula experienced a fall in plasma zinc ar reduced synthesis of lean tissue compared with the on a milk-based ration.[43] Whether other minerals are al made less available by soy, and what the compensato supplementation of soy-based recovery formulas shou be, remains to be clarified by future research

Vegetable-protein mixtures with good essential amin acid complementation have become popular dieta supplements in the developing world Many are suitab for nutritional rehabilitation diets for children wi moderate or severe PEM. They are prepared in mar countries, usually from locally available grains ar legumes, and are enriched with vitamins, minerals ar energy sources (lipids or carbohydrates) Protein in the mixtures is 10% to 20% less digestible than are anima proteins This makes it necessary to feed large amounts c the mixtures to meet protein needs The bulki consistency of some vegetable mixture preparation makes it difficult to provide 4 to 5 g protein per kg per da to small, severely malnourished children Three grams pe kg can usually be consumed comfortably by childre recovering from malnutrition These considerations ar pertinent to the present strategy to educate mothers in th preparation of weaning foods from blends of locall available vegetable protein sources

Mild and Moderate Malnutrition

The less severe forms of PEM should be treated in a ambulatory setting by supplementation of the child home diet with easily digested foods that contain protei of high biological value and a high energy density Th quantity of food will vary, depending on the degree o malnutrition and on the relative deficit of proteins an energy. As a general guideline, the goal should be t provide a total intake — including the child's home diet – equal to at least twice the protein and 1 5 times the energ requirements For preschool children this would mea daily intake of 2 to 2 5 g of high quality protein and 120

TABLE 4

CATCH-UP GAINS OF 24 CHILDREN WITH PROTEIN-ENERGY MALNUTRITION TREATED AT INCAP'S CLINICAL CENTER WITH COW'S MILK FORMULAS FOR 20-49 DAYS*

Severity of PEM at the beginning	Number	Age, months	Initial weight-for-height percent of expected†	Weight gain, g/day	Weight gain, g/kg/day
Weight-for-height					
<80% of expected†	12	26 ± 6‡	76 ± 2	76 6 ± 15 5	8 7 ± 1.7
		(14 - 37)	(70 - 79)	(58 1 - 100 0)	(6 3 ± 11 4)
Weight-for-height					
≥80% of expected†	12	29 ± 13	84 ± 3	79 0 ± 32 1	7.8 ± 2 3
		(18 - 66)	(80 - 88)	(39 5 - 151 9)	(4.1 - 12.1)
Total	24	28 ± 10	80 ± 5	77.7 ± 24 7	8 2 ± 2 0

*The diets provided 3 to 4 g protein, 5 to 6 g lactose and 150 Kcal/kg/day, and they were fully consumed by the children
†Relative to 50th percentile of well-nourished standards weights after disappearance of edema
‡Mean ± SD Range within parentheses
Reproduced with permission from Torun B, Solomons NW Viteri FE Arch Latinoam Nutr 1979, 29 445-494

150 Kcal per kg of body weight

Two important factors should never be overlooked in the treatment of mild and moderate PEM 1) ensuring the intake of the food supplements by the target (the malnourished child) and 2) avoiding a major substitution effect on the household diet (ie, a decrease in the usual food intake) The ingestion of the food supplement by the malnourished child is more likely to occur if it is appetizing to both the child and the mother, if it is ready-made or easy to prepare, if additional amounts are provided to feed the siblings, and if it does not have an important commercial value outside the home that would make it easy and profitable for the family to sell the item for cash. A substitution effect on the home diet is almost unavoidable, but it can be reduced to a minimum by using low-bulk supplements of high protein and energy densities Special attention should be given to maintenance of breast feeding The supplements for breast fed infants should be paps or solid foods, which will not quench the infant's thirst and thus not change the infant's demand for breast milk (Table 5)

As in severe PEM, the diets should be supplemented with minerals and vitamins, as needed, and infections should be treated

PREVENTION AND CONTROL OF INFANTILE MALNUTRITION

The main goal of nutritional programs is the eradication of infantile malnutrition through preventive measures They include the availability and rational use of foods that optimize utilization of nutrients, control or reduction of infections that decrease appetite, reduce intake, increase nutrient losses, and tax the child's reserves, and education programs relating to nutrition

Availability of Food

Food may be unavailable because of poverty, cultural food taboos, cyclical climatic conditions, and natural and manmade disasters Solution of some of these conditions is beyond our control, however, the pediatrician, nutritionist, public health worker and educator can play an active role in ameliorating or solving those that are Among these, one can provide instruction about more nutritious combinations of foods available to the household and about better infant feeding practices

It will often be necessary to convince the child's parents about the safety of using foods that, in some cultures, are fed only to adults and older children This is especially true in the case of weaning foods Trials have shown that it is feasible to feed pablums based on legumes, a cereal and vegetable oil, to babies as young as three months without causing intestinal discomfort, and *without decreasing intake of breast milk* (Table 5).

Presence of a malnourished child in a family is an indicator that other members of the household might also be malnourished Therefore nutritional and health education must not be restricted to the rehabilitation of the index case, but to prevention of nutritional deterioration of other family members, especially siblings and pregnant and lactating women Similarly, a high

TABLE 5

PAPS TO COMPLEMENT BREAST MILK, USING COMMON FOODS AND BASED ON COMBINATIONS OF A LEGUME, A GRAIN AND VEGETABLE OIL

	A	B	C	D
Cooked beans*	25†	20	20	25
Vegetable oil	12	7	7	10
Corn dough‡	20	—	—	—
White bread**	—	10	—	—
Boiled rice	—	—	22	—
Boiled potatoes	—	—	—	31
Protein, g/100g††	5.6	7.1	6.1	5.5
Energy, kcal/100g††	312	268	269	232

*Black beans (Phaseolus vulgaris), cooked and strained according to Guatemalan customs.
†Amounts of ingredients in grams
‡Cooked, lime-treated corn dough
**Moistened with about 50% water.
††Protein and energy content of 100g of pap, ready to eat.

prevalence of children with malnutrition (wasted) or growth retardation (stunted) indicates that their entire community is at some risk of impaired nutrition. Consequently, education programs must also be devised for community leaders, civic action groups and the community as a whole.

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32

Protein-Energy Malnutrition

Protein-energy malnutrition (PEM) encompasses a wide spectrum of general nutritional conditions that range clinically from almost unrecognizable symptoms to the florid pictures of starvation and kwashiorkor.

PEM can be primary or secondary, that is, the result of a primary deficit in food intake or the consequence of other primary alterations that impair food intake, absorption, or utilization, or that increase energy and/or protein needs or losses. This chapter focuses on primary PEM, a prevalent nutritional deficiency condition among populations in most developing countries. PEM generally is associated with poverty, limited availability of food, unsanitary environments, high rates of infection, and marked socioeconomic inequalities. Clearly, PEM can assume epidemic proportions as a consequence of natural, political, or sociodemographic calamities.

The clinician can diagnose PEM among population groups by being aware of characteristic social settings (even in the absence of specific clinical signs), functional consequences and patterns of morbidity and mortality. Affected population groups are generally deprived. Food intake is monotonous and food often is scarce. Physiologic performance is suboptimal (i.e., poor growth, high prevalence of small babies at term, substandard mental performance, lower relative physical activity levels in tasks that demand energy). A few cases of severe, clinically evident PEM are seen, the endemic rate of infections (mostly gastrointestinal) is elevated, and infant and preschool mortality rates are high.

At the individual level, the diagnosis of mild or even moderate PEM is often difficult without adequate information about the setting and conditions of the family and the community as a whole. Even then, in the isolated patient, PEM is often an exclusion diagnosis arrived at after chronic infection, malignancy, other secondary causes, and primary, nonnutritional alterations in physiological performance have been discarded.

Another problem in diagnosing PEM is the duration of the process as well as its sequelae. Acute and severe PEM is often superimposed on chronic mild to moderate PEM. Frequently sequelae related to the inadequate environment and previous PEM (stunted,

poorly developed individuals) lead to the diagnosis of PEM when it is no longer present. At the population level these sequelae can be functionally significant. Thus, large-scale prevention, early detection, and prompt and effective correction of protein and energy deficits are imperative.

Etiology

Primary PEM results from prolonged deprivation of essential amino acids and total nitrogen and/or of energy substrates. The limiting nutritional factor(s) at the onset of the process leading to PEM can be protein-nitrogen (essential amino acids and nonessential nitrogen) and/or total energy. Each of these deficiencies can occur singly, that is, in the presence of adequate or excessive amounts of the other nutrients, or as combined deficiencies. However, as the severity and duration of a specific deficiency advances, the other factors also become deficient. For example, in pure energy deficiency protein nutriture can be spared initially; however, in more advanced energy deficiency, protein is utilized for energy. Similarly, as protein-nitrogen becomes less available, the efficiency of energy utilization declines. In practice, then, except for very acute situations, the vast majority of cases with moderate to severe PEM present with a combined protein-nitrogen and energy deficiency either part of which still may predominate.[1]

In the absence of complicating factors, which could alter the absorption, transport, and utilization of protein-nitrogen and energy, the cause of these deficits at the cell level is inadequate intake. Inadequate intake is defined as intake not sufficient to meet the individual's needs. The levels of essential amino acids, total nitrogen, and energy have been defined (chapters 1 and 2) in terms of both minimal requirements and recommended intakes.

Conditioning Factors

From the standpoint of the deficiency or adequacy of protein and energy intakes in relation to the etiology of PEM, several conditioning factors must be considered. First, the staple foods and preparation techniques typical of individual cultures, together with other cultural determinants of total food intake must be known in order to evaluate energy and protein intakes at the population level. Second, although total food intake may be adequate for the population as a whole, it may be inadequate for certain groups that require more protein or energy per kg body weight. The above consideration recognizes the importance of: patterns of food intake at different ages and intrafamilial food distribution; protein and energy density of foods and differences in food preparation techniques; and food bulk and satiety.

Finally, protein sources must be known in order to judge whether they provide adequate amounts of the essential amino acids in bal-

anced proportion (protein quality) as well as adequate amounts of total nitrogen. Protein quality is especially important when protein needs are higher per kg body weight (early childhood). In this age group animal protein is normally fed (breast milk, other milk preparations) to satisfy protein needs. Other animal or selected vegetable sources of protein, which are often mixed to complement their essential amino acid contents, can serve as substitutes for milk (for example, corn and beans, providing 50% of protein from each source; formulated vegetable protein mixes).

The causes of inadequate food intakes that lead to PEM now can be analyzed from the standpoints of the individual, the family unit, and the population as a whole.

Causes of PEM in Infants and Children

The persons most often afflicted with PEM are children under 5 years of age.[2] These children appear to be the most vulnerable group because both the proportion of the population afflicted and the incidence of severe PEM are higher in this group than in any other age group. This situation is determined by host, environmental, and agent factors.[3]

Host Factors: The host factors are as follow.

1. A child under the age of 5 years has high protein and energy requirements on a body weight basis, particularly if he/she was small at birth (premature, small for date, or both).
2. A child under 5 years of age has a limited capacity to ingest large amounts of food at a single sitting.
3. A 5-year-old or younger child has no access, or only limited access, to food at will.
4. Once the child is malnourished, his/her condition is complicated further by lowered defenses against infectious agents, resulting in more frequent illness, anorexia, irritability, listlessness, and deterioration of appearance and affective interaction with caregivers as time elapses.

Environmental Factors: The environmental factors are as follow.

1. A woman malnourished prior to and/or during pregnancy and lactation is more likely to produce an underweight baby.[4] Lactation in these cases often is inadequate and affective interaction is impaired.
2. Poverty almost always is an underlying cause of PEM. Living quarters are overcrowded, the environment is often dirty and lacks the most basic hygienic conditions (particularly in slums and camps), and often the parents do not care for the child. Thus the child is weaned at an early age and is exposed to infection due to lack of proper attention. Substitute food preparations under these circumstances are added sources of infection and of improper nutrition. Infection and undernutrition act synergistically to aggravate both conditions.[5]

3. Cultural considerations in poverty-stricken populations are essential in the analysis of environmental factors in PEM. On the one hand, in cultures where breastfeeding is still universal and lasts for the greater part of the first 12 or 24 months, PEM begins during the third and fourth month of life and is progressive because breast milk alone cannot provide enough energy and protein beyond 3 months to 4 months of age. Although complementary foods are essential, often they are introduced late and inappropriately. Thus, weaning becomes a critical nutritional period. On the other hand, socioeconomic demands and improper practices of assimilation, particularly in urban settings, have resulted in a marked decline in breastfeeding. Improper feeding practices (nonhygienic preparation of overdiluted formula or substitution of milk for unsanitary sugar water or starch gruels) result in early-age severe PEM. The whole weaning process encompasses a very delicate period for the child under these circumstances; but, even after weaning, in the face of scarcity, the small child receives the smallest and most inadequate proportion of the family pot. Moreover, cultural practices often dictate a restricted food intake when the child is sick; such children may be given only "medicinal" or "safe" beverages that have essentially no nutritional virtues and that even may be toxic.

Agent Factors: The primary agents in these cases are the scarcity and/or poor quality of the diet ingested by the child.

1. Insufficient intake occurs in the child principally as a result of one of three causes: (a) the child is offered little food and is still unable to get more by him/herself (for example, restricted intake during illnesses or prolonged exclusive breastfeeding); (b) the child is offered ample food but of an improper quality for his/her needs, resulting from low protein and/or low energy densities or from improper preparation for the gastrointestinal and general functional capacity at his/her age (for example, diluted formula, cereal- and root-based gruel or porridge, unmodified cow's milk given to newborns and premature babies, and improperly prepared complementary foods fed to infants); and (c) the child is given food to satiety only a few times per day or when he/she is anorectic, resulting in diminished total intake in either case.

2. Children frequently ingest a poor quality diet because they often are given overdiluted milk formulas and/or foods that are bulky, starchy, and poor in protein content, a result of a low protein concentration (low protein density) and/or an imbalanced amino acid composition. In this case the proportion of protein utilized for synthetic purposes is, at best, that of its most limiting amino acid (see chapter 1). In terms of energy, food preparations that are rich in starches and undigestible fiber, bulky, and very poor in fat content (low energy density) usually cannot provide the required energy. Moreover, imbalanced diets produce anorexia. Protein-poor but carbohydrate-rich foods are particularly prone to produce acute severe protein deficiency through mechanisms that are discussed below (see section on pathophysiology).*

Causes of PEM in Older Children and Adults

In addition to children under the age of 5 years (and especially under 3 years), the elderly, pregnant and lactating women, and adolescents are also vulnerable groups for some of the same reasons already discussed but also for the following specific factors more prevalent for their different ages and physiologic conditions.

The Elderly: The elderly often are unable to care for themselves properly and, with advancing age, their energy requirements fall as a consequence of inactivity and of slight reductions in maintenance energy requirements. Their protein needs, however, do not seem to diminish at the same rate. Therefore, the food consumed must be more carefully balanced in terms of protein density and quality. In addition, a more sedentary life, the frequent existence of other nutritional deficiencies, and alterations in behavior often lead to anorexia and neglect in eating habits.

Pregnant and Lactating Women: Pregnant and lactating women require both more energy and more protein than nonpregnant, nonlactating women of reproductive age. At the same time, pregnant women often suffer nausea in the early periods of pregnancy and their gastric capacity is somewhat reduced as pregnancy advances. In primitive cultures pregnant and lactating women remain active and probably do not reduce their energy output as much as those women in developed societies do. Adequate energy and protein intakes appear to be essential during pregnancy and lactation to ensure satisfactory reproductive performance.[7]

The Adolescent: In primitive societies the adolescent participates in the labor-intensive chores of the adults and at the same time undergoes rapid growth often complicated by teenage pregnancy. Therefore, the adolescent's protein and energy needs are high. In developed societies the abundance of diet fads can predispose teenagers to some degree of PEM.

Older Children and Adults: Older children and adults in developing countries, although nutritionally less likely to develop moderate or severe PEM, also often suffer moderate, and predominantly mild, energy deficits. This energy deficiency can result in lower physical activity both at school or work and outside of work, with consequences more evident in the spheres of productivity, social and family interactions, and community development activities.

Family and Community Etiologic Factors

Since describing PEM from the family or community standpoint is not the primary purpose of this chapter, the factors conducive to primary PEM at family and community levels will be analyzed only briefly here. In general, PEM affects the family as a unit even though different members may present with deficiencies in varying degrees of severity. Where poverty and ignorance are prevalent, malnourished mothers with severely malnourished children are a

common sight; however, obese mothers with severely malnourished children are also seen. Mothers of the latter type often relate the beginning of PEM to an infection that was followed by repeated bouts of diarrhea, anorexia, and progressive PEM. In these cases, older or younger siblings often appear healthy or only mildly malnourished. An analysis of the situation may disclose that the mother progressively had withdrawn foods from the sick child while he/she was being given medicines and multivitamin preparations prescribed by physicians or other health workers, employees at drug stores, traditional healers, or relatives. The point is that, just as the woman appears ignorant of her own and her family's dietary practices, there is also ignorance and a general impression of impotence in trying to bring health back to severly malnourished children once a vicious cycle of PEM and other diseases is established. (See the section on pathophysiology for the role of infection as a precipitating cause of severe PEM).

Families of malnourished children are often disorganized usually with uneducated parents. Alcoholism and other social diseases are evident among many malnourished families. In general, a malnourished child clearly indicates a lack of well-being in the family as a whole; the family must be investigated and must become the center of rehabilitative measures. The same general thinking applies to the community where malnourished families exist. Malnutrition implies social disease and requires prompt attention.

Many schemes have been drawn to explain the factors that, at a macro level (community-national-regional levels), are conducive to PEM.[8] All indicate multiple interactions among poverty, population growth, food production and general food policies, food preservation and distribution, health status, education, and migration. All agree that malnutrition is the ultimate result and, at the same time, often a perpetuating factor in very complex and diverse social-political-economic conditions originating far back in the development of cultures and nations or as a result of recently developed pressures. Consequently, abolishing malnutrition requires diverse and often bold actions. Malnutrition in Chile, northwestern Argentina, tropical Africa, India, and even rural and urban Guatemala is the result of different yet often comparable etiological factors. Therefore, it is essential to understand the etiologic details in each region to design effective strategies for controlling and preventing PEM.

Epidemiology

Based on the etiologic considerations discussed above most of the epidemiologic characteristics of PEM can be described in terms of global magnitude, general trends in populations undergoing rapid urbanization, and the problem of effective food distribution.[9]

Global Magnitude

The global magnitude of PEM is difficult to estimate with precision. However, rough estimates of the affected population in different regions and countries can be obtained by evaluating the proportion of individuals who chronically consume food in amounts that provide less than 1.2 times their basal energy expenditures. This estimate is based on a series of assumptions that makes it somewhat imprecise. Two main variables are the precision by which chronic food intake is measured and the value of individual basal energy expenditures used as cut-off points. The variance from both these factors easily can add up to 30%. In spite of these limitations, the figure of 1.2 times basal energy expenditure is useful as a relative standard that, in theory, is the minimum intake necessary to live a very sedentary life.[10] Therefore, it reflects the lower limit below which energy deficiency undoubtedly would occur. There are various terms for this level, one of which is physiologic energy needs (PEN). Food intake at the population level, however, must be enough to allow the population to fulfill its function properly, in accordance with its life style and optimal developmental rate. Many persons can fulfill their PEN but still be limited in their functional performances by their food intakes. The number of malnourished persons can be much higher according to this criterion (the recommended energy allowance or REA) than that computed on the basis of the PEN. Therefore, in spite of inaccuracies, the estimate based on PEN still can be conservative, particularly if it is realized that developing societies often depend on energy-intensive life styles and, therefore, on relatively high REAs.[11]

PEM Trends

With this understanding in mind, the proposed next step links income (and poverty) to food (and energy) intake and projects the estimated population that, on the basis of income (or poverty level), cannot acquire enough food to fulfill its PEN. The inaccuracy of these projections extends beyond the simple fulfillment or nonfulfillment of PENs. However, it links the estimate of destitute populations, or of the marginal population in "extreme poverty" or "extreme underdevelopment," with the nutritional component. Obviously, populations in these categories not only are undernourished but, in general, are in a desperate situation in terms of life fulfillment and of health as defined by the World Health Organization (WHO).

The Food and Agricultural Organization (FAO) [12] and the World Bank have provided estimates of the global magnitude of PEM. These estimates indicate a total number of PEM victims as between 450 million and one billion persons. Almost all of these people are in developing countries; 56% are in developing countries classified as "most seriously affected" in terms of the world economic crisis.

Population distribution by regions as of 1972–74, according to the Fourth World Food Survey,[12] is as follows:

Region	Number below PEN	Percentage of Population
Far East	297 million	29
Africa	83 million	28
Latin America	46 million	15
Near East	20 million	16

Food Distribution

Estimates of food availability, translated into energy and protein supplies, can be summarized for the years 1969–71 from the 1974 UN World Food Congress[13] as follows.

The energy supply (kcal/person/day) and the protein supply (g/person/day) data available from 33 developed countries indicated that the lowest energy intake was in Japan: 2,510 kcal/person/day (107% of the estimated requirements). The overall mean energy intake, based on country means, was 3,136 kcal/person/day (S.D. 280). The percentage of estimated supplies to fulfill requirements ranged from 99 to 136. In terms of protein, the range was from 74 g/person/day in Albania to 109 g/person/day in New Zealand.

In contrast, data available from 95 developing countries showed a wide range of values in both energy and protein supply. Only 37 (39%) of these countries averaged energy supplies above 100% of estimated requirements. Thirteen percent of these countries showed dietary energy supplies below 2,000 kcal/person/day, which is lower than 86% of estimated requirements (range, 72% to 85%). In terms of protein, the range is from 33 g to 106 g/person/day; however, only 9 of 93 developing countries with available data had 74 g protein supply/person/day, the lowest level found among the developed countries.

Global projections of future food supply indicate that the current differences between countries with different degrees of development will increase. Projected food demands showed increases of 26% for developed countries and 70% for developing countries between 1970 and 1985. Given these conditions, even at a calculated high rate of increase in food availability, the global per capita supply would be stationary at best. The situation becomes more serious for developing than for developed societies because the former have a near threefold increase in demand rate and because the distribution of food and resources is known to be unequal between more affluent groups and those with scarce assets.

As indicated previously, in the face of food scarcity, young children (infants and preschoolers), the elderly, pregnant and lactating women, and adolescents are more vulnerable to PEM.

PEM Indicators In Children

Growth retardation, weight and height in relation to age, type of infant feeding, and mortality rates are a few indices of the relative magnitude and severity of PEM.[14]

Growth Retardation

A manifestation of PEM in children is growth retardation. If PEM occurs for a prolonged period of time in relation to the child's age and if it occurs early in life, when linear growth rate is higher, stunting is one result. The recovery or catch-up in linear growth is a slow process and can occur only in situations that ensure optimal conditions in terms of health, nutrition, and general stimulation. On the other hand, acute severe PEM at any age causes weight loss and mild to moderate PEM at least reduces weight gain. Under adequate conditions catch-up in weight can be dramatic and complete. PEM, therefore, affects both components of growth — linear and body mass increments; however, these components are affected differently and, in a way, the attained stature at a given age determines the maximal body mass (weight) a child can achieve. Weight, then, generally should be interpreted in terms of height: as weight for height.

Weight and Height

When only a child's weight is available and it is below normal, it can mean, in terms of PEM, that the child either *is* or *was* malnourished. If the height is also below normal, the process has been chronic, but one still cannot determine if the process exists in the present or existed in the past. If weight and height are compared and weight is found to be adequate for height, this being subnormal, the child previously has been stunted by PEM but currently has adequate body mass for height. If the body weight is below normal for the child's subnormal height, the child *is* and *has been* malnourished.

Most estimates of PEM prevalence are based only on weight determinations. On this basis, children with weight deficits greater than 40% for their age and/or having edema are considered to be suffering from severe PEM. Those with deficits between 10% and 40% may be moderately malnourished but the risk exists of calling a child malnourished when he/she is only stunted from previous PEM and now has adequate weight for height. With these limitations on the estimates, roughly 75% of preschool children in developing countries show some degree of PEM. In any case they have been malnourished and point out the poor overall community situation. Roughly 3% of the children in Asia, Africa, and Latin America present with severe PEM (range, .05% to 20% according to 25 different surveys from 1963 to 1973) and 20% present with moderate forms (range, 3.5% to 46.4% according to the same surveys).[2]

Infant Feeding and Age

In populations at risk, PEM is generally seen at a later age in children who have been breastfed than in children fed by bottle. In these PEM cases, energy deficiency is predominant and is aggravated by frequent bouts of infectious diarrhea. Severe marasmus is the predominant form of PEM in early infancy and kwashiorkor occurs later in the weaning period or in preschoolers.[15]

Mortality Rates

Mortality patterns also reflect malnutrition in childhood. Four characteristics are particularly useful: total mortality in children under 5 years old; ratio of infant mortality to that of the 1- to 4-year-old age group and, within the infant group, the ratio of neonatal to postneonatal mortality; mortality rate associated with low birth weight and "immaturity"; and mortality rate due to diarrheal disease. The inter-American research on mortality in childhood illustrates the usefulness of two of these characteristics.[16]

Mortality in Children under 5 Years: Total mortality in children under 5 years of age was 48 and 50/1,000 in rural Bolivia and rural El Salvador, respectively; in Sherbrooke, Canada and suburban California, it was only 4.1/1,000. Santiago, Chile, and San Juan, Argentina, each had a total mortality of 13/1,000.

Infant/1- to 4-Year-Old Mortality Ratio: The ratio of infant mortality to that of the 1- to 4-year-old was lowest in the rural areas of El Salvador and Bolivia (ratios of 4.6 and 5.7/1,000 respectively) and highest in the cities of San Juan and Santiago (ratios of 33.8 and 30.5/1,000 respectively). Sherbrooke and suburban California each showed a ratio very close to 23/1,000. These data suggest that late chronic PEM exists predominantly in areas with low infant/1- to 4-year-old mortality ratios; these areas also have very high mortality rates in both age groups. In San Juan and Santiago, infant mortality was almost three times higher than that in Sherbrooke and suburban California; the 1- to 4-year-old group mortality rate was nearly twice as high in San Juan and Santiago as in Sherbrooke and suburban California. These comparisons show early urban malnutrition as a predominant problem in Santiago and San Juan.

The neonatal to postneonatal mortality ratios further clarify this problem: in Sherbrooke and suburban California the neonatal mortality was nearly three times higher than the postneonatal mortality. In Santiago and San Juan this ratio was near 1/1,000; and in rural El Salvador and rural Bolivia it was 0.7 and 0.4/1,000 respectively.

These statistics illustrate the well-known fact that, as child health and medical care improve, mortality in children under 5 years is concentrated in the neonatal group; the statistics also show that poor child health and nutrition shift the highest mortality rate to the postneonatal period because the less favorable circumstances extend the elevated death rate beyond the first year of life. Conversely, mortality in the 1- to 4-year-old group is the first to be reduced as

nutrition and other preventive health measures directed to the child are improved.

Pathophysiology

Four basic concepts define the pathophysiology of PEM. [1,17-19]

1. PEM is a dynamic state to which the subject adapts and survives in a compensated state.
2. Severe deficiencies or the superimposition of stressful situations can cause decompensation, which is translated into severe disease.
3. PEM induces harmonic changes in: (a) intracellular energy and amino acid metabolism; (b) intracellular electrolyte concentrations; (c) changes in enzyme activities (organ-specific as well as general); (d) hormone levels and end-organ action; and (e) body composition with all its functional consequences.
4. Adaptation to deficiencies in protein and/or energy imply functional repercussions and alter host-environment interactions.

Energy Equilibrium

In the compensated state, energy equilibrium is achieved in the reduced energy intake phase by reducing energy expenditure. Depending on the severity of the energy deficit, diverse mechanisms come into play: mild deficits can result in only a diminution of physical activity and/or a slightly increased energy reserve (adipose tissue) mobilization. As deficits become more severe, the impact on these mechanisms increases and utilization of body protein (primarily muscle) begins to be used for energy. This process, together with utilization of visceral protein, is greatly accentuated in severe energy deficits (starvation). In these cases a prompt initial reduction in basal metabolic rate is followed by a progressive reduction that parallels the diminution in body protein (lean body and active tissue masses).

Energy Reserve Mobilization

Mobilization of energy reserves is accomplished by neurohormonal mechanisms, including decreased insulin activity due to diminished stimulation from food intake, increased epinephrine and norepinephrine production, decreased intracellular potassium, and elevated free fatty acid levels as a result of increased growth hormone, glucagon, glucocorticoid, and catecholamine levels. These hormonal changes also favor the mobilization of amino acids from muscle and their visceral utilization for gluconeogenesis; moreover, amino acid nitrogen is spared by more efficient recycling, by the promotion of specific transamination reactions, and by a reduction in urea cycle enzyme activities. As the need for oxygen declines, the hypothalamohypophyseal thyroid axis diminishes thyroxine and

triiodothyronine levels. This general adaptation mechanism can be upset by infection, which induces hormonal alterations that lead to diminished utilization of fat and increased dependence on carbohydrate metabolism and amino acid catabolism for energy purposes.[20] Carbohydrate intake produces an increase in insulin activity and a consequent decrease in the hormonal mechanisms that lead to lipolysis and amino acid transport from muscle to viscera. Insulin promotes lipogenesis and amino acid deposition in muscle, thus upsetting the internal adaptative shift of protein synthesis from muscle to viscera. This, in turn, results in acute amino acid depletion at the visceral level and decompensation, as manifested by decreased albumin, apolipoprotein, and other transport protein synthesis and by a reversal of enzymatic systems that had resulted in adaptative increases in efficiency of amino acid utilization at the visceral level.

Kwashiorkor and Marasmus

Characteristics: The differences between kwashiorkor (decompensated PEM) and marasmus are primarily the presence of edema and of fatty liver. Edema results from sodium retention and excessive extracellular fluid accumulation with absolute intracellular fluid deficit (parallel to the reduction in body cell mass) but elevated cell water/g cell solids; intravascular spaces are preserved or even decreased (hypovolemia). Relative increases in extracellular fluid volume in the absence of clinical edema occurs in marasmus and in moderate PEM. The relative role of hypoalbuminemia, increased aldosterone and renin activities, altered renal and cardiac functions, and defects in the cell sodium pump as explanations for increased sodium retention are still debatable.

Potassium and magnesium deficits and mild levels of acidosis also are present in both kwashiorkor and marasmus and have two origins: (1) a decreased intracellular capacity to retain potassium associated with protein deficiencies and an accumulation of free acids (metabolites and amino acids); and (2) excessive losses of potassium, magnesium, bicarbonate, and other electrolytes as consequences of diarrhea and altered renal functions.[21,22]

Fatty liver primarily results from a decrease in beta-lipoprotein synthesis and, thus, decreased fat mobilization from the liver. It has also been proposed that liver fat synthesis increases.

The decline in albumin and other protein synthesis is associated with an overall reduction in the catabolism of proteins. Thus, total protein turnover is markedly depressed in malnutrition. During recovery, protein synthesis increases while protein catabolism lags behind, increasing later as protein repletion proceeds. In fact, with accelerated rates of growth, parallel increases in protein turnover occur, which also depend more on the levels of protein intake than on the levels of energy intake.[23]

Causes: Many of the clinical manifestations and fatal consequences of severe decompensated malnutrition result from infection

and/or forced carbohydrate feeding without adequate protein intake. On the other hand, many functional manifestations of malnutrition, whether mild, moderate, or severe, result either from alterations of functional capacity conditioned, in part, by the changes in body and organ composition already referred to or from the progressive adaptation of enzyme systems and organ function to a persistently reduced stimulus (such as: chronic meager food intake or, specifically, extremely reduced fat intake; lack of physical activity; reduced tissue O_2 needs because of progressive loss of active tissue mass) to which a chronic force of infection is superimposed. Thus, hemoglobin and red cell production are reduced to assure the necessary levels of O_2 transport as demanded only by the lower oxygen requirements that are defined by the diminished active tissue mass of malnourished children. Yet, red cell and hemoglobin production respond to hypoxia even in the presence of severe PEM; pancreatic lipase production is reduced but can be stimulated to high levels in the majority of severe PEM cases by administering fat; antibody production can be substantial in the presence of infection in spite of severe PEM; the hypophyseal thyroid system is less active but responds well to hypothalamic thyrotropin releasing factor; cardiac function is reduced but can respond moderately to increased circulatory demands, but a low cardiac reserve and a reduced oncotic pressure easily result in "wet lungs" and dependent edema. In other words, with the proper stimulation many functions "adaptatively" depressed in PEM can respond to additional demands, even in the presence of severe protein and energy deficiencies, although with certain limitations.[1,24]

An important alteration in severe PEM is the inadequate response to bacterial infection,[25] an alteration particularly critical in the gastrointestinal and respiratory tracts, which have their own ecologies as open systems. Bacterial overgrowth takes place in both systems, resulting in increased incidences of diarrheal episodes and of both upper and lower respiratory infections. In the intestines, the mucosal cells are shorter and have slower turnover rates (as is the case for all mucosal and rapid-turnover cell systems), the production of local antibodies is reduced, bacterial overgrowth results in increased free (unconjugated) bile acids at the upper intestinal level, and the micellarization capacity for fat is reduced. This process is essential for long-chain fatty acid absorption. In addition, the free bile acids are toxic to the gut cells. Severe PEM reduces the rates at which facilitated and active transport mechanisms absorb carbohydrates.[26] The gastric and enteric barriers to bacterial penetration are faulty and thus the gastrointestinal tract becomes an important source of bacteremia, urinary tract infections, and septicemia with fatal consequences. In the respiratory system, "wet lungs" clearly promote bacterial overgrowth. Cell-mediated immunity in general is impaired. Leukocyte migration, phagocytic capacities, and T cell production and function are reduced, leading to defective tissue defense mechanisms, including delayed hypersensitivity reactions.[27]

Histopathology

Acute infections (respiratory, gastrointestinal, urinary, septicemic) and superimposed specific nutrient deficiencies often are evident macroscopically and upon histopathological examination.

General pathology reveals tissue atrophy without any specificity except fatty infiltration of the liver, edema, and skin changes evident in predominant severe protein deficiency.[28] More atrophy occurs in tissues with greater turnover (intestinal mucosa, red bone marrow, pancreatic acini, testicular epithelium). Periportal fat appears first and advances centripetally as severity increases. The skin changes consist of dermal atrophy, ecchymosis, ulcerations, and hyperkeratotic desquamation, seen primarily in areas subjected to irritation and not necessarily restricted to exposed areas, as in the case of pellagra. Intestinal villi are flattened, and the enterocytes lose their columnar appearance. Gastric, colonic, and rectal mucosal atrophy are evident. Special staining techniques and electron microscopy can reveal many other minute alterations, not all of which result specifically from primary protein-energy malnutrition but do reflect generalized atrophy and the effects of infection as they affect specific cell types.

With nutritional recovery, these changes revert to normal, although some residual lesions may persist for some time, as in the case of diaphysoepiphyseal junctions. There is some disagreement about the completeness of pancreatic and intestinal recoveries.

Clinical Syndromes

Mild PEM

As indicated in the section on etiology, mild PEM cannot be diagnosed clinically with certainty. In children, some retardation in growth, apathy, and decreased physical activity plus a history of inadequate food intake and frequent infections can lead to a tentative diagnosis of mild PEM. The whole socioeconomic structure of the community and the family, as well as the presence of other specific nutritional deficiencies such as vitamin A and iron, may also suggest the diagnosis. In older children and adults, PEM is often difficult to diagnose.[28]

Moderate PEM

Moderate PEM results in an accentuation of the symptoms of mild PEM: greater deficiencies in height and weight with certain losses in lean body mass, flaccidity, apathy, repeated infections, and signs of other associated deficiencies. In women, inadequate weight gain during pregnancy, the delivery of small-for-date babies, and poor lactation performance also lead to moderate PEM diagnosis.

Severe PEM

Severe PEM[29] is the end result of a continuum that, when compensated by the efficient operation of adaptive mechanisms, is primarily manifested as tissue waste resulting in the clinical picture of marasmus in a small child and emaciation in older children and adults (e.g. World War II concentration camp victims). The marasmic child is primarily a very lean, hypotonic, hungry, "monkey-faced" child with a disproportionately big abdomen and head in relation to very thin limbs, evident rib cage, and sunken cheeks and eyes. Severely marasmic children may suck their thumbs and other fingers or may be too apathetic to do even that; they may be interested in their environment and cry actively, or they may be depressed to the point of coma. Normally, severely marasmic children are constipated or may pass small mucous stools, but these children also can suffer diarrhea and dehydration. Generalized infection and septic death are not uncommon. Hair is thin, dry, and fragile, like that of a doll, and falls out easily (fig. 32.1).

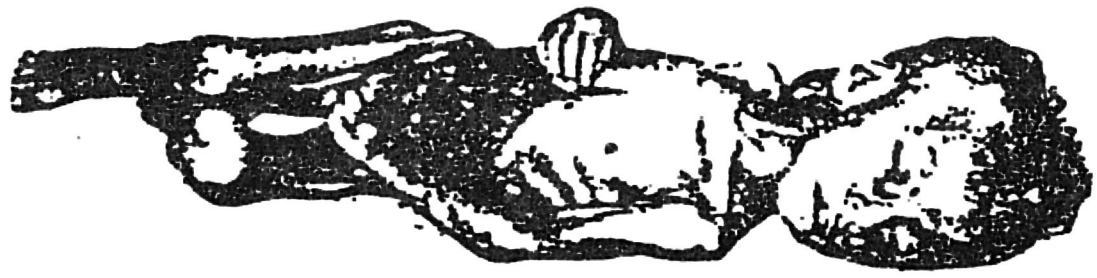

Figure 32.1. Sixteen-month-old child with marasmus. No edema or skin changes. Principal feature: emaciation.

The uncompensated state (kwashiorkor)[30] results from acute severe protein deficiency. This deficiency can exist alone (in cassava-eating populations or where children are force-fed starch or other carbohydrate-rich, protein-deficient foods) or as a consequence of infection. Kwashiorkor is characterized by: edema, soft-hepatomegaly (the fatty liver possibly extending down to the iliac crest), extreme apathy and irritability, and hair discoloration (reddish blond) with bands of dark and light hair reflecting the past nutritional history (flag sign), mucosal and cutaneous lesions that range from thinness, dryness, scaliness, and depigmentation through

hyperkeratotic large-scale skin desquamation of pigmented, mosaic-like lesions to deep ulcerations. Petechiae and ecchymosis are not infrequent with infection (figs. 32.2 and 32.3). In both kwashiorkor and severe marasmus, patients can develop acute corneal ulceration as a result of infection superimposed on severe vitamin A deficiency. These signs may result from: (1) malnutrition per se or (2) sequestration of vitamin A in the liver, as occurs also with fat, because of the marked deficiency of transport apoproteins (retinol-binding protein and beta-lipoproteins).

Figure 32.2. Eighteen-month-old child with kwashiorkor marasmus: edema, skin lesions, and loss of fat evident in rib cage.

Laboratory Findings

Hematologic, clinical, and nutritional chemistry findings can be summarized as follows.[28-30]

1. In the erythron, low hemoglobin concentration and low hematocrit are the rule, although the values may be within normal ranges. A diagnosis of anemia due to protein deficiency usually is false since hematopoietic-factor deficiencies responsible for anemia interact with hemodilution due to PEM. Iron and folate deficiencies, singly or together, are not uncommon, particularly when these substances are not provided in adequate amounts during nutritional recovery, which is accompanied by rapid expansion of the erythron.[1]

2. White cell and platelet changes compatible with folate deficiency are not uncommon and lymphopenia (especially of T cells) is the rule in severe PEM, accompanied by thymic atrophy. In children with severe PEM, the leukocytic response to infection may be curtailed, but changes resulting from septicemia and intravascular

coagulation can be noted as clearly as in well-nourished children with massive infections.

Figure 32.3. Thirty-two-month-old child with acute kwashiorkor of the sugar-baby type: edema, mild skin changes, and preservation of subcutaneous fat.

3. When protein intake is low and no renal impairment is present, the blood urea level is low. When PEM is decompensated, levels of serum albumin and transport proteins (transferrin, apolipoproteins, retinol-binding protein, transcortin) are low. In contrast, gammaglobulins may be elevated, particularly if infections are, or have been, present. Plasma amino acids are low, the branched-chain amino acids and tyrosine being more affected. Some nonessential amino acids may be present in higher concentrations. Serum enzymes (cholinesterase, alkaline phosphatase, amylase, and lipase) are low.

4. When protein intake is low and when muscle mass is reduced, urinary excretion of urea and creatinine, respectively, is low. Timed creatinine excretion, related to that of a normal child of the same height, can help estimate the degree of muscle mass deficit; this estimate gives results similar to those determined by total body potassium. Urinary hydroxyproline and 3-methylhystidine are also reduced, indicating low protein turnover (collagen and muscle,

respectively). unfortunately, infection can alter these nutritional indicators.

5. Serum levels of fat-soluble vitamins (A and E) as well as prothrombin time (responsive to vitamin K administration) are compatible with deficiencies of these nutrients. However, often they improve as protein nutrition improves and, as a result of transport proteins synthesis, they are mobilized from accumulated fat in the liver.

Often, biochemical indicators of water-soluble vitamin and mineral (trace elements) deficiencies are reported in different parts of the world, where such deficiencies tend to be more prevalent even among otherwise well-nourished populations.

PEM Classifications

Several classifications of malnourished children have been proposed for different reasons. A Mexican group proposed a classification based on body weight for age by which *children with a clinical diagnosis of malnutrition* were ranked on the basis of their risk of death.[31] Malnourished children were classified as grades 1, 2, or 3 if their body weight for age deficits were 10% to 25%, 25% to 40%, and greater than 40%, respectively. Children with edema also were classified as grade 3.

This classification has been used clinically and in survey work to identify nutritional deficiencies at the family and community levels. It has been misused when, on the basis of body weight for age alone, *children with no evidence of clinical malnutrition* have been classified as presently malnourished (see the discussion on etiology).

As discussed above, height and height for age must be known in order to define precisely the history of malnutrition and its type (marasmus, kwashiorkor, and marasmic-kwashiorkor) as well as to be able to monitor recovery and its completeness. The Joint FAO/WHO Expert Committee on Nutrition proposed the classification shown in table 32.1.[32]

Table 32.1. Simplified classification of protein-energy malnutrition

Condition	Body Weight (% of Standard)*	Edema	Deficit in Weight for Height
Underweight child	80–60	0	Minimal
Nutritional dwarfing	<60	0	Minimal
Marasmus	<60	0	Severe
Kwashiorkor	80–60	+	Severe
Marasmic-kwashiorkor	<60	+	Severe

*Source. From a report to the Wellcome Trust, 1968 [32]

*Standard taken as fiftieth percentile of the Harvard values [33]

+Weight for height=(weight of patient)/(weight of normal subject of same height)×100

These classifications are useful, but they obscure the fact that PEM is a continuum in which a progressive energy deficit results primarily in loss of fat and, only when late and very severe, in a substantial loss of protein, whereas protein deficiency results

primarily in loss of muscle protein in the presence or absence of body fat deficit.

To simplify, the greater the weight-for-age deficit in a malnourished population of children, the greater the risk of death; the greater the deficit in height, the more chronic and the earlier the problem of malnutrition appears; and the greater the weight-for-height deficit, the more severe present malnutrition is. Height and weight must be considered to evaluate the immediate correction of present malnutrition (by weight-for-height changes) and the long-term correction of chronic malnutrition (by height-for-age and weight-for-age changes).

Treatment

The treatment of a severely malnourished child is divided in three phases: the emergency phase, the initiation of cure, and the nutritional consolidation phase. [34-36]

Emergency Phase

The emergency phase deals with complications that normally hospitalize a child with PEM: infection, water and electrolyte disturbances, hypoglycemia and hypothermia, cardiac, renal, and respiratory failures, and other associated nutritional deficiencies.

Infection: Suspected infection and septicemia in any severely malnourished child can lead to septic death. Careful clinical examination and auxiliary laboratory analyses, and their interpretation, must be accompanied by the awareness that normal responses to infection, such as leukocytosis and fever, often are depressed. The presence of petechiae, hypothermia and hypoglycemia, diarrhea, shock, or general hypotonia usually indicate severe infection. At the slightest suspicion of infection, start aggressive treatment; investigate the identity of the infective organism, but do not delay treatment with broad-spectrum antibiotics while waiting to institute more specific therapy. Treat septicemia and intravascular coagulation syndromes aggressively, regardless of the nutritional condition of the patient.

Water/Electrolyte Disturbances: Water and electrolyte disturbances have two origins: (1) the nutritional status per se and (2) associated alterations as a result of infection and diarrhea. The first alterations, intracellular potassium deficits and whole body sodium excess associated with hyposmolality, are corrected during nutritional recovery. Treat superimposed dehydration accompanied by aggravation of the potassium deficit (which would reduce total body potassium to below 30 meq to 35 meq/kg and which could be reflected in hypokalemia) and magnesium deficiency with oral rehydration and, if necessary, intravenous fluids. Various solutions have been proposed and have been shown successful in treating this complication. In general, the primary aim of rehydration is maintaining

renal function. No more than 5 (nor fewer than 3) meq sodium/kg/day, together with 4% to 5% dextrose and approximately 1 meq magnesium/kg/day, can be safely administered by mouth or intravenously to provide between 120 ml and 140 ml water/kg/day. If renal function is adequate, 4 meq to 8 meq potassium can be administered without surpassing 40 meq KCl/liter solution. If impending shock and anuria are detected, rapidly administer 30 ml to 40 ml/kg Hartman's solution or, in its absence, saline solution, giving 20 ml/kg in the first half hour. If hypoalbuminemia is extremely severe (less than 1 g/dl), plasma can be added, in repeated 20-ml doses.

Cardiac, Renal, and Respiratory Failures If a child is severely anemic (hemoglobin concentration, below 5 g/dl) and/or shows signs of impending cardiorespiratory decompensation, administer small transfusions of packed red cells or whole blood, taking care not to bring the hemoglobin concentration above 8 g or 10 g/dl.

In the process of oral rehydration, essentially the same fluids can be fed as were administered by vein, but potassium content can be raised to provide up to 8 meq or 10 meq/kg/day. Do not raise sodium intake (or sodium administered parenterally) above 5 meq/kg/day since a child's body already contains a large amount of sodium and greater concentrations of this cation may be fatal.

Careful rehydration and evaluation of other causes of cardiac failure can prevent this complication. Administer diuretics only if necessary and only after careful evaluation. Rapid digitalization can proceed (always with extreme care) if hypokalemia is not present.

Liver failure in connection with malnourishment is extremely rare but, when it exists, a careful progression in protein intake should be used, together with all other measures routinely used in liver failure in nonmalnourished populations.

Other Nutritional Deficiencies. Keep in mind other acute specific nutritional deficiencies, particulary severe vitamin A deficiency, which can develop rapidly into keratomalacia. For this reason, one should routinely administer 50,000 units of a water-dispersable preparation of vitamin A to a malnourished patient upon admission. Hypocalcemia, hypomagnesemia, and zinc, copper, and chromium deficiencies have been described, keep these deficiencies in mind if muscle twitching, tetany, convulsions, hyperglycemia and glycosuria, cutaneous ulcers, or leukopenia are present. Diet therapy should include all of the above-mentioned trace minerals and vitamins and essential fatty acids in amounts sufficient to achieve the four- to fivefold rate of normal tissue growth induced by adequate nutritional repletion.

Initiation of Cure

Start diet therapy as soon as possible, keeping in mind the following three general principles.

1. The malnourished child has reached this stage through prolonged adaptation. Therefore, metabolic systems cannot handle sudden energy and protein loads.

2. Anorexia is a very common sign of uncompensated and complicated malnutrition. Patience in feeding these children, together with corrections of complications, will result in progressively larger intakes and smooth recovery.

3. Severely malnourished children with diarrhea of infectious origin can present with decreased lactose tolerance. Therefore, carefully evaluate milk tolerance initially. Also, avoid osmolar loads in these children. Use calcium caseinate, half-milk/half-casein, low-lactose milk, and/or other animal or vegetable protein mixtures of high protein quality to start diet therapy. Actual intolerance to physiologic milk intake and to progressively administered whole or fat-rich milk preparations is rare and its prevalence has been exaggerated; however, genetically determined lactose intolerance may be important in certain populations.

Simple schemes for progressively increasing protein and energy intakes are effective in treating severely malnourished children. A common program starts with 1 g protein/kg/day, 50 to 75 kcal/kg/day, 20% to 30% of which is provided by fat (preferably rich in polyunsaturated fatty acids), with supplementary vitamins and minerals. Depending on the child's tolerance and appetite, greater concentrations of nutrients can be administered at two- to four-day intervals, as follows:

Protein (g/kg)	Energy (kcal/kg)
2	100-150
3	150-200
4	200-300

Nutritional Consolidation

The consolidation of cure in terms of nutrition can start as soon as edema disappears and the child begins to gain weight rapidly. One should rapidly and progressively introduce other foods, taking into account local eating habits, to lead to a varied and healthy diet.

Throughout recovery, the child must be stimulated both mentally and physically to promote physical activity and emotional well-being.

Ideally, severely malnourished children without complications should be treated at home, and both food assistance and nutritional-health education should be provided for the family. The child with complications that merit hospitalization should be kept in the hospital only as long as necessary, and efforts should be made to ensure the complete nutritional rehabilitation of the child and the family. Longer hospitalization increases the chance of further infection and is unhealthy from the standpoint of physical, mental, and emotional recovery and development. Since many of these children suffer from poor general care, health personnel can take advantage

of this contact to promote immunizations and other necessary health and hygienic measures in addition to caring for the immediate problem; however, nutritional recovery must precede immunizations in children with severe PEM.

Children with PEM often present with intestinal parasites. Unless there are clinical reasons to suspect massive loads or clinical signs of protozoal disease (amebiasis, giardiasis), delay treatment until the child is well into nutritional recovery. However, if there are clinical signs of malaria it should be treated immediately.

Sequelae

It has been suggested that children who have suffered from severe or moderate PEM are not normal even when they have recovered fully.[37] These children have been deprived not only of nutrition but also of opportunities for development, and they may have missed the critical period for acquisition of different concepts, abilities, and reactions that lead to a harmonic maturation, both physically and mentally. Physically, these children usually show retarded development, primarily in height. Weight for height can be restored easily, but this still leaves a child who is dwarfed and underweight for age. Malnourished children may grow and tend to mature at their biologic age rather than at their chronologic age. That is, if a 5-year-old child has the stature and bone maturation of a 3-year-old child, his rate of growth and maturation would be more like that of a 3-year-old child. Mentally, severely malnourished children appear to have residual problems in terms of creativity and social interaction; however, the roles of malnutrition and poor environment are not easily dissociated.

Persistent altered insulin secretion, increased rate of glucose intolerance, and chronic pancreatic insufficiency have been suggested as long-term sequelae from severe PEM, but the validity of many of these observations has been questioned.

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Chapter 112

Protein-Energy Malnutrition

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Protein-energy malnutrition (PEM) is the most important nutritional disease in the developing countries because of its high prevalence and its relationship with child mortality rates, impaired physical growth, and inadequate social and economic development. While associated deleterious effects on mental growth and maturation have been demonstrated in experimental animals [1,2] and they seem to occur in humans [3,4], it has not been possible to disassociate completely the nutritional factors from other environmental conditions, nor to ascertain the irreversibility of the nutritional mental damage

PEM mainly affects infants and preschool-aged children It occurs more frequently when infections impose additional demands or induce greater losses of dietary energy, total nitrogen, and essential amino acids, and when living conditions demand greater energy expenditure, as in heavy physical work. The inability to satisfy the needs for these nutrients leads to PEM of varying degrees of severity It is estimated that in many developing countries between 20 and 66 percent of all children under 5 years of age had or presently have PEM [5] Mild and moderate forms of adult PEM affect the physical and physiological performance of many millions of individuals

PEM encompasses a wide spectrum of clinical syndromes conditioned by the relative intensity of protein or energy deficit, the severity and duration of the deficiencies, the age of the host, the etiology of the deficiency, and the association with other nutritional or infectious diseases Its severity ranges from weight loss, without other clinical manifestations to kwashiorkor or marasmus Its origin can be *primary*, as a result of inadequate food intake, or *secondary*, as a result of other diseases that lead to low food intake, inadequate nutrient utilization, and/or increased nutritional requirements.

This chapter deals only with *primary PEM of a relatively chronic onset*, where inadequate energy and/or protein intakes lead to the nutritional disease The metabolic alterations and clinical characteristics of famine and of specific vitamin and mineral deficiencies are described in other sections of this book.

NUTRIENTS

Primary PEM results from insufficient food intake or from the ingestion of foods with proteins of poor nutritional quality Dietary energy and protein deficiencies usually occur together, but sometimes one predominates and, if severe enough, may lead to the distinct clinical syndromes of *kwashiorkor* (predominant protein deficiency), *marasmus* (mainly energy deficiency), or *marasmic kwashiorkor* (chronic energy deficiency with chronic or acute protein deficit) It is difficult to recognize which deficit predominates in milder forms of the disease

ABSORPTION AND UTILIZATION

Energy

The main dietary energy sources are carbohydrates and fats, but proteins can also provide energy In order to be absorbed, carbohydrates must be hydrolyzed to monosaccharides by the action of amylases and disaccharidases, fats must be converted into fatty acids and monoglycerides, which requires bile salts and lipases, and proteins must be hydrolyzed into amino acids by several gastrointestinal proteases and peptidases Assuming that carbohydrates, fats, and proteins are 99, 95, and 92 percent absorbed, respectively, and that each gram of urinary nitrogen represents 1.25 kcal of protein energy that was not utilized by the human body, Atwater proposed that the "metabolizable" energy contents of those food components were 4, 9, and 4 kcal/g, respectively. It is now known that the proteins of most predominantly vegetable diets are only 65 to 85 percent absorbed and total energy absorption from mixed animal-vegetable diets is usually 90 to 95 percent [6] Nevertheless, the Atwater factors are still practical and their use results in a relatively small error

Protein

The utilization of dietary proteins depends on their digestibility (i e , absorption) and their amino acid composition A protein that is deficient in one or more essential amino acids is not used adequately for the body's protein metabolism, although the nonutilized amino acids are potential energy sources when dietary carbohydrates and fats do not provide sufficient energy The rational combination of poor-quality proteins to provide a

surplus amount of the essential amino acid that each one lacks will improve the protein quality of a diet This quality can be expressed as a chemical or amino acid score, relative to a standard essential amino acid pattern If the score is corrected by the protein digestibility, a good estimate of the protein's nutritional value is obtained [7] Protein deficiency can result from the intake of insufficient amounts of digestible protein (total nitrogen deficit), from the ingestion of poor-quality protein (essential amino acid deficit), or from a combination of both A deficient dietary energy intake will also contribute to the development of protein deficiency by reducing the efficiency of protein utilization, altering amino acid metabolism, and increasing the nutritional requirements for protein [8]

ENERGY AND PROTEIN DENSITIES OF FOODS

Some vegetable foods have proteins and energy of good nutritional quality, but they are bulky and become more so as a result of the water absorbed during cooking Consequently, their energy and protein densities (i e , energy and protein per gram of cooked food, ready to be eaten) are low and they must be consumed in relatively large amounts to meet the body's requirements for these nutrients. This may lead to PEM, particularly in infants and preschool children whose appetites are satisfied and whose stomachs are filled with quantities of bulky foods that do not provide sufficient amounts of proteins or energy [9]

INTERACTIONS WITH OTHER NUTRIENTS

Poor energy and protein intakes are accompanied by insufficient intakes of other essential nutrients In severe PEM there can be deficiencies of vitamins, such as A, E, folic acid, and B_{12}, trace minerals such as iron, zinc, selenium, and chromium, and electrolytes such as potassium and magnesium Their clinical and metabolic significance depend on the severity of the specific micronutrient deficit relative to that of PEM. In kwashiorkor and marasmus manifestations of energy and protein insufficiency usually predominate and some of the other nutrient deficiencies only become clinically evident during the course of protein-energy repletion This can be either because the derangement caused by severe PEM overshadows other symptoms or because the functional requirements for some micronutrients diminish in severely malnourished patients and increase only during the period of nutritional rehabilitation The latter situation is exemplified by iron patients with kwashiorkor and marasmus usually have low hemoglobin concentration, even when the levels of serum iron and plasma ferritin are normal, the administration of additional iron does not produce a reticulocyte response nor an increase in hemoglobin synthesis until dietary therapy with energy and protein begins replenishing the depleted body mass The reduced synthesis of hemoglobin is not a "functional" anemia but a physiological adaptation to low protein intakes in the presence of decreased demand for oxygen transport as a consequence of the reduced lean body mass and low physical activity characteristic of severe PEM [10]

These hidden" nutrient deficits are important during treatment of PEM For example, functional anemia and hypoxia may develop if hematinics are not provided as tissue synthesis and oxygen demands increase, failure to replete nearly exhausted vitamin A stores can precipitate severe ocular manifestations of hypovitaminosis A, muscular tone and other cell functions will recover very slowly unless enough potassium is provided to overcome the intracellular depletion of this electrolyte, covert zinc deficiency may retard catch-up growth

PATIENT

PATHOPHYSIOLOGY AND ADAPTIVE RESPONSES

PEM develops gradually over many days or months This allows a series of metabolic and behavioral adaptations which result in decreased nutrient demands and in a nutritional equilibrium compatible with a lower level of cellular nutrient availability. Patients whose PEM develops slowly—as is usually the case in marasmus—are better-adapted to their current nutritional status and maintain a less fragile metabolic equilibrium than those with more acute PEM, as in kwashiorkor of rapid onset

Energy mobilization and expenditure

A decrease in energy intake is quickly followed by a decrease in energy expenditure, accounting for shorter periods of play and physical activity in children [11,12] and for longer rest periods and less physical work in adults [13] When the decrease in energy expenditure cannot compensate for the insufficient intake, body fat is mobilized with a decrease in adiposity and weight loss Lean body mass diminishes at a slower rate, mainly as consequence of muscle protein catabolism with increased efflux of amino acids, primarily alanine As the cumulative energy deficit becomes more severe, subcutaneous fat is markedly reduced, and protein catabolism leads to muscular wasting Visceral protein is preserved longer, especially in the marasmic patient In marasmus, these alterations in body composition lead to increased basal oxygen consumption (i e , basal metabolic rate) per unit body weight In kwashiorkor, the severe dietary protein deficit leads to an earlier visceral depletion of amino acids that affects visceral cell function and reduces oxygen consumption, therefore, basal energy expenditure decreases per unit of lean or total body mass Blood glucose concentration remains normal, mainly at the expense of fats

and gluconeogenic amino acids, and it falls in very severe PEM or when complicated by serious infections or fasting

Protein metabolism

The most striking changes are a marked recycling of amino acids and a reduction in urea synthesis and excretion The poor availability of dietary amino acids decreases protein synthesis in viscera and muscles. This is followed by increased muscle protein catabolism, modifies composition of the free amino acid pool, and increased visceral amino acid availability. In the steady state, the amount of free amino acids entering the body pool is equal to the amount leaving it The latter is represented by the amino acids synthesized into body protein and the amount of amino acid nitrogen that is excreted. On a normal protein intake, 25 percent of the amino acids leaving the total body pool are excreted as nitrogenous compounds and 75 percent are recycled or reutilized for protein synthesis. This latter fraction may rise to 90 to 95 percent when protein intake is reduced [*14*]. Therefore, the adaptive change is not so much a reduction of total nitrogen or amino acid turnover but an increase in the proportion turned over that is used for synthesis and a corresponding reduction in the proportion of nitrogen that is excreted.

The half-life of some proteins increases The rate of albumin synthesis decreases, but after a time lag of a few days the rate of breakdown also falls [*15*]. In addition to its increased half-life, a shift of albumin from the extravascular to the intravascular pool assists in maintaining adequate levels of circulating albumin in the face of reduced synthesis, until protein depletion becomes so severe that it disrupts these adaptive mechanisms. The ensuing reduction in intravascular oncotic pressure and the outflow of water into the extravascular space contribute to the development of the edema of kwashiorkor.

These adaptations lead to the sparing of body protein and the preservation of essential protein-dependent functions. The gradual and inevitable loss of body protein as a result of long-term dietary protein deficit is primarily from skeletal muscle. Some visceral protein is lost in the early development of PEM but then becomes stable until the nonessential tissue proteins are depleted, the loss of visceral protein then increases, and death may be imminent unless nutritional therapy is successfully instituted.

Endocrine changes

Hormones play an important role in the adaptive metabolic processes. Endocrine changes may not be wholly explained by

Table 112-1. Some metabolic effects and secretion or circulating levels of selected hormones usually seen in severe protein-energy malnutrition

Hormone	Stimulus	Metabolic effects of hormone	Hormonal activity	
			In energy deficit	In protein deficit
Insulin	↑ Glucose	↑ Protein synthesis (muscle)	Decreased	Decreased
	↑ Amino acids	↑ Lipogenesis		
		↑ Growth		
Somatomedins		↑ Protein synthesis (muscle, cartilage)		Decreased
		↑ Lipogenesis		
		↑ Growth		
		↑ Collagen synthesis		
Growth hormone	↓ Glucose	↑ Protein synthesis (muscle, visceral)	Normal or moderately increased	Increased
	↑ Amino acids	↑ Lipolysis		
		↑ Growth		
Glucocorticoids	↓ Glucose	↑ Protein catabolism (muscle)	Increased	Normal or moderately increased
	↓ Amino acids	↑ Protein turnover (visceral)		
		↑ Lipolysis		
		↑ Gluconeogenesis		
Thyroid hormones		↑ Protein turnover	Normal or decreased	Variable, usually decreased
		↑ Lipolysis		
		↑ Glucose oxidation		

the circulating levels of hormones, since cellular responses to hormonal stimulation may also be altered in PEM. Table 112-1 summarizes the main changes in hormonal activity seen in patients with severe energy or protein deficiencies. The functional capacities of the hypothalamic-pituitary axis and the adrenal medulla are preserved. Consequently, patients can still show endocrine and metabolic responses to stress conditions.

Some endocrine adaptive functions in severe PEM are related to energy metabolism (Fig. 112-1). (1) The decreased food intake tends to reduce plasma concentrations of glucose and free amino acids which, in turn, *reduce insulin* secretion and *increase epinephrine* release. The low plasma amino acid levels, seen mainly in kwashiorkor, also *stimulate the secretion of human growth hormone*. (2) The *low plasma somatomedin* activity, also seen mainly in kwashiorkor, probably contributes to the high circulating levels of growth hormone, due to the absence of the feedback inhibition postulated for somatomedins. (3) The stress induced by the low food intake and further amplified by fever, water and electrolyte losses, and other manifestations of the infections that frequently accompany PEM, also *stimulates epinephrine release* and *corticosteroid secretion*, more so in marasmus than in kwashiorkor, probably because of the greater severity in energy deficit that characterizes marasmus. (4) The plasma concentrations of T_3 *and* T_4 *decrease*, by mechanisms that are not yet defined, the iodination of tyrosine may be involved, as the reduction in T_3 (3,5,3'-triiodothyronine) is accompanied by an increase in the circulating levels of the metabolically inactive reverse-T_3 (3,5,5'-triiodothyronine). All these changes contribute to the maintenance of energy homeostasis through increased glycolysis and lipolysis, increased amino acid mobilization, decreased storage of glycogen, fats, and proteins, and decreased energy metabolism. They also participate in the preservation of visceral protein through increased breakdown of muscle protein and increased availability and turnover of amino acids in viscera, particularly liver. Some investigators [*16*] have postulated that the evolution of PEM into either kwashiorkor or marasmus may be partly related to differences in adrenocortical response, whereby the better response will preserve visceral proteins more efficiently and lead to the better-adapted syndrome of marasmus.

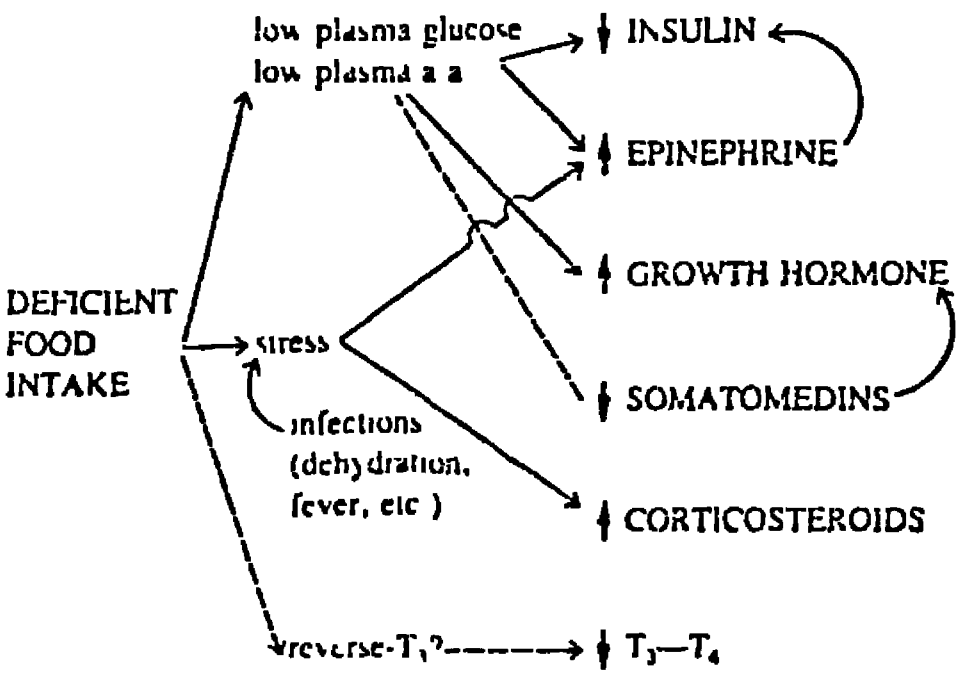

Figure 112-1 Endocrine adaptive functions in severe PEM related to energy metabolism

Disruption of adaptation

Patients with severe PEM adapt to a new, but fragile, state of metabolic equilibrium. The adaptive mechanisms can be upset by large increases in the intake of energy relative to proteins, by infections, and by a sudden, large increase in energy and/or protein intake. For example, the abrupt administration of high-carbohydrate diets with poor protein intake will induce insulin secretion and reduce the release of epinephrine, growth hormone, and cortisol. Consequently, fat oxidation and gluconeogenesis decrease and the availability of muscle amino acids for liver protein synthesis diminishes. These changes may lead to the development or exacerbation of kwashiorkor.

Patients with kwashiorkor suddenly fed large amounts of proteins or given large transfusions of plasma or blood may experience a rapid increase in intravascular protein concentration and entry of extracellular fluid into the vascular compartment leading to cardiovascular insufficiency and pulmonary edema. In fact, a too early introduction of high-energy or high-protein diets to a severely malnourished patient may be fatal [*17*].

ASSESSMENT OF NUTRIENT STATUS

The assessment and classification of moderate forms of PEM is based on anthropometric measurements, since biochemical indexes usually do not show changes unless the disease is well advanced. More accurate measurements, such as assessment of body composition, are not practical or feasible in most of the settings where PEM occurs, and the so-called functional indicators (Chap. 22) are not as yet well defined or standardized. Severe PEM can be classified qualitatively to distinguish kwashiorkor, marasmus, and intermediate forms, based on clinical and biochemical criteria.

Anthropometric measurements

The anthropometric assessment of nutritional status employs a standard reference of comparison but not necessarily an ideal or a target. Any set of reliable anthropometric data can be used as the standard, but the interpretation of their use (i.e., the line

that separates "normal" from "deficient" and further subdivisions into "mild," "moderate," and "severe" forms) is a matter of judgment. In order to allow international comparisons, it is sensible to use the same standard of reference for various populations. The value judgment comes into play when deciding whether the expected normal value for a given population should be 100 percent, 90 percent, or other proportion of the standard. Setting different cutoff points relative to a single standard is more practical than constructing local standards which, in a country with heterogeneous population groups, may pose the same problem as a "foreign," commonly used reference. The World Health Organization presently recommends the data from the U.S. National Center for Health Statistics (NCHS) [*18*] as reference.

The choice of anthropometric indexes will depend on the simplicity, accuracy, reproducibility, and sensitivity of the measurements, and on the availability of measuring instruments. The most widely used index for children, although not the best, is *weight for age*. This was the basis for classifying PEM into three degrees [*19*]: first degree = 90 to 75 percent of standard, second degree = 74 to 60 percent, third degree = less than 60 percent. The use of this index, however, does not differentiate between a truly underweight child and one who is short in stature but well-proportioned in weight. Furthermore, the information about chronological age is not always reliable.

The measurement of height or length, in addition to weight, is important. It allows the use of two indexes: *weight for height*, as an index of *current* nutritional status, and *height for age*, as an index of *past* nutritional history which, when deficient, may represent a short period of growth failure at an early age or a longer period at a later age. Waterlow [*20*] suggested the term "wasting" for a deficit in weight for height, and "stunting" for a deficit in height for age. Children may fall into four broad categories that are qualitatively different: (1) normal, (2) wasted but not stunted (suffering from acute PEM), (3) wasted and stunted (suffering from acute and chronic PEM), and (4) stunted but not wasted (past PEM with present adequate nutrition, or "nutritional dwarfs"). The severity of wasting and stunting can be graded using, respectively, weight as percentage of the expected median weight of a standard child of the same height, and height as percentage of the median standard height for age. The grading shown in Table 112-2 is suggested for most countries. It may be convenient to use different points of demarcation for some populations (e.g., normal height for age in groups that are genetically short could be less than 95 percent of the standard).

Other anthropometric indexes have been used, such as the developmental quotient for weight or height (weight-age or height-age divided by the chronological age) [*21*], midarm circumference in absolute terms [*22*] or relative to height (QUAC-stick) [*23*], or weight, ratio of arm circumference to head circumference [*24*]. It seems, however, that an international classification of PEM should be based primarily on weight, height, and, when available, age [*20*].

Table 112-2. Grading of severity of current ("wasting") and past or chronic ("stunting") malnutrition

	Normal	Mild	Moderate	Severe
Weight for height (deficit = wasting)	90–110*	80–89	70–79	<70
Height for age (deficit = stunting)	95–105	90–94	85–89	<85

*Percentage of the median NCHS standard (Ref. 23)
Source: From [*24*]

Body composition

Measurements of adiposity and lean body mass provide a better assessment of mild and moderate PEM than anthropometric measurements in adults. Since energy deficiency is usually more common than protein deficiency, the most striking change is a reduction of adiposity below the average 12 and 20 percent expected in normal, well-nourished men and women, respectively.

Fat stores are reduced in severe PEM and virtually depleted in marasmus, a notable exception are the classic cases of kwashiorkor where patients have had an adequate energy intake with a very poor protein intake. Body protein decreases at a slow rate, most of it from muscle, and the greater loss of adipose tissue results in a relative increase of total body water (i.e., per unit of body mass), mainly as intracellular water. In severe protein deficiency (kwashiorkor) there is also an increase in extracellular water. The intracellular concentrations of potassium and magnesium decrease and that of sodium increases, although the serum concentrations of electrolytes do not necessarily reflect these alterations [*25*].

Functional alterations

Physical activity and energy expenditure decrease with insufficient dietary energy intakes [*11–13*], but the methods to assess such changes are complex. Other functional assessments related to immunocompetence, intellectual and behavioral responses, and gastrointestinal functions have been or are currently being investigated. Their application to assess nutritional status is complicated by the environmental conditions and high morbidity rates that usually prevail where PEM develops. Nevertheless, this is a promising line of research that may also indicate important physiological or social implications of moderate PEM that are frequently overlooked.

CLINICAL MANIFESTATIONS

Mild and moderate PEM

The main clinical feature of mild and moderate PEM in children is a retardation in physical growth. Present malnutrition results in wasting (low weight for height) and past malnutrition in stunting (low height for age). The combination of wasting and stunting suggests chronic malnutrition with present inadequate nutritional status. In adults, mild to moderate or chronic PEM results in leanness with a more or less marked reduction in subcutaneous tissue.

Nonspecific manifestations include reduced physical activity, frequent episodes of diarrhea and apathy, lack of liveliness, and short attention spans.

Marasmus

Severe muscular wasting and absence of subcutaneous fat give the patient a "skin-and-bones" appearance (Fig. 112-2). Marasmic persons frequently have 60 percent or less of the weight expected for their height, with marked retardation in longitudinal growth. The hair is sparse, thin, and dry; the skin is usually dry, thin, with little elasticity and wrinkles; and lymph nodes are easily palpable. The patient is weak and frequently cannot stand without help. Heart rate, blood pressure, and body temperature may be low. Hypothermia of 35°C or less can occur, especially after fasting a period, and is often accompanied by hypoglycemia.

The marasmic child is apathetic but usually aware and with a look of anxiety on his or her face. These features and the

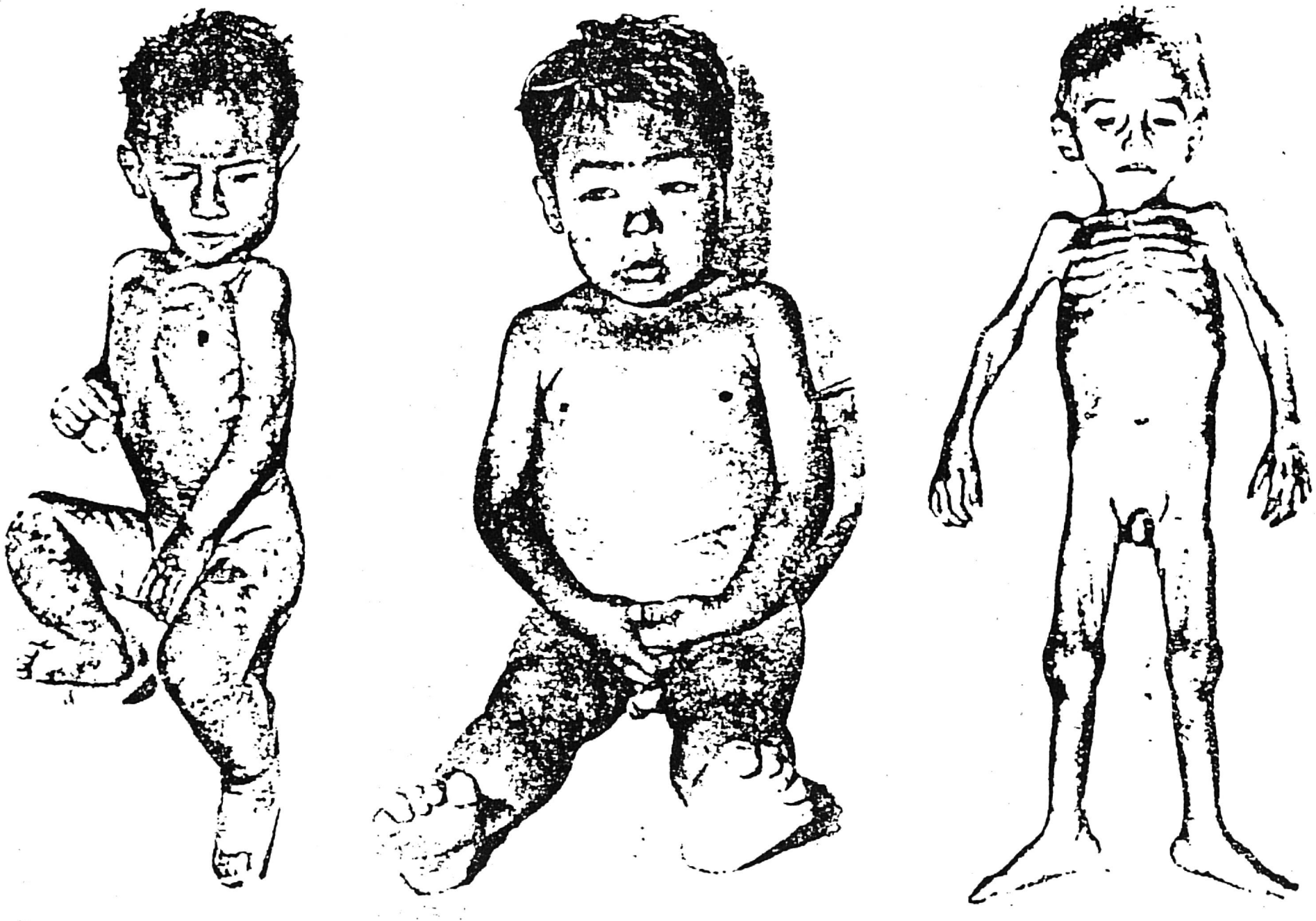

Figure 112-2. "Skin-and-bones" appearance of marasmic patient.

sunken cheeks caused by disappearance of the Bichat fat-pads, which are among the last subcutaneous adipose depots to disappear, give the marasmic child's face the appearance of a monkey's or an old person's. Some patients are anorexic while others are ravenously hungry, but they seldom tolerate large amounts of food and vomit easily

Common complicating features are acute gastroenteritis, dehydration, respiratory infections, eye lesions due to hypovitaminosis A, and skin infections Systemic infections can be present without an appropriate febrile response, tachycardia, or leukocytosis

Kwashiorkor

The predominant feature is soft, pitting, painless edema, usually in the feet and legs, but extending to perineum, upper extremities, and face in severe cases (Fig. 112-2) Subcutaneous fat is preserved, although there may be some muscle wasting Weight deficit, after accounting for the edema, is not as severe as in marasmus Height is variable and may be normal or retarded, depending on the chronicity of the current episode and on past nutritional history The hair is dry, brittle, without its normal sheen, and can be pulled out easily and without pain Curly hair becomes straight, and there usually are changes in pigmentation, becoming dull brown, reddish, or even yellowish-white Alternating periods of poor and relatively good protein intake can produce alternating bands of depigmented and normal hair, which have been termed the "flag sign" Skin lesions, often confused with pellagra, are very characteristic of kwashiorkor They occur in many but not all patients more frequently in the areas of edema, continuous pressure (e g , buttocks and back), or frequent irritation (e g , perineum and thighs) In those areas the skin may be erythematous and it glistens in the edematous regions with zones of dryness, hyperkeratosis, and hyperpigmentation, which tend to become confluent. The epidermis peels off in large scales, exposing underlying tissues that are easily infected The patients may be pale, with cold and cyanotic extremities Hepatomegaly with a soft, round edge, caused by severe fatty infiltration is usually present The abdomen is frequently protruding because of distended stomach and intestinal loops Peristalsis is irregular Muscle tone and strength are greatly reduced and tachycardia is common Both hypothermia and hypoglycemia can occur after short periods of fasting.

Patients are simultaneously apathetic and irritable and have an expression of misery and sadness Anorexia, sometimes necessitating nasogastric tube feeding, postprandial vomiting, and diarrhea are common These improve without specific gastrointestinal treatment as nutritional recovery progresses

Diarrhea and respiratory infections are more frequent and severe in kwashiorkor compared to marasmus Severe, even fatal infections may occur as in marasmus, but without fever, tachycardia, respiratory distress, or leukocytosis

Marasmic kwashiorkor

This form of edematous PEM combines clinical characteristics of kwashiorkor and marasmus The main features are the edema of kwashiorkor, with or without its skin lesions, and the muscle wasting and decreased subcutaneous fat of marasmus (Fig 112-2) When edema disappears during early treatment, the patient's symptoms resemble a case of marasmus Biochemical features of both marasmus and kwashiorkor are seen, but the alterations of severe protein deficiency usually predominate.

DIAGNOSIS

Mild and moderate PEM

The diagnosis is based on dietary history and anthropometric measurements Biochemical indicators are of little help, although the patients may have low urinary excretions of urea nitrogen, creatinine, hydroxyproline, and 3-methylhistidine, and a small decrease in serum concentrations of branched-chain essential amino acids, albumin, and transferrin

Severe PEM

The diagnosis is principally based on dietary history and clinical features. The most common biochemical findings are that serum concentrations of total proteins and albumin are markedly reduced in edematous PEM, and normal or moderately low in marasmus, hemoglobin and hematocrit are usually low, more so in kwashiorkor than marasmus, the ratio of nonessential to essential amino acids in plasma is elevated in kwashiorkor and usually normal in marasmus, serum levels of free fatty acids are elevated, particularly in kwashiorkor, blood glucose level is normal or low, especially after fasting 10 to 12 h, urinary excretions of creatinine, hydroxyproline, 3-methylhistidine and urea nitrogen are low, children usually have low urinary creatinine excretions in relation to their height, leading to a low creatinine-height index [26], whereas marasmic children may have a normal or somewhat low index.

Plasma levels of other nutrients vary and tend to be moderately low. They do not necessarily reflect the body stores For example, serum iron and retinol may be normal with almost depleted body stores, or in kwashiorkor they may be relatively low with adequate stores because of alterations in the transport proteins, transferrin, and retinol-binding protein

Many other biochemical changes have been described in severe PEM They have little practical diagnostic importance

but give an insight into the pathophysiological changes (Table 112-3)

PROGNOSIS AND RISK OF MORTALITY

Treatment usually takes longer in marasmus than kwashiorkor. Mortality rates in severe PEM can be as high as 40 percent. Immediate causes of death are usually infections. Table 112-4 lists the characteristics that generally indicate a poor prognosis

Anthropometric characteristics are also associated with mortality rates, as in the classification of severe PEM into first, second, or third degrees, based on weight for age [*19*]. A higher mortality rate is associated with the more intense anthropometric deficits but not with mild or moderate deficiencies [*27*].

Table 112-4. Manifestations in patients with protein-energy malnutrition that generally indicate a poor prognosis

1. Age less than 6 months
2. Deficit in weight for height of greater than 30%, or in weight for age of greater than 40%
3. Extensive exfoliative or exudative cutaneous lesions or deep decubitous ulceration
4. Dehydration and electrolyte imbalances, especially hypokalemia and severe acidosis
5. Clinical jaundice or elevated serum bilirubin concentrations, with or without elevations in the transaminases
6. Hypoglycemia or hypothermia
7. Total serum protein concentrations less than 3 g/dL
8. Severe anemia with hypoxia
9. Petechiae or hemorrhagic tendencies (purpura is usually a sign of septicemia or a viral infection)
10. Intercurrent infections, particularly measles and bronchopneumonia
11. Persistent tachycardia and/or respiratory difficulty
12. Coma, stupor, or other alterations in mental status and consciousness

Source Modified after B Torún, FE Viteri, Rev Col Med (Guatemala) 27 43–62, 1976

TREATMENT

Severe PEM

Whenever possible, patients with noncomplicated PEM should be treated on an outpatient basis Hospitalization increases the risk of cross-infections and the unfamiliar setting may increase apathy and anorexia in children, making feeding more difficult. When hospitalization is necessary, treatment strategy can be divided into three stages (1) resolving life-threatening conditions, (2) restoring nutritional status without disrupting homeostasis, and (3) ensuring nutritional rehabilitation

Table 112-3. Selected biochemical changes observed in severe protein-energy malnutrition

	Marasmus	Edematous PEM
Body composition		
Total body water	High	High
Extracellular water	High	Higher
Total body potassium	Low	Lower
Total body protein	Low	Low
Serum or plasma		
Transport proteins*	Normal or low	Low
Branched-chain amino acids	Normal or low	Low
Tyrosine/phenylalanine ratio	Normal or low	Low
Enzymes (in general)†	Normal	Low
Transaminases	Normal or high	High
Liver		
Fatty infiltration	Absent	Severe
Glycogen	Normal or low	Normal or low
Urea cycle and other enzymes‡	Low	Lower
Amino acid–synthesizing enzymes	High	Not as high

*For example, transferrin, ceruloplasmin, retinol-, cortisol-, and thyroxine-binding proteins, α- and β-lipoproteins
†For example, amylase, pseudocholinesterase, alkaline phosphatase
‡For example, xanthine oxidase, glycolic acid oxidase, cholinesterase

RESOLVING LIFE-THREATENING CONDITIONS

Most in-hospital deaths occur in the first week of treatment. Nutritional rehabilitation can be delayed until emergencies are solved The most frequent complications that require immediate treatment are

1. Fluid and Electrolyte Disturbances The assessment of dehydration is not easy in severe PEM, as classic signs of dehydration, such as sunken eyeballs and decreased skin turgor, are frequently found in well-hydrated patients, while hypovolemia may coexist with subcutaneous edema. Useful signs are low urinary output, weak and rapid pulse, and low blood pressure and a declining state of consciousness, which indicate impending circulatory collapse

Whenever possible, oral or nasogastric rehydration should be used Intravenous fluids must be used in severe dehydration with hypovolemia, impending shock, frequent vomiting, and persistent abdominal distension The therapeutic approach differs from that in well-nourished patients because of hydroelectrolytic peculiarities of severe PEM, namely, (1) hypoosmolarity with moderate hyponaturemia, frequently with intracellular sodium excess; (2) intracellular potassium depletion, usually without hypokalemia, (3) mild-to-moderate met-

abolic acidosis, which decreases or disappears when the patient receives dietary or parenteral energy, and electrolyte balance is reestablished, (4) high tolerance to hypocalcemia, partly because of the acidosis, which produces a relative increment in ionized Ca^{2+}, and partly because of hypoproteinemia, which makes less protein available to bind Ca^{2+}; (5) decreased body magnesium, with or without hypomagnesemia

The volume of fluids will depend on diuresis and the clinical signs of dehydration. Fluid repletion should allow a diuresis of at least 200 mL in 24 h in children and 500 mL in adults, or a micturition every 2 to 3 h As a guideline, 10 mL/(kg h) by mouth or nasogastric tube every 1 to 2 h can be given initially to be modified according to patient response The following treatment plan is based on extensive experience at the Institute of Nutrition of Central America and Panama (INCAP) Patients with edema who are urinating should receive about 6 meq K, 2 to 3 meq Na, 2 to 3 meq Ca, and 20 to 30 kcal/day per kilogram of body weight. This can be accomplished by dissolving in 1 L of water, 3 g KCl, 1 g table salt (NaCl), 2 g $CaCl\ 6H_2O$ (or 4 g calcium gluconate), and 50 g glucose or cane sugar Potassium should be withheld when there is no diuresis Additional fluids must be given to compensate for the losses of diarrhea and vomiting, providing about 35 meq Na and 30 meq K per kilogram of excreta (i e , 2 g table salt and 2 g KCl per liter) Dietary formula with calcium should be started as early as possible, if necessary alternating with the electrolyte solution Total K intake should be raised to 8 to 10 meq/(kg day) while for Mg 0 5 to 1 meq/(kg day) should be given

When intravenous infusions are necessary, osmolarity must be kept low (200 to 280 mosmol/L), K and Na should not exceed 6 and 3 meq/(kg day), respectively, and glucose must provide 15 to 30 kcal/(kg day) During the first hour, 10 to 30 mL/kg is infused, depending on the patient's condition Subsequent volumes are calculated at 2- to 4 h intervals Additional losses through diarrhea and vomiting must be compensated with about 3 meq Na, 3 meq K, 6 meq Cl, and 15 kcal per 100 g (i e , 20 mL isotonic saline, 2 mL of 10% KCl, and 78 mL of 5% dextrose per 100 g excreta) An increase in pulse and respiratory rate with weight gain after accounting for weight of excreta, pulmonary rales, and appearance or exacerbation of edema indicates overhydration An increase in pulse and respiratory rate with weight loss, low urine output, and continuing losses from diarrhea and vomiting suggests insufficient fluid therapy

Patients with severe hypoproteinemia (less than 3 g/dL), anuria, and signs of hypovolemia or impending circulatory collapse should be given 10 mL plasma per kilogram in 1 to 2 h, followed by 20 mL/(kg h) of a mixture of two parts of 5% dextrose and one part of isotonic saline, for 1 or 2 h This will increase plasma protein concentration by about 0 5 to 1 g/dL and help prevent the rapid exit of water from the intravascular compartment If diuresis does not improve, the dose of plasma can be repeated 2 h later Further treatment is similar to that of well-nourished patients

Some clinicians advocate the routine use of lactate- or bicarbonate-containing solutions However, the mild metabolic acidosis of malnutrition usually disappears with energy intake Therefore, treatment for acidosis should be withheld unless blood pH is below 7 25, urinary pH is below 5, or there are clinical signs of severe acidosis

When there is hypomagnesemia or clinical signs similar to hypocalcemia that do not respond to calcium infusion, magnesium should be given intramuscularly as a 50% solution of magnesium sulfate in doses of 0 5, 1, and 1 5 mL, respectively, for patients who weigh less than 7, between 7 and 10, and more than 10 kg The dose can be repeated as required every 12 h

2. Infections Malnourished patients are particularly prone to infections While these are often severe and life-threatening, paradoxically, clinical manifestations may be mild and the classic signs of fever, tachycardia, and leukocytosis absent Antigen-antibody reactions are often impaired and skin tests, such as tuberculin, often give falsely negative results

Antibiotics should not be used prophylactically, but when an infection is suspected appropriate antibiotic therapy must be started immediately, even before obtaining the results of microbiological cultures The choice of drug will vary with the suspected etiological agent, the severity of the disease, and the pattern of the drug resistance in that area Clinicians should be aware that gastrointestinal, hepatic, and renal alterations that might accompany severe PEM could potentiate a drug's toxic effects Where septicemia is suspected, a broad-spectrum antibiotic or a combination, such as ampicillin and gentamicin, is usually given intravenously Other supportive treatment may also be necessary, as for respiratory distress, hypothermia, and hypoglycemia

Treatment for intestinal parasites is rarely urgent and can be deferred until nutritional rehabilitation is underway This will decrease the risks of potential toxicity, including the possibility of absorbing drugs normally not absorbed by a healthy intestine.

3. Hemodynamic Alterations Cardiac failure may develop during or after administration of intravenous fluids, or shortly after the introduction of high-protein and high-energy feedings, leading to pulmonary edema and secondary pulmonary infection These alterations may be the result of impaired cardiac function, sudden expansion of the intravascular fluid volume, severe anemia or impaired membrane function Diuretics such as furosemide (10 mg IV or IM repeated as necessary) should be given, as well as other supportive measures Many clinicians advocate the use of digoxin (0 03 mg/kg IV, every 6 to 8 h) The use of diuretics merely to accelerate the disappearance of edema in kwashiorkor is contraindicated

4. Severe Anemia Blood transfusions should be given only in cases of severe anemia with less than 4 g hemoglobin per deciliter, or with signs of hypoxia or impending cardiac failure. Whole blood (10 mL/kg) can be used in marasmic patients, but it is better to use packed red blood cells (6 mL/kg) in edematous PEM The transfusion should be given slowly, over 2 to 3 h, and repeated if necessary after 12 to 24 h. The routine use of blood transfusions endangers the patient, and hemoglobin levels will improve with proper dietary treatment supplemented with hematinics.

5. Hypothermia and Hypoglycemia Body temperature below 35 5°C and plasma glucose concentration below 60 mg/dL can be due to either impaired thermoregulatory mechanisms, reduced fuel substrate availability, or severe infection. Asymptomatic hypoglycemia can be treated (and prevented) by the frequent feeding of small volumes of glucose-containing diets and solutions Severe symptomatic hypoglycemia must be treated intravenously with 10 to 20 mL of 50% glucose solution followed by oral administration of 25 to 50 mL of 5% glucose solution at 2-h intervals for 24 to 48 h

Body temperature usually rises in the hypothermic patient with frequent feedings of glucose-containing diets or solutions Caution and close monitoring of body temperature must be used with external heat sources and devices to reduce the loss of body heat, as these patients may rapidly become hyperthermic It is best to keep the seminude patients in an ambient temperature of 30 to 33°C

6. Severe Vitamin A Deficiency Severe PEM is often associated with vitamin A deficiency A large dose of vitamin A should be given on admission, since ocular lesions can develop as adequate protein and energy feeding begins and the metabolic demands for retinol increase Water-miscible vitamin A should be given orally or IM on the first day, at a dose of 50,000 to 100,000 IU for infants and preschool children, or 100 000 to 200,000 IU for older children and adults, followed by 5000 IU orally each day for the duration of treatment The initial dose should be repeated two more days in symptomatic cases Corneal ulcerations should be treated with ophthalmic drops of 1% atropine solution and antibiotic ointments or drops until the ulceration heals.

HOMEOSTATIC RESTORATION OF NUTRITIONAL STATUS

The next objective of therapy is to replace tissue deficits as rapidly and as safely as possible Based on the premise that the patient is adapted to the malnourished state, nutritional treatment must begin slowly Various regimens provide a diet that meets daily maintenance requirements for a few days, followed by a gradual increase in nutrient delivery Table 112-5 shows a therapeutic schedule for children, based on INCAP's experience. The only difference between kwashiorkor and marasmus is that the latter often requires larger amounts of dietary energy, which must be raised at 5-day intervals, depending on the patient's weight gain. The intervals for the dietary increments in Table 112-5 can be lengthened to 3 to 5 days in very severely malnourished children, especially those with plasma protein less than 3 g/dL or with serious metabolic disturbances

It is best to begin with a liquid formula fed orally or by nasogastric tube, divided equally into 5 to 12 feedings per day, depending on the patient's age and general condition This frequent feeding of small volumes avoids vomiting and prevents the development of hypoglycemia and hypothermia Intravenous feeding is rarely justified in primary PEM

The attitude of the person who feeds the patient and the appearance, color, and flavor of the foods influence appetite For older children with good appetite, the liquid formula can be partly substituted with solid foods that have a high density of good quality, easily digestible nutrients.

The diet must be supplemented to provide 8 to 10 meq of potassium, 3 to 5 meq of sodium, 5 to 8 meq of calcium, and 1 to 2 meq of magnesium per kilogram of body weight per day This can be accomplished by adding 0 3 g KCl and 0 1 g NaCl per 100 mL to milk formulas, or by adding appropriate amounts of the mineral mixture shown in Table 112-6 to most other diets Additional supplements should include daily doses of 60 to 120 mg elemental iron, 10 mg elemental zinc, 0 3 mg folic acid, 5000 IU vitamin A, and other vitamins and trace elements in the doses provided by most commercial preparations

The protein source must be of high biological value and easily digested Cow's milk is frequently available but some

Table 112-5. Example of a dietary therapeutic regimen for children based on dry skim milk, sugar, and vegetable oil*

Days from beginning of treatment	Protein, g	Energy, kcal	Milk, g	Sugar, g	Oil, mL	Water, mL
1	0 8–1	80–100	3	17	2	100
3	1 5–2 5	110–120	6	20	2	130
5	2 5–3 5	140–150	9	20	4	150
7	3 5–4 5	150–160	12	20	4	160
12 (marasmust†)	3 5–4 5	175†	12	20	6†	160
17	3 5–4 5	195	12	20	8	160
22	3 5–4 5	215	12	20	11	160
etc.	3 5–4 5	†	12	20	†	160

*All amounts per kilogram of body weight per day. The liquid formula must be supplemented with adequate levels of vitamins, minerals, and electrolytes

†Marasmic patients may require more dietary energy Two to three milliliters of vegetable oil per kilogram per day should be added at 5-day intervals until the rate of weight gain becomes adequate.

Source From FE Viteri, B Torun, in RS Goodhart, ME Shils (eds) *Modern Nutrition in Health and Disease*, 6th ed, Philadelphia, Lea and Febiger, 1980.

Table 112-6 Mineral mixture to complement liquid formulas

Salt	Amount, g	1 g mixture provides, meq	
KCl	44	K^+	8 5
NaCl	9	Na^+	3 5
Na_2HPO_4	7	Ca^{2+}	1 4
$CaCO_3$	5	Mg^{2+}	0 6
$MgSO_4\ 7H_2O$	5	HPO_4^{2-}	1 4

clinicians worry about the possibility of lactose malabsorption in severe PEM. Recent studies [28,29], however, have shown that cow's milk is well-tolerated and assimilated by severely malnourished children and can be safely advocated Eggs, meat, fish, soy isolates, and some vegetable-protein mixtures are also sources of good protein Most vegetable mixtures have protein digestibilities that are 10 to 20 percent lower than animal proteins, making it necessary to feed larger amounts. Their bulk might pose a problem in feeding small children

The initial response to diet is either no change in weight or a decrease due to loss of edema, accompanied by large diuresis After some time, commonly 7 to 15 days, there is a period of rapid weight gain or "catch up." The rate of catch up usually is slower in marasmus than kwashiorkor In children, this rate of weight gain generally is 10 to 15 times that of a normal child of the same age, and it can be as high as 20 to 25 times greater Some patients only show a four- or fivefold increase in catch up, most times this is associated with insufficient energy intakes (formula inadequately prepared, insufficient amounts of formula given at each feeding, too few feedings per day, anorexia, or lack of patience of the person who feeds the child) or with overt or asymptomatic infections Urinary infections and tuberculosis are among the most commonly seen asymptomatic diseases

ENSURING NUTRITIONAL REHABILITATION

This last stage of treatment may begin in the hospital and continue on an outpatient basis, but making sure that the patient continues eating adequate amounts of protein, energy, and other nutrients, especially when traditional foods are introduced into the diet Emotional and physical stimulation must be provided, and persistent diarrhea, intestinal parasites, and other minor complications must be treated Children can be vaccinated during this period as well

1. Introduction of Traditional Foods Other foods, especially those available at home, are gradually introduced into the diet in combination with the high-energy, high-protein formula This should be done when edema has disappeared, the skin lesions are notably improved, the patient becomes active and interacts with the environment, appetite is restored, and adequate rates of catch-up growth have been achieved A daily minimum intake of 3 to 4 g of protein and 120 to 150 kcal per kilogram of body weight (or more in marasmus) must be ensured To achieve this, the energy density of solid foods must be increased with oil or fat, and protein density and quality must be high, using animal proteins, vegetable protein mixtures, or soybean protein concentrates and isolates Local traditional foods can be used in appropriate combinations, *in addition to the liquid formula*, as in the following examples: (1) one part of a dry pulse or its flour (black beans, soybeans, kidney beans, cowpeas) and three parts of a dry cereal or flour (corn, rice, wheat), fat or oil should be added to the mashed or strained pulse during or after cooking, in amounts equal to the weight of the dry pulse or flour, and to the cereal preparations in amounts of 10 to 30 mL oil per 100 g dry cereal product, depending on the type of preparation. (2) Four parts of dry rice and two parts of fresh fish; fat or oil should be added in amounts equal to 20 to 40 percent of the dry weights. The foods can be served as separate dishes or they can be mashed or blended and fed as paps to infants and young children.

2. Emotional and Physical Stimulation The malnourished child needs affection and tender care from the beginning of treatment This requires patience and understanding by the hospital staff and the relatives Involvement of parents or relatives is usually very helpful Hospitals should be brightly colored, cheerful, with audible stimulation such as music As soon as the child can move without assistance and is willing to interact with the staff and other children, he or she must be encouraged to explore, to play, and to participate in activities that involve body movements Relatively small increments in physical activity and energy expenditure during the course of nutritional rehabilitation result in faster longitudinal growth and accretion of lean body tissues [*12*]

Parents should be encouraged to stimulate and teach their children by playing and talking Toys and play materials can often be made from discarded local articles

3. Persistent Diarrhea and Other Health Problems Mild diarrhea does not interfere with nutritional rehabilitation, as long as fluid and electrolyte intakes maintain satisfactory hydration, and often disappears without specific treatment as nutritional status improves Persistent diarrhea can contribute to the development of a new episode of PEM and should be treated This is determined by the underlying cause of diarrhea, usually intestinal infections, excessive bacterial flora in the upper gut that ferment food substrates and deconjugate bile salts, intestinal parasites (particularly amebiasis, giardiasis, and trichuriasis), and intolerance to food components Among the latter, lactose, milk protein, and gluten have often been held responsible. This is often founded on inadequate diagnostic procedures (e g , intolerance to 2 g lactose per kilogram in aqueous solution, rather than to the 7 to 15 g lactose contained in a milk meal) [*30*] When food intolerance is suspected the diet should be modified, taking care to preserve its nutritional

quality and nutrient density. Before branding a patient as intolerant to a given food, it should be reintroduced into the diet to confirm the diagnosis and adequate diagnostic tests should be done.

4. Criteria for Recovery The most practical criterion is weight gain. A patient should be discharged from in-hospital or outpatient treatment when he or she has reached a body weight equal to or near the expected weight for height. A premature discharge increases the risk of a recurrence of malnutrition. If urine can be collected for 24 h in children, the creatinine-height index [26] can be used as an indicator of body protein repletion. Specific treatment of other nutritional problems (e.g., iron deficiency) must be prolonged beyond discharge for PEM.

When discharged, patients or their parents must be taught about the causes of PEM, emphasizing rational and nutritious use of household foods, personal and environmental hygiene, appropriate immunizations, and early treatment of diarrhea and other diseases.

Mild and moderate PEM

The less-severe forms of PEM should be treated in an ambulatory setting, supplementing the home diet with easily digested foods that contain proteins of high biological value and a high energy density. In some instances, therapy can be achieved merely by instructing the adult patient about adequate eating habits and a better use of food resources or by instructing mothers in improved child-feeding practices and in more nutritious culinary habits. It is almost always necessary, however, to provide both nutritious food supplements and instructions in their use.

The quantity of food supplements will vary depending upon the degree of malnutrition and the relative deficit of proteins and energy. As a general guideline, the goal should be to provide a total intake—including the home diet—of *at least* twice the protein and 1.5 times the energy requirements. For preschool children, this would signify a daily intake of about 2 to 2.5 g of high-quality protein and 120 to 150 kcal per kilogram of body weight, and for infants under 1 year, about 3.5 g protein and 15 kcal/(kg·day).

The ingestion of the food supplement by the malnourished person must be ensured. This is more likely to occur if it is appetizing to both the child and the mother, if it is ready-made or easy to prepare, if additional amounts are provided to feed the siblings, and if it does not have an important commercial value outside the home that would make it easy and profitable for the family to sell the item for cash. A substitution effect on the home diet (i.e., a decrease in the usual food intake) is almost unavoidable, but it can be reduced by using low-bulk supplements of high protein and energy densities. Special attention should be given to avoid a decrease in breast-feeding; the supplements for breast-fed infants should be paps or solid foods that will not quench the infant's thirst and thus not change the infant's demand nor the mother's attitude toward lactation.

Adequate amounts of vitamins and minerals must be assured, although mild deficiencies can be overcome by the micronutrients in the food or using fortified vehicles such as iron-enriched bread or sugar fortified with retinol.

POPULATION

The epidemiology of PEM is discussed in Chap. 23. Certain aspects, however, should be further emphasized.

POPULATION ECOLOGY

PEM can affect all age groups but it is more frequent among children whose growth increases nutritional requirements, and especially among the very young who cannot ensure adequate food intakes by their own means. Older children usually have milder forms of PEM because they can cope better with social and food availability constraints, because infections and other precipitating factors become less severe, and early survival may imply a natural selection of the more fit. Pregnant and lactating women can also have PEM but the consequences of the dietary deficiencies are seen mainly in the growth, nutritional status, and survival rates of their fetuses, newborn babies, and infants. Adult men and nonpregnant, nonlactating women usually have the lowest prevalence and the mildest forms of the disease, because of greater opportunities to obtain food and social and cultural practices that protect the productive members of the family.

Poverty, low food availability, and infectious disease stress are causes of PEM (see Chaps. 23, 24, 25). In some families or societies, ignorance may lead to poor infant- and child-rearing practices, misconceptions about the use of certain foods, inadequate feeding practices during illnesses, and improper food distribution within the family members. Poor environmental conditions favoring infections, and social problems such as child abuse, maternal deprivation, alcoholism, and drug addiction can lead to PEM in children and adults. Other circumstances that contribute to or precipitate PEM are agricultural patterns and climatic conditions leading to cyclic or sudden food scarcities, social and cultural practices which impose food taboos, the migration from traditional rural settings to urban slums, and a decline in the practice or duration of breast-feeding.

A profile of risk factors can indicate which individuals or societies are more prone to PEM. Thus, the most likely victims are children under 2 years of age from low socioeconomic strata whose parents have a series of misconceptions concerning the use of foods, whose families are known to have a high prevalence of alcoholism and unstable marriages, who live under poor sanitary conditions in urban slums or in rural areas

frequently subject to droughts or floods, and whose societal beliefs prohibit the use of many nutritious foods.

PREVENTION AND CONTROL OF PEM

Measures that will prevent the recurrence of PEM or the appearance of new cases include the availability and rational use of foods that optimize nutrient utilization, the control or reduction of infections, and health and nutrition education programs for the individual, the family, and the community.

Food availability

Inadequate food availability caused by poverty, cultural customs, cyclical climatic conditions, and natural disasters and those of human origin is a major constraint in the control of malnutrition. The solution of some conditions is dependent on social and economic changes while others, as natural disasters, are beyond human control. However, the pediatrician, nutritionist, public health worker, and educator can and *must* play an active role in ameliorating or solving other conditions.

Animal foods are the best protein sources but they tend to be expensive, not always available, or prohibited by religious practices. Under such circumstances, the staple foods can be complemented or substituted with vegetable foods combined in ways to permit a good essential amino acid complementation and improve the biological value of dietary protein For example, corn and black bean combinations that provide proteins in a proportion of about 60 40, equivalent to about three parts of dry corn and one part of dry beans, have an excellent amino acid composition and permit adequate growth and function [9,33] The same is true of a series of combinations of grains and/or legumes [6] The relatively low nitrogen digestibility of these vegetable sources must be considered in recommending the amounts to be eaten Energy density can be increased by adding fats or carbohydrates.

It will often be necessary to convince parents about the safety of using foods which, in some cultures, are fed only to adults and older children This is especially true in the case of weaning foods Trials at INCAP have shown that it is feasible to feed pablums based on legumes, a cereal, and vegetable oil to babies as young as 3 months without intestinal discomfort and without decreasing breast-milk intakes. Examples of such paps are shown in Table 112-7 Promotion of breast-feeding must accompany the recommendation for weaning foods

Table 112-7. Paps to complement breast milk, using common foods and based on combinations of a legume, a grain, and vegetable oil

	A	B	C	D
Cooked beans*	25 g	20 g	20 g	25 g
Vegetable oil	12 g	7 g	7 g	10 g
Corn dough†	20 g	—	—	—
White bread‡	—	10 g	—	—
Boiled rice	—	—	22 g	—
Boiled potatoes	—	—	—	31 g
Protein, g/100 g§	5 6	7.1	6 1	5 5
Energy, kcal/100 g§	312	268	269	232

*Black beans (*Phaseolus vulgaris*), cooked and strained according to Guatemalan customs
†Cooked, lime-treated corn dough
‡Moistened with about 50 percent water
§Protein and energy content of 100 g of pap, ready to eat
Source From F E Viteri, B. García, B Torún, unpublished observations.

Reduction of morbidity rates

This is a logical consequence of the interactions of nutrition with infection. Since young children are at higher risk of malnutrition, high priority must be given to immunizations, sanitary measures to reduce fecal contamination, and early oral rehydration of children with diarrhea [34]

Education

The presence of a malnourished child in a family suggests that other members of the household might also be at risk of malnutrition Therefore, nutritional and health education must not be restricted to the rehabilitation of the index case, but to prevention of nutritional deterioration of other family members, especially siblings and pregnant and lactating women. Similarly, a high prevalence of children with malnutrition or growth retardation indicates that the entire community is at some risk of impaired nutrition Consequently, education programs must be devised for community leaders, civic action groups, and the community as a whole Such programs must emphasize promotion of breast-feeding, appropriate use of weaning foods, nutritional alternatives using traditional foods, personal and environmental hygiene, feeding practices during illness and convalescence, and early treatment of diarrhea and other diseases. Personal and communal involvement should be pursued through commitments to apply the recommendations Toward this aim, it is very important that all educational programs incorporate the people's own assessment of their nutritional problems and their feelings toward personal participation to contribute to the solution

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Malnutrition in Tropical America

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INTRODUCTION

The concepts about the causes of and the solutions to the food and nutrition problems in Third World nations have been substantially modified during the last two decades [Joy and Payne, 1975]. It is now generally accepted that chronic malnutrition in children results from inadequate access to and utilization of health and educational services and/or from the low purchasing power of families. Therefore, if malnutrition is to be effectively dealt with, governments should strengthen those programs oriented to reducing significantly the existing levels of poverty.

This chapter discusses the present nutritional and health conditions in Tropical America (TA) and the changes that have occurred in the principal health indicators over time. TA includes 17 countries that include approximately 16 million km² of national territory and 297 million inhabitants. It is subdivided into Continental Middle America (CMA), including Belize, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, and Panama, with 93 million people; and Tropical South America (TSA), which comprises Brazil, Bolivia, Colombia, Ecuador, Guyana, Paraguay, Peru, Suriname, and Venezuela, with 204 million inhabitants [PAHO, 1982a]. TA in general has a hot and humid climate, although temperature and rainfall vary dramatically by altitude. A mixture of indigenous and Spanish-speaking cultures forms the majority of the populations. The remaining, predominantly indigenous populations are found in the highlands or in bordering isolated communities. African-American populations are mostly concentrated on the Atlantic coasts. Approximately 43% of the population of the region is under 15 years of age. The adult literacy rates range from 47% in Guatemala to 90% in Costa Rica and Mexico [PAHO, 1982a]. Poverty affects 71% of the population in Guatemala and 65% in Honduras [MIDEPLAN, 1983]. Less than 40% of house-

holds in eight countries (Bolivia, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Paraguay, and Peru) have access to adequate water supply systems [PAHO, 1982b].

MALNUTRITION IN TROPICAL AMERICA

The data available in TA since the 1940s had identified protein-energy malnutrition, anemias associated with iron and folate deficiencies, hypovitaminosis A, and iodine deficiency as the most pressing nutritional problems of the area.

In the following section, the most recent data related to nutritional and health conditions are reviewed. Most data sources consulted are derived from national nutrition surveys that did not provide details about sampling procedures, the validity and reliability of the data, the methods of data collection, the growth standards used, or the procedures for data editing and processing. Thus, in most countries it was not possible to estimate or adjust for the confounding effects imposed by different methodologies. However, for some countries, the changes observed in rates cannot be attributed solely to methodologic differences in the data sets. Despite those difficulties of interpretation it is important to get a general notion of trends in light of the health goals proposed for the year 2000.

National Prevalence and Changes Over Time

Mortality. Mortality and indicators of growth retardation to a large extent reflect prevailing deficiencies of energy and protein. The mortality figures reported in this chapter are derived from national health statistics. While infant and child deaths are underestimated by official statistics, the present trend in most countries is towards improving the reporting system. Thus, if reductions in mortality are observed, these are generally underestimations of the true changes occurring over time. The information on infant mortality (IM) in TA in the 1970s is presented in Table I. The most important annual declines in IM are seen in Paraguay (5.7 deaths of children under 1 year of age per 1,000 live births), Costa Rica (4.2/1,000), Peru (3.8/1,000), and Mexico (3.6/1,000). Belize (2.5/1,000), Ecuador (2.2/1,000), Guatemala (1.9/1,000) and Panama (1.9/1,000) have also shown important reductions in IM during the 1970s. Some countries in Central America report IM that underestimate the true figures. In spite of that, five countries in TA still have IM above 50/1,000, the maximum acceptable figure established in health for all in the year 2000.

The 1- to 4-year mortality figures (1–4 YM) for the year 1970 and the period 1977–1981 in TA are shown in Table II [PAHO, 1982a; OPS, 1981; MS, 1983; Baum and Arriaga, 1981]. Marked annual reductions in this indicator are reflected in all countries, particularly in Guatemala (1.46/1,000) and El Salva-

TABLE I. Infant Mortality in Tropical America in 1970 and 1977–1981

Country	Years		Average annual reductions[a]
	1970	1977–1981	
Paraguay	93 8	48.1	5.7
Costa Rica	61.5	19 0	4.2
Peru	65.1	35.1	3.8
Mexico	58.5	39.7	3 6
Belize	50 7	27 5	2.5
Ecuador	76.6	61 0	2.2
Panama	40.5	21.5	1 9
Guatemala	87.1	70 2	1.9
Venezuela	49 2	32 1	1.7
Colombia	50.5	39.5	1.6
El Salvador	66.7	53 0	1.5
Brazil[b]	92 0	85.2	1 0
Honduras	33.2	24 9	0 9
Guyana	34.7	28 5	0 6
Suriname	36.7	35.1	0.2
Bolivia[b]	151 6	151 0	0.1
Nicaragua	42 8	42.9	0 0

[a]Reference period varies from 6 to 11 years

[b]From Baum and Arriaga [1982], and based on census and household surveys.

TABLE II. Mortality for Children 1–4 Years of Age in Tropical America in 1970 and 1977–1981

Country	Years		Average annual reductions
	1970	1977–1981	
Guatemala	27.0	12 4	1 46
El Salvador	13 0	4 1	1.11
Mexico	10 6	3 3	0 91
Peru	12 5	5 2	0 91
Ecuador	14 9	8.1	0 85
Nicaragua	9.5	3 6	0 84
Honduras	11 4	4.3	0.79
Panama	7 6	2.1	0 55
Belize	4 3	1 6	0 45
Venezuela	5 2	2 6	0 35
Colombia	6 8	4 5	0.33
Costa Rica	4.4	0.9	0 32
Suriname	4 3	1.4	0.31
Paraguay	6 7	4 1	0 26
Guyana	3 2	1.9	0 08

dor (1.11/1,000), where previous rates were among the highest in the region. The less dramatic annual reductions are seen in countries with previously low levels of 1–4 YM in 1970. With the exception of Colombia, Ecuador, Guyana, and Paraguay, all countries had a drop of at least 50% in the 1–4 YM during the period of analyses.

Incidence of growth retardation. A child with a weight for age below 75% of the median of an internationally accepted reference pattern is defined here as suffering from weight retardation (Gómez II and III) [Gómez et al, 1956]. The latest reports of incidence of growth retardation in children are shown in Table III. The highest rates of second- and third-degree malnutrition in children are found in Guatemala (30.5%) [Valverde et al, 1981], and Honduras (29.5%) [INCAP/CDC, 1972]; while in Colombia and Costa Rica the respective figures are 8.3% and 4.8% [Mora, 1982; Jaramillo, 1983]. The rates of growth retardation, 15% or less, reported from Nicaragua, Panama, El Salvador, and Venezuela [Parillón, 1982; INCAP, 1983; PAHO, 1982c] are also low compared to rates observed in other developing nations.

Comparable data on weight for age are not available for other countries. Nevertheless, the nutrition survey of Bolivia, conducted in 1981 [INAN, 1983], disclosed that 49% of children 6–59 months old had heights below two standard deviations of the reference pattern, as compared to only 22.4% of Colombian children [Mora, 1982]. Other countries, such as Peru and Ecuador, have reported rates of growth retardation based on growth patterns or reference values (25th percentile) that underestimate the true incidence of growth retardation [Amat and Cunurisy, 1981; PAHO, 1982c].

The information on changes in the incidence of weight retardation in TA countries is shown in Table IV. Important improvements occurred in El Salva-

TABLE III. Percentage of Children Under 5 Years of Age Weighing Below 75% of Standard Weight for Age (W/A) in Tropical America

Country	Year	Incidence (%)
Costa Rica	1982	4.8
Colombia	1977–1980	8.3
El Salvador	1978	10.4
Panama	1980	11.6
Venezuela	1974	13.6
Nicaragua	1966	15.0
Belize	1973	19.2
Brazil	1968	19.9
Honduras	1967	29.5
Guatemala	1977	30.5

TABLE IV. Percentage of Children Under 5 Years of Age Weighing Below 75% of Standard Weight for Age in Tropical America, 1965-1968 and 1974-1982

Country	Years 1965-1968	1974-1982	Average annual reductions
El Salvador	27.5	10.4	1.32
Venezuela	19.0	13.6	0.68
Colombia	15.7	8.3	0.62
Costa Rica	13.5	4.8	0.54
Guatemala	33.6	30.5	0.28
Panama	11.9	11.6	0.02

dor, Costa Rica, Colombia, and Venezuela. Panama maintained in 1980 [Parillón, 1982] the same low prevalence as that observed in 1967 [INCAP/CDC, 1972]. Guatemala showed a slight decline in the proportion of children with growth retardation, 33.6% in 1965 [INCAP/CDC, 1972] and 30.5% in 1977 [Valverde et al, 1981]. Data from Brazil that compare results from surveys conducted in the 1960s and 1970s also demonstrate a decline from 68.3% to 46% in the percentage of children under 5 years of age who are below 90% of appropriate weight for age [Dutra et al, 1981].

Incidence of vitamin A deficiency. Vitamin A deficiency is defined here as any case with a serum retinol level below 20 μg/dl (low and deficient levels). The latest reports of rates for children and for the total population in TA countries are presented in Table V. In El Salvador 31.3% of children below 60 months of age had low or deficient levels of serum retinol [MSPAS/INCAP, 1977] Panama reported a vitamin A deficiency incidence in children of 18.4% [INCAP/CDC, 1972]. The more recent figures for children from Costa Rica (1.6%) [Novygrodt, 1983], Guatemala (9.2%) [Arroyave et al, 1979] and Honduras (less than 2.8%) [CID, 1980] indicate that vitamin A deficiency is no longer a public health problem in these three countries.

The proportions of the total population exhibiting vitamin A deficiency in Bolivia and Brazil are extremely high, being 45.1% and 13.0%, respectively [OPS, 1981]. The national nutrition survey conducted in Bolivia in 1981 reported a national incidence of night-blindness of 2.1% in children aged 6 to 59 months, confirming the existence of a severe deficiency of vitamin A in that country [INAN, 1983].

Table VI presents data on changes in vitamin A deficiency in children in the 1960s and from 1976 to 1980 [INCAP/CDC, 1972; MSPAS/INCAP, 1977; Novygrodt, 1983; Arroyave et al, 1979; CID, 1980]. The results show a marked decline in the incidence of vitamin A deficiency in all countries. Fur-

TABLE V. Incidence of Vitamin A Deficiency (20 μg/dl) in Children Under 5 Years of Age and in the Total Population in Tropical America

Country	Year	Incidence (%)
Children		
Costa Rica	1981	1.6
Honduras[a]	1980	2.8
Guatemala	1977	9.2
Panama	1967	18.4
Nicaragua	1966	19.8
El Salvador	1976	33.3
Total population		
Venezuela	—	4.9
Paraguay	—	6.6
Guyana	—	9.5
Colombia	1977-1980	12.4
Brazil	—	43.0
Bolivia	—	45.1

[a]The latest information from Honduras [CID, 1980] reported a percentage of cases below 30 μg/dl of 2.8%. Therefore, no more than 2.8% of cases are below 20 μg/dl.
(—) No information about the year was available [OPS, 1981].

TABLE VI. Incidence of Vitamin A Deficiency (20 μg/dl) in Children Under 5 Years of Age in Tropical American Countries During the 1960s and 1976-1980

Country	Period	Incidence (%)		Average annual reductions
		Previous survey (1960s)	Latest survey (1976-1980)	
Honduras	1967-1980[a]	39.5	2.8	2.82
Costa Rica	1966-1981	32.5	1.6	2.06
El Salvador	1966-1976	50.0	33.3	1.67
Guatemala	1965-1977	26.2	9.2	1.42

[a]For 1967, information from INCAP/CDC [1972]. Regarding figure for 1980, see footnote a, Table V

thermore, two surveys conducted in children under 5 years of age in six communities of rural Honduras—one in 1978 prior to the initiation of a program designed to fortify sugar with vitamin A and one in 1980 after 2 years of sugar fortification—showed that the proportion of children with serum retinol levels below 30 μg/dl was reduced from 35% to 2.8% [CID, 1980]. In Honduras, Guatemala, and Costa Rica, national programs fortifying sugar with retinol palmitate were implemented in the 1970s.

TABLE VII. Incidence of Endemic Goiter in the Total Population of Tropical America

Country	Year	Incidence (%)
Colombia	1965	2
Costa Rica[a]	1979	3
Panama	1975	6
Mexico	1972	8
Guatemala[a]	1979	10
Venezuela[a]	1966	13
Brazil[a]	1976	14
Peru	1975–1976	15
Honduras	1966	17
Paraguay	1976	18
Nicaragua	1981	20
El Salvador[a]	1973	24
Bolivia	1981	61

[a]School-age children.

Incidence of iodine deficiency. The incidence of iodine deficiency has been evaluated by either the percentage of the total population or of the school-age population with any clinical evidence of goiter.

The latest reports documenting the incidence of endemic goiter in the total population in TA are presented in Table VII. Bolivia, Ecuador, Peru, Paraguay, Brazil, Guyana, Venezuela, El Salvador, Honduras, Guatemala, and Nicaragua have rates above 10% [INCAP/CDC, 1972; OPS, 1981; INCAP, 1982; DeMaeyer et al, 1979; Quezada, 1979]. Colombia and Costa Rica have successfully eliminated clinical cases of iodine deficiency, as less than 5% of the populations have goiters. In Suriname, Mexico, and Panama the latest reported figures on incidence of goiter are less than 10% [DeMaeyer et al, 1979; Flores et al, 1981, Parillon, 1979].

The changes in the incidence of endemic goiter have been well documented in TA countries as reflected in Table VIII. With the exception of Paraguay and Brazil, dramatic improvements have been seen in endemic goiter rates in most countries.

Incidence of anemia. No current national statistics on the magnitude of iron- and folate-related anemias are available for TA countries. The data available by the end of the 1960s describing the proportion of pregnant women with hemoglobin levels below the World Health Organization (WHO) norm (less than 11.0 gm/liter) in different regions or cities of TA countries are shown in Table IX [Royston, 1982]. The Pan American Health Organization collaborative study, conducted in the early 1970s in cities of Brazil, Colombia, Guatemala, Mexico, Peru, and Venezuela, showed anemia rates of 28.5% in pregnant women, 17.3% in nonpregnant women, and 3.9% in adult males

TABLE VIII. Incidence of Endemic Goiter in Different Periods in Tropical American Countries

Country	Period	Incidence (%)		Average annual reductions
		First survey	Latest survey	
Nicaragua	1978-1981	33	20	4.3
El Salvador	1967-1973	48	24	4.0
Colombia	1945-1965	45	2	2.2
Panama	1967-1975	16	6	1.2
Costa Rica	1966-1979	18	4	1.1
Guatemala	1954-1979	38	10	1.1
Peru	1967-1976	22	15	0.8
Mexico	1950-1972	20	8	0.5
Brazil	1956-1976	18	14	0.2
Paraguay	1965-1976	18	18	0.0

TABLE IX. Estimates of Percentage of Pregnant Women With Levels of Hemoglobin Below the Norm* in Tropical American Countries

Country	Year	(%)
El Salvador	1969	15
Brazil	1968	20
Colombia	1968	22
Guatemala	1965	34
Peru	1968	35
Mexico	1963	38
Venezuela	1968	54
Guyana	1971	55

*Less than 11 gm/liter.

[Cook et al, 1971; Royston, 1982]. Iron-deficiency anemia was widespread in both high and low socioeconomic groups. Serum folate deficiency was found in 10% of women. Serum B_{12} deficiency was identified but only in pregnant women [Royston, 1982].

Variation in Mortality and Malnutrition Within Countries

The following analyses of variation in mortality and in the nutritional status of children within TA countries are based on data available from Costa Rica, Guatemala, and Panama.

A survey of schoolchildren's height conducted by Costa Rican teachers in 1979 showed dramatic differences among the 80 "cantones" in the numbers of children with attained height below 90% of the expected height for age. Five cantones had a rate of height retardation above 22%, and in another five, the proportion of children with heights below 90% ranged from 4.4 to 6.3% [Valverde et al, 1980b].

A survey of schoolchildren's height was conducted in Panama in 1982 [MS/ME, 1983]. The information was disaggregated for the 514 municipalities into which the country is divided. The percentage of children with a height more than two standard deviations below the median height of the (US) National Center for Health Statistics (NCHS) reference pattern [Hamill et al, 1979] was 21.8%. However, a total of 14 municipalities had rates of height retardation (>2 SD below the NCHS median) above 70%, whereas in 34 municipalities, no children were found whose height was >2 SD below the reference median. Similar data are available from other countries [Mora, 1982; SGCNPE/INCAP, 1980].

Data documenting differentials in the nutritional status of children according to the occupation of the head of household also have been reported. Information available from a national nutrition survey conducted in Guatemala in 1980 showed that in families whose heads of household were farmers with less than 0.7 hectare of land, 57.1% of children were reported with height retardation, as compared to 34.7% in those families where the head of household was a skilled employee [SGCNPE/INCAP, 1980]. Similar findings have been communicated from other TA countries [SIN/MS, 1980; Franklin et al, 1982].

Variation in IM in 1978, at the canton level, in Costa Rica is illustrated in Figure 1. The hatched areas represent cantones with IM above 35/1,000, areas

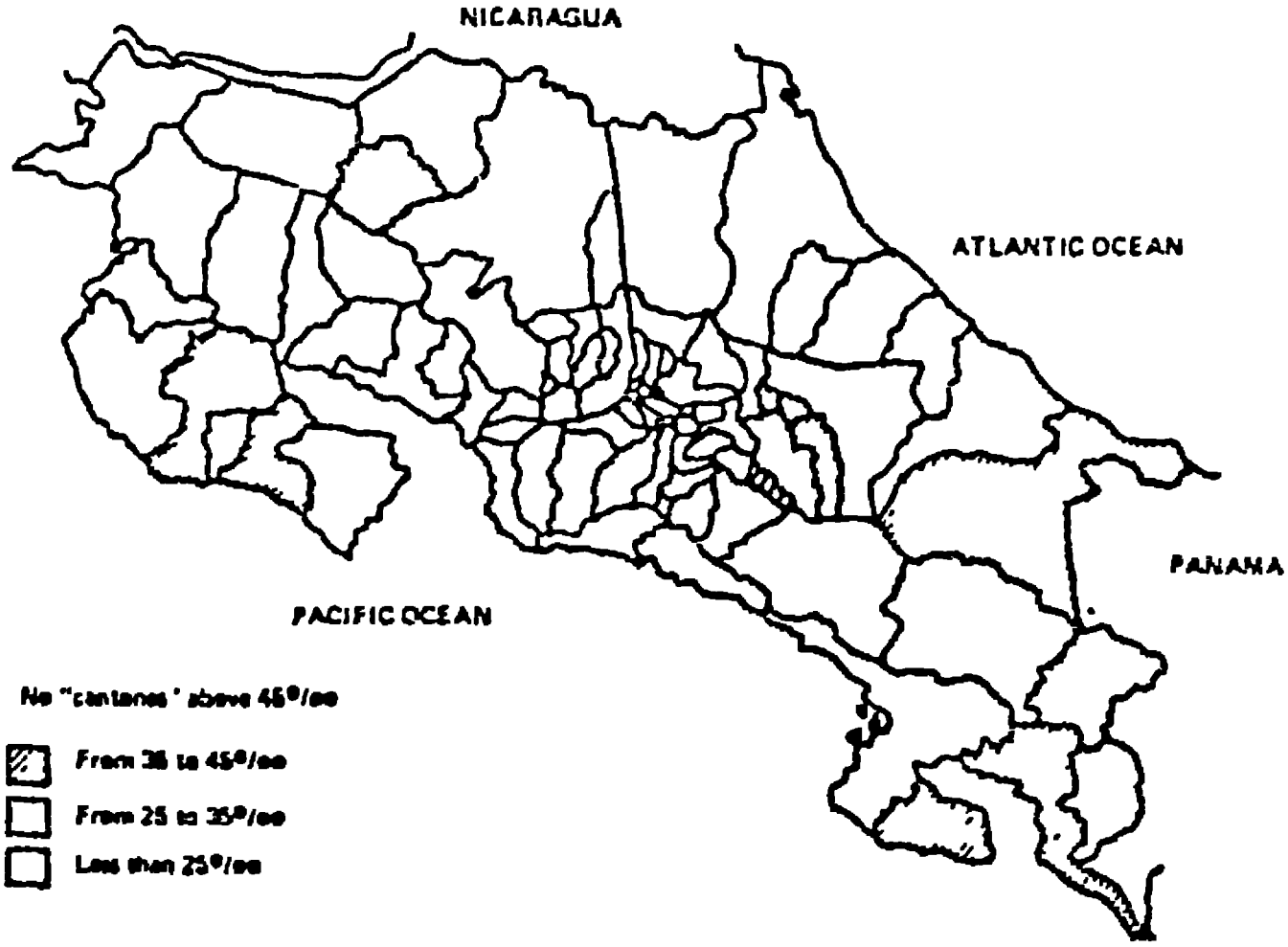

Fig 1. Infant mortality by canton, Costa Rica, 1978

in white are cantones exhibiting IM below 25/1,000 [Bermúdez, 1980]. Similar data describing differentials in IM in the 66 districts of Panama for 1982 have been reported [MS, 1983].

The probability of dying during the first 24 months of life has been reported by region in Guatemala [Haines et al, 1981]. The probability ranged from 92/1,000 children in the Central Region to 176/1,000 children in the Southern Region. During the period 1964–1973 the annual decline was observed mostly in nonindigenous populations (4.0/1,000) and to a lesser extent in indigenous groups (1.2/1,000).

Ecology dictates the differentials described. Poverty and malnutrition are concentrated mostly in rural communities. For example, the prevalences of height retardation in different ecological regions of El Salvador have been reported elsewhere [Valverde et al, 1980a]. Half of the children in coffee-growing areas are height-retarded, whereas in the urban slums only 33% are found in the same category. On the other hand, data gathered on schoolchildren in Costa Rica and Panama have shown that the areas inhabited by a higher proportion of Indians exhibit the highest levels of malnutrition [Valverde, 1980a; MS, INE, 1983]. Coincidentally these are also the most deprived regions within countries.

The coastal regions and lowlands are dedicated to banana, cotton, sugar, and other cash crops, which are grown on large plantations employing full-time or part-time laborers. The low-quality land is left for small farmers cultivating staple foods

The high-quality land on the mountain slopes or the highlands is dedicated to coffee or other cash export crops, which are also grown on large plantations employing permanent and seasonal laborers. The poor land in the highlands also is left to subsistence farmers cultivating staple foods. These populations also form the seasonal labor force employed in the cotton and coffee harvests. Seasonal migration also entails family disruption and greater exposure to diseases.

DISCUSSION

The data show that nutritional deficiencies still exist in several TA countries. Within countries, important variation was identified in mortality and in the nutritional status by geographical location and occupation of the head of household.

Significant improvements in the incidence of protein-energy malnutrition and vitamin A and iodine deficiencies have occurred in several TA countries. These changes may be the result of the extension of health service coverage, improvements in agricultural production and local marketing systems and/or the efficient operation of food fortification programs.

Another contribution to improving the nutritional status of the region has been the decision to conduct periodic diagnoses of food and nutrition conditions and set up permanent nutrition information systems. These efforts have promoted political concern, both internationally and nationally, and facilitated the more rational allocation of existing resources to those families and/or communities in greatest need of social, health, and nutrition services.

The improvements in vitamin A status observed in Costa Rica, Guatemala, and Honduras can be attributed directly to the implementation of national programs adding vitamin A to sugar. However, in Colombia and El Salvador, where fortification of this type has not been implemented, the major contribution to improvements in vitamin A status and other nutritional deficiencies may be the extension of social services to dispersed communities. For example, in El Salvador a nationwide program, operating in 1973 and 1974, distributed vitamin A capsules through the health infrastructure [Sommer, 1976]. In many countries iron supplements are routinely distributed to pregnant women.

The analyses of changes in the nutritional conditions of the population of TA were based on incidence rates. However, population growth occurring during the study period may overshadow the nutritional improvements measured by these rates. In some countries in which national figures report less severe health and nutritional problems than in the past, more individuals are currently suffering from malnutrition in spite of the reductions in overall rates. For planning purposes and action programs the total number of persons at risk is often more useful than incidence.

Some CMA countries are now more exposed to man-made disasters owing to the rapid depletion of natural resources and to regional political conflicts. The latter has caused the displacement of entire communities and greater difficulties of access to basic services. Significant declines in the production of basic foods are also occurring in the same areas. Refugee problems are reported in Mexico, Guatemala, Honduras, and Costa Rica, and to a lesser extent in Panama.

The international crisis has also limited the capacity of governments to extend the coverage of social and nutritional services. Priority has been given again to direct government investments in productive activities, as opposed to the allocation of additional resources to social services. The deterioration of the purchasing power of national currencies has also imposed constraints on the normal operation of programs such as the fortification of salt and sugar, since the potassium iodate and the retinol palmitate are imported.

On the other hand, in almost all countries, governments have made efforts to identify and locate geographically the most deprived families and communities so that action programs can be better targeted. This has led to a more efficient provision of basic health and nutrition services to regions and commu-

nities that were traditionally excluded from these benefits. Still the lack of current valid and reliable health and nutritional data evidence the need for providing more support to the development of permanent food and nutrition information systems. At the same time, the likely impact of economic crises on health and nutrition indicators shpuld not be overestimated. In spite of a severe economic crisis that occurred in Costa Rica from 1980 to 1982, the important improvements in health and nutrition conditions observed during the 1970s were maintained in the 1980–1982 period [Jaramillo, 1983]. The results of the 1977–1980 national survey in Colombia [Mora, 1982] provide similar evidence. Likewise, poor Guatemalan communities have not suffered a deterioration in health and nutritional conditions, in spite of the economic crisis and/or more limited access to social services [Delgado et al, 1983].

What changes in nutritional conditions can be expected from government interventions? This question is discussed in Gwatkin et al [1980], Delgado et al [1983] and Valverde et al [1983]. Undoubtedly, efficient food fortification programs have eradicated iodine and vitamin A deficiencies in many countries [Arroyave et al, 1979, DeMaeyer et al, 1979]. To estimate the expected nutritional effects of social and economic interventions by government, let us examine data from coffee plantations located in Western Guatemala. Families in these plantations were afforded a medical care program, an increase in minimum wages, and the distribution of an improved protein corn, Opaque-2, for 17 months [Valverde et al, 1983]. The overall incidence of weight retardation declined from 32.4% to 22.2% one year after a new wage scale was enacted. In those populations receiving the Opaque-2 corn, a medical care program, and an increase in wages, children's growth was better than in comparison populations with only medical care and improvements in wages.

The provision of medical care alone has been reported to produce declines in IM and 1–4 YM [MOH/INCAP, 1982; Delgado et al, 1983], but the effects are not immediately reflected in children's growth. In spite of dramatic declines in IM and 1–4 YM in Western Guatemala [Delgado et al, 1983] no reductions were seen in the percentage of children weighing less than 75% of standard weight for age after the communities were exposed for 3 years to an effective simplified medical care program [Valverde et al, 1983].

The variety of lifestyles should be a major consideration in designing interventions for deprived groups. For example, an increase in minimum wages will improve the purchasing power of laborers in coffee plantations but will not affect subsistence farmers or other laborers whose salaries are "above" minimum wages. On the other hand, small farmers will be positively affected by programs distributing land and credit, which to a much lesser extent may also affect other poor groups. Subsidies, through low-price shops, will not benefit populations residing in isolated communities, as these services are usually located in cities or in concentrated semiurban areas.

To conclude, mortality, anthropometric, and other data reflecting vitamin A, iodine, iron, and folate deficiencies indicate that nutritional problems still persist in TA countries. These deficiencies are often more dramatic when the data are analyzed by region and family type. Finally, nutritional problems in TA are not going to be eradicated by "a program" but rather by the operation of a set of programs of an economic and social nature under the responsibility of personnel who understand the behavior and the likely responses of communities to the proposed program activities. Furthermore, there is not—and let's not keep looking for—a single technological solution to overcome food and nutritional problems. It has to be accepted that if resources available are not directed efficiently to poor families, and if decisions of policy makers to implement effectively the proposed actions are not taken, malnutrition will continue to affect an important proportion of the population residing in Tropical American countries.

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