VOL. 2. No. 4. PRICE 5/- ($0.70) MARCH, 1957

THE JOURNAL OF TROPICAL PEDIATRICS

Devoted to all problems of Child Health in Sub-tropical and Tropical Countries of the World.

PROTEIN AND FAT BALANCE STUDIES IN CHILDREN RECOVERING FROM KWASHIORKOR*

by

UNA ROBINSON†, MOISÉS BÉHAR, FERNANDO VITERI, GUILLERMO ARROYAVE *and* NEVIN S. SCRIMSHAW

(Institute of Nutrition of Central America and Panama (INCAP) Guatemala, C. A.)

The clinical, biochemical and physiological characteristics of kwashiorkor have received wide-spread attention, and have been the subject of several reviews (TROWELL, 1954 ; *Conference on protein malnutrition*, 1953 ; SCRIMSHAW et al., 1956). However, most studies have been confined to the acute and initial recovery stages of the syndrome. Despite the fact that the successul rehabilitation of children with kwashiorkor requires long and costly hospital treatment, little information is available on the metabolic characteristics of children in the late stages of recovery.

The amount of protein and fat and the number of calories per kilogram of body weight which will produce optimal recovery are also uncertain. Furthermore, there is little information as to how much the diarrhoea, which the child recovering from malnutrition frequently acquires in an open pediatric ward, affects recovery.

HOLEMANS and LAMBRECHTS (1955) have studied the nitrogen retention of children recovering from kwashiorkor on daily protein intakes ranging from 0.5 to 7.8 gm. per kg. of body weight and found that within this range the amount of nitrogen retained increases with the amount of protein fed. GÓMEZ et al. (1956) have reported a linear relationship in children with kwashiorkor between the amount of protein consumed and both the nitrogen absorbed and retained within a range of 2.2 to 4.1 gm. per kg. of milk protein. However, absorption and retention of nitrogen were both relatively poor on similar children fed corn and beans. GÓMEZ et al. (1956) have also reported the absorption of fat to be reduced in such cases but to improve steadily as recovery occurs. The only data on children in the late recovery phase are those of DEAN (1953) who reports the absorption of nitrogen and fat in three cases to be still somewhat reduced.

The present paper presents the results of 12 periods of metabolic study in four children who were in the stage of late recovery, or what is referred to by BROCK et al. (1955) as " consolidation of cure." Although more cases must be studied in order to resolve the uncertainties mentioned, the data reported are already helping to improve the management of our patients with kwashiorkor and provide suggestions of value for public health programmes directed toward the prevention of protein malnutrition.

* Assisted by Grant-in-aid No. A-981 from the National Institute of Arthritis and Metabolic Diseases of the United States Public Health Service, and by funds from the World Health Organization and the Williams-Waterman Fund of the Research Corporation.

† Professor of Home Economics, Indiana University, Bloomington, Indiana, and Visiting Investigator, INCAP, February-July, 1956. INCAP Scientific Publication I-63.

Material

Four children were admitted to the hospital with moderate or severe kwashiorkor. In each case their signs and symptoms included growth retardation, oedema, apathy and anorexia, skin and hair changes and diarrhoea. Biochemical findings included lowered blood serum protein and albumin and reduced activity of serum amylase, pseudo-cholinesterase and alkaline phosphatase. They had completed initial recovery on a mixed diet highi n milk protein and were gaining weight at the time that the metabolic balance studies were begun. Other pertinent clinical data for each case can be summarized as follows :

F.A., a boy aged 2 years and 7 months, was admitted with severe kwashiorkor 10 weeks before the first balance period. He had been hospitalized for the same condition one year previously. On admission he weighed 9.8 kg. and dropped to 7.0 kg. with the loss of oedema. His height was 77.5 c.m.

F.C., a boy aged 8 years and 11 months, was admitted with moderately severe kwashiorkor 6 weeks before the first balance period. His weight on admission was 18.3 kg. and dropped to 12.1 kg. with the loss of oedema. His height was 104 cm.

T.A., a boy aged 1 year and 5 months, was admitted with severe kwashiorkor of a pronounced marasmic type 6 weeks before the first balance period. On admission his weight was 7.4 kg. and dropped to 5.6 kg. when all oedema was lost. The child was still thin and gaining weight slowly when the metabolic studies were begun. His stools were semi-formed and numbered 5-6 per day. He developed bulky stools during the first balance period but these improved during the second and his rate of weight gain increased. Presumably, due to the drastic drop in the amount of protein given to him, his weight decreased during the adaptation period preceding the third balance trial, but remained stable from 3 days before the trial was actually begun until the experiment ended.

R.L., a girl aged 5 years and 11 months, was admitted 4 weeks before her first balance period with mild kwashiorkor of long standing. Her initial weight was 14 kg. but dropped to 11.6 kg. when her oedema was lost. Her weight was 100.5 cm. Her recovery was clinically and biochemically well advanced at the time of the first trial period and her clinical recuperation was considered complete 8 weeks after admission.

Methods

In order to insure complete collection of urine and faeces during each five-day balance period, the two older children were closely supervised and the two younger ones strapped in a specially adapted bed. The urine was collected under toluene in flasks surrounded by ice. Faeces were collected in a small pot and subsequently washed with distilled water into a glass jar. Both urine and faeces were refrigerated or frozen daily until the collection was completed and the analyses could be done on the composite 5-day sample. One hundred mg. of carmine were administered with the first meal of the period and the collection begun when the dye appeared in the faeces. Five days later an equal amount of carmine was given and the collection of faeces terminated when red stained stools appeared.

The diet ingredients were weighed with an accuracy of 0.1 gm. and a one-tenth aliquot of each food set aside in the refrigerator for subsequent analyses. Nitrogen was determined in the diet, urine and faeces samples by the Kjeldahl method (Hamilton and Simpson, 1946) and fat by that recommended by the A.O.A.C. (1950).

The dietary intakes of protein and calories were designed to meet specific levels considered desirable for the study. The food composition values obtained by INCAP (1953) were used for these calculations which, in general, agreed well with the analytic values for the whole diet. Caloric adjustments were made by varying the quantities of sugar, corn starch and fat included in the diet. During the period of the metabolic studies all children received a vitamin mixture daily which supplied : Vitamin A, 5,000 I.U. ; Vitamin D, 1,000 I.U. ; Thiamine HCl, 1.5 mg. ; Riboflavin, 1.2 mg. ; Niacin, 10 mg. ; Ascorbic acid, 50 mg. ; Pyridoxine HCl, 0.5 mg.

The nitrogen absorbed was calculated as equal to the nitrogen intake minus the nitrogen excreted in the faeces. The nitrogen retained was assumed to be the quantity absorbed less that excreted in the urine. In accordance with Macy (1942) and Allison (1955), but in contrast to Holemans and Lambrechts (1955), no correction for faecal nitrogen was made in calculating the nitrogen absorbed.

Results

The amount of protein, fat and calories consumed per kg., the amount of protein per 100 cal. and the body weight and clinical status in each period are shown in Table I together with the data on nitrogen and fat absorption and nitrogen retention. When recovery was progressing satisfactorily, the absorption of nitrogen was high but the retention varied from 16.4 to 52.9 per cent. The milligrams of nitrogen per kilo actually retained ranged from 95 to 259. Under the same circumstances the percentage of fat absorbed varied from 31.9 to 88.5 per cent.

TABLE I. Metabolic data in children recovering from kwashiorkor.

Patient	Weight in kg.	Clinical status	Principal Protein source	Dietary Intake				Nitrogen			Fat % Abs.
				Protein		Fat	Cal.	Abs.	Retained		
				gm./kg.	gm./100 Cal.	gm./kg.	kg.	%	%	mg./kg./day	
R.L.	12.7	Good recovery	Acid whole milk[1]	2.9	2.2	1.9	130	78.4	44.0	205	88.5
R.L.	14.3	Good recovery	Skimmed milk[2]	3.1	2.6	0.8	115	85.5	52.9	259	71.3
F.A.	9.6	Good recovery	Acid whole milk[1]	5.3	3.7	3.6	144	79.8	27.7	240	78.0
		Diarrhoea 1 day						13.5	−1.0	−6	60.8
F.A.	9.8		Skimmed milk[2]	3.8	3.1	1.0	122				
		Post ,, 4 days						57.5	4.6	28	59.6
F.A.	10.4	Slightly bulky stools	Skimmed milk[3]	4.0	3.5	0.7	115	75.1	17.3	112	31.9
F.A.	10.8	Good recovery	Skimmed milk[3]	4.1	3.6	1.3	114	81.5	23.1	150	77.5
F.A.	11.2	Good recovery	Skimmed milk[2]	2.6	2.4	0.9	108	74.1	23.0	95	52.9
T.A.	7.1	Bulky stools	Half sk. milk[4]	7.3	5.4	1.8	135	75.1	11.7	137	87.2
T.A.	7.4	Slightly bulky stools	Skimmed milk[2]	9.4	7.1	0.9	132	84.2	16.4	247	57.8
T.A.	7.5	Stationary weight	Skimmed milk[2]	2.6	2.6	0.4	99	86.6	3.2	13	77.6
F.C.	14.6	Good recovery	Skimmed milk[2]	6.2	5.8	0.8	106	82.2	14.0	138	78.7

1. " Pelargon "—Supplied by Nestlé Co. 2. Supplied by UNICEF. 3. " Golden State." 4. " Nesbrum "—Supplied by Nestlé Co.

The balance period in F.A., in whom diarrhoea occurred during the first day, followed by relatively loose bulky stools for the remaining four days, showed a very marked adverse effect of the diarrhoea on both the absorption and retention of nitrogen. The former dropped from 79.8 to 13.5 per cent. in the first day and returned only to 57.5 per cent. in the following four days. The latter dropped from 27.7 per cent. to a negative 1 per cent. and returned only to 4.6 per cent.

There was a general tendency for the amount of nitrogen and fat absorbed per kg. per day to increase linearly with the amounts fed. This is illustrated for nitrogen in Fig. 1 and for fat in Fig. 2. These figures include the linear regression equation and line for each correlation. The percentage of nitrogen retained showed great variation from one child to another. There was no tendency for the amount of nitrogen retained per kg. per day, to show a correlation with either the amount of nitrogen consumed or absorbed. The relationship between the amount of fat consumed and that absorbed was highly variable. Unlike the absorption of nitrogen, the absorption of fat does not appear to be affected by a period of diarrhoea.

Discussion

When no diarrhoea was present, the percentage of nitrogen absorbed by these children was remarkably uniform and the average value of 80.2 per cent. is probably a good indication of the amount of absorption to be anticipated under the circumstances of these trials. This average is less than the 90 per cent. given by MACY (1942) for well nourished children. Our figure may indicate a slight impairment of absorption even late in recovery.

Surprisingly, the average per cent. absorption of nitrogen in the present study is almost the same as that reported by HOLEMANS and LAMBRECHTS (1955) for 28 balance periods in children with acute kwashiorkor. In view of the evidence that gastrointestinal enzymes are drastically reduced in acute kwashiorkor (TROWELL et al., 1954 ; *Conference on protein malnutrition*, 1953 ; THOMPSON and TROWELL, 1952 ; and GÓMEZ et al., 1954), this would confirm a very rapid recovery of the proteolytic enzymes (VEGHELYI, 1948) before the child could be placed on the metabolic trial. From the standpoint of practical therapy it means that the large quantities of protein customarily administered in the treatment of kwashiorkor are digested and the nitrogen absorbed. A very rapid recovery has also been noted for serum protein and albumin and for several of the serum enzymes (TROWELL et al., 1954 ; SCRIMSHAW et al., 1956).

The percentage of absorbed nitrogen retained by the body may be expected to show a great deal more variation. When the quality of protein is constant the most important cause of this variation will be the degree of depletion of body stores. In early recovery the retention may be expected to be relatively large, but this is bound to decrease as the tissue needs are met and normal balance is approached. On the other hand, the percentage of nitrogen retained at the stage when tissue deficits have been satisfied will depend upon the total amount of nitrogen absorbed and the rate of growth.

The question should be asked, however, whether or not the feeding of very high levels of protein in recovery actually results in more nitrogen being retained by the body or simply causes an increased urinary and faecal nitrogen excretion. The figures obtained together with those of HOLEMANS and LAMBRECHTS (1955) and GÓMEZ et al. (1956) suggest that there is an essentially linear relationship between the amount of nitrogen fed and the amount retained per kg. per day, as long as the body is depleted of protein. However, this no longer applies to children who have been fully repleted of protein and who have

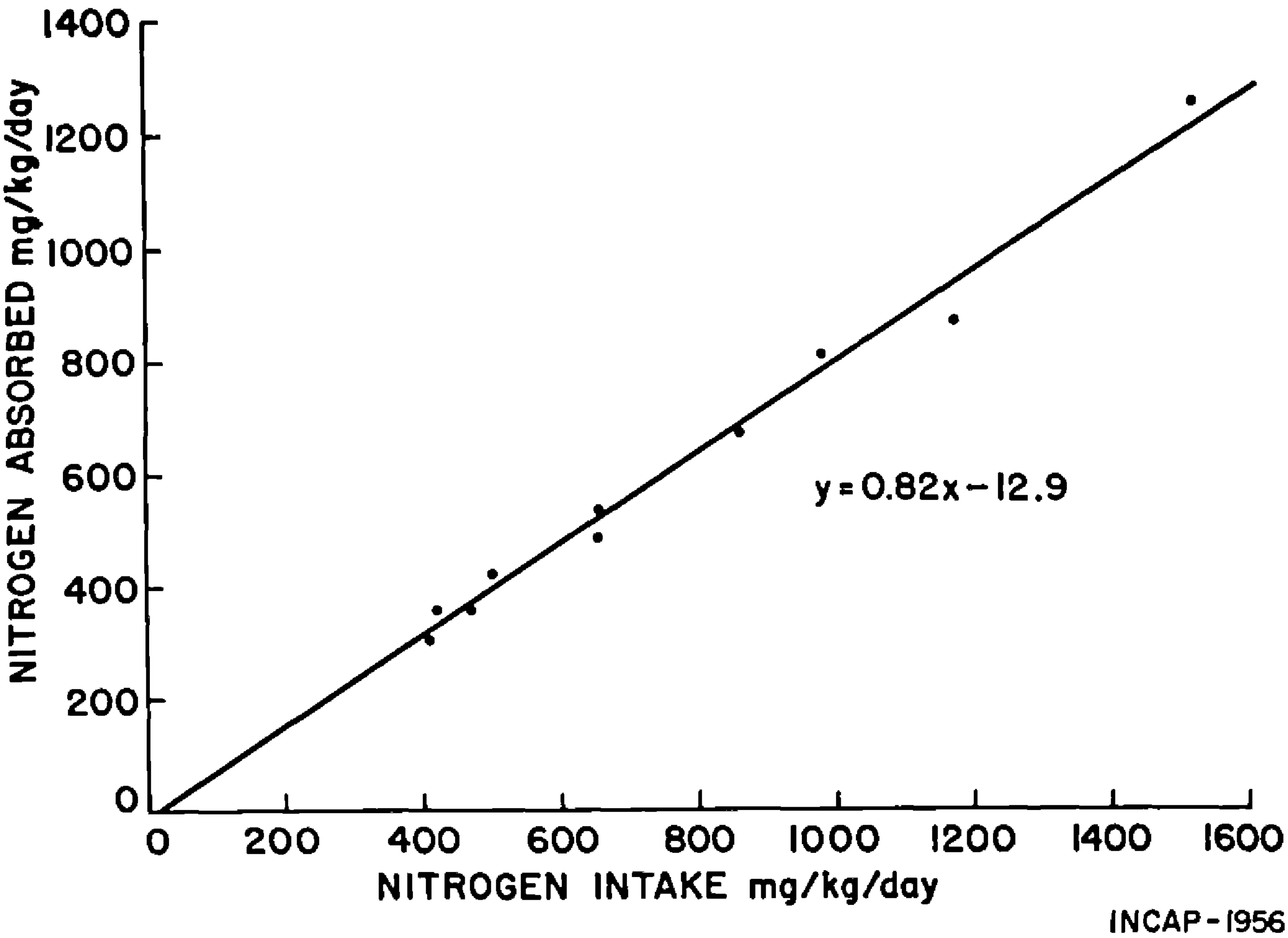

FIG. 1. Relationship between nitrogen intake and nitrogen absorption in children recovering from kwashiorkor.

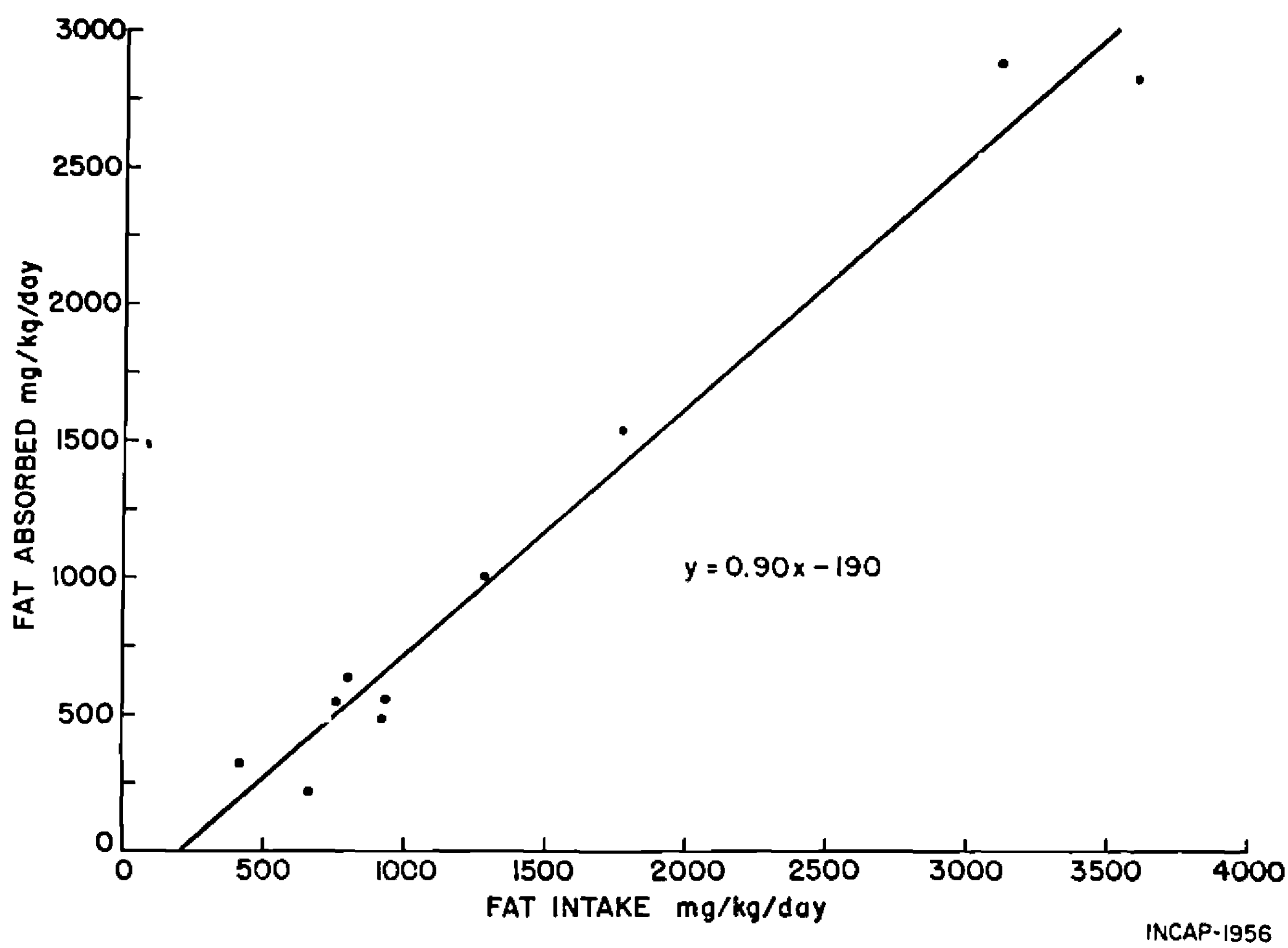

FIG. 2. Relationship between fat intake and fat absorption in children recovering from kwashiorkor.

regained the appropriate weight for their height. This would explain why R.L. retained 259 mg. of nitrogen per kg. per day on an intake of only 3.1 gm. per kg., while F.C. retained only 138 mg. on an intake of 6.2 gm. of protein per kg., even though the protein came from skim milk in each case.

The data appear to justify relatively high protein intakes for therapy during the active recovery period. In fact, the case of T.A. illustrates the danger of not maintaining a high enough protein intake. This child was showing excellent clinical progress and weight gain at the beginning of the balance studies. When given 7.3 gm. of protein per kg. he retained 137 mg. per kilo and when this was increased to 9.4 gm. his retention increased to 247 mg. per kilo. However, when his intake was reduced to 2.6 gm. per kg. he was barely able to maintain a positive nitrogen balance and weight gain not only stopped, but his weight stayed stationary as long as the protein intake was held at this relatively low level.

It is of great interest that the child with diarrhoea neither absorbed nor retained nitrogen well, although a one-day balance is subject to a relatively large experimental error. Additional studies of children with diarrhoea are obviously indicated. The data presented support the suggestion that diarrhoea may be a very important factor in the original development of acute kwashiorkor (AUTRET and BÉHAR, 1954 ; SCRIMSHAW et al., 1955) and in the relatively slow recovery of cases in open pediatric wards where infections producing diarrhoea are common (SCRIMSHAW et al., 1956). This may be due in part to the drop in duodenal enzymes reported by VEGHELYI (1948) for children with infectious diarrhoea.

Neither acid whole milk, nor half skimmed milk appeared to have any advantage over skimmed milk, although too few cases were involved for conclusions on this point. As would be expected, the degree of recovery of the child was more significant in determining the nitrogen retention than the number of weeks in the hospital. Too few cases were studied to allow comments on the effect of either the age or the weight of the child on the values cited. Since the children were not studied metabolically until recovery was deemed satisfactory, it is not likely that severity of the kwashiorkor entered importantly into the trials.

The factors responsible for the relatively large variation in the amount of fat absorbed are not readily apparent. In general, the percentage of ingested fat absorbed was considerably less than the 97 per cent. for normal children given by MACY or 90-95 per cent. cited by DOCHAIN and LAMBRECHTS (1954). It was also lower than that reported by HOLEMANS and LAMBRECHTS (1955) for acute kwashiorkor, but higher than in most of the cases studied by GÓMEZ et al. (1956). It should be noted that the determination of fat absorption was only an incidental part of the study and most of the fat intakes were relatively low. Only additional studies can indicate the value or adverse effect of higher fat intakes in the treatment of kwashiorkor. From the present study, it does not appear that the amount of fat present in whole acid milk is less readily handled by the child than the small amount of fat in the skimmed milk.

SUMMARY

The nitrogen absorption and retention of four children recovering from acute kwashiorkor of the marasmic type were determined in twelve metabolic balance periods begun after initial recovery. When milk protein was given in amounts varying from 2.6 to 9.4 gm. per kg., nitrogen absorption in uncomplicated kwashiorkor varied from 74.1

to 85.5 per cent., with an average of 80.2 per cent. The nitrogen retained per kg. per day showed no correlation with the protein intake or absorption. Both nitrogen absorption and retention were drastically reduced by an episode of diarrhoea. A daily level of 2.6 gm. of protein per kg. was barely sufficient for positive nitrogen balance in a boy 18 months of age and did not support growth. The fat intakes ranged from 0.4 to 3.6 gm. per kg. per day and the fat absorbed showed a positive linear correlation with the amount fed.

REFERENCES

Allison, J. B. (1955). *Physiol. Rev.*, **35**, 664. Biological evaluation of proteins.

Association of Official Agricultural Chemists (1950). *Official Methods of Analysis.* 7th Ed. Washington, D.C. : Association of Official Agricultural Chemists.

Autret, M. and Behar, M. (1954). Sindrome Policarencial Infantil (Kwashiorkor) and its prevention in Central America. *FAO Nutritional Studies No.* 13. Rome, Italy, Food and Agriculture Organization of the United Nations.

Brock, J. F., Hansen, J. D. L., Howe, E. E., Pretorius, P. J., Davel, J. G. A. and Hendrickse, R. G. (1955). *Lancet*, **269**, 355. Kwashiorkor and protein malnutrition. A dietary therapeutic trial.

Dean, R. F. A. (1953). *Bull. Wld. Hlth. Organ.*, **9**, 767. Treatment and prevention of Kwashiorkor.

Dochain, J. and Lambrechts, A. (1954). *Rev. Med. Liége*, **9**, 15. Problémes diététiques du lait. III. Influence de l'homogénéisation du lait sur l'absorption des graisses par l'enfant normal. (Cited by Holemans and Lambrechts).

Gómez, F., Ramos Galván, R., Cravioto, J. and Frenk, S. (1954). *Pediatrics*, **13**, 544. Studies on malnutrition in children. Enzymatic activity of the duodenal content in third grade malnutrition in children.

———, ———, ———, ———, De la Peña, C., Moreno, M. E. and Villa, M. E.(1956). Protein metabolism in chronic severe malnutrition (Kwashiorkor). I. Absorption and retention of nitrogen from a typical diet (in press).

———, ———, ———, ———, Vazquez, Santaella, J. and De la Peña, C. (1956). Studies on the undernourished child. XX. Fat absorption in chronic severe malnutrition (In press).

Hamilton, L. F. and Simpson, S. G. (1946). *Talbot's Quantitative Chemical Analysis.* 9th Ed., p. 355. New York : The Macmillan Co.

Holemans, K. and Lambrechts, A. (1955). *J. Nut.*, **56**, 477. Nitrogen metabolism and fat absorption in malnutrition and in Kwashiorkor.

Instituto de Nutrición de Centro América y Panamá (1953). *Suplemento No.* 1 *del Boletin de la Oficina Sanitaria Panamericana*, " Publicaciones Cientificas del Instituto de Nutrición de Centro América y Panamá, p. 129. Tercera edición de la Tabla de Composición de Alimentos de Centro América y Panamá.

Macy, I. G. (1942). *Nutrition and chemical growth in childhood.* Vol. I. *Evaluation.* Springfield, Ill. : Charles C. Thomas.

" Protein Malnutrition " (1955). Proceedings of a Conference in Jamaica, 1953. Sponsored jointly by the Food and Agriculture Organization, World Health Organization and Josiah Macy Jr. Foundation. New York : University Press, Cambridge.

Scrimshaw, N. S., Behar, M., Pérez, C. and Viteri, F. (1955). *Pediatrics*, **16**, 378. Nutritional problems of children in Central America and Panama.

———, ———, Arroyave, G., Viteri, F. and Tejada, C. (1956). *Fed. Proc.*, **15**, —. Characteristcs of Kwashiorkor (Sindrome Pluricarencial de la Infancia). (In press).

———, ———, ———, Tejada, C. and Viteri, F. (1956). J.A.M.A. Severe protein malnutrition (Kwashiorkor) in children and its response to protein therapy. (In press).

Thompson, M. D. and Trowell; H. C. (1952). *Lancet*, **262**, 1031. Pancreatic enzyme activity in duodenal contents of children with a type of Kwashiorkor.

Trowell, H. D., Davies, J. N. P. and Dean, R. F. A. (1954). *Kwashiorkor.* 1st Ed. London, England : Edward Arnold Ltd.

Veghelyi, P. V. (1948). *Acta Paediatrica*, **36**, 483. Pancreatic function in different clinical conditions.

PROPHYLAXIS OF TUBERCULOSIS IN CHILDHOOD*

by

Arvid J. Wallgren

(*Emeritus Professor of Pediatrics, Pediatric Department of Karolinska, Sjukhuset, Stockholm, Sweden.*)

Prevention of tuberculosis in childhood includes two objectives, prevention of infection and prevention of the development of tuberculous disease from the infecting bacilli. By prevention of infection the children are, of course, protected in the most efficient way against tuberculosis. If there is no tuberculous infection, there can be no tuberculous disease. To protect children from infection, however, is often very difficult. even if all available public health measures are applied. These measures include a satisfactory milk hygiene and control of the health of people who have professionally to do with children. In countries with a very high tuberculosis morbidity rate, the sources of infection are so numerous that almost no children escape infection. In countries with a moderate morbidity rate about half of the children become infected, while in countries with a very low mortality rate, such as in Scandinavia, only a few children run the risk of exposure, and the prevention of infection is therefore an easier task.

Once tuberculous infection has occurred it depends largely upon the resistance of the child whether tuberculous disease will be manifested. If the resistance is high, no disease will occur, while, if the resistance is low, the child may die from tuberculosis. The factors that determine the degree of resistance may be divided into two groups: non-specific and specific. The non-specific, natural resistance depends upon the age of the child when infected and upon genetic, constitutional and environmental factors. The specific resistance is due to immunity conferred by a previous infection. It has long been known that a tuberculous infection produces an increased specific resistance against subsequent infections. This immunity is without doubt of benefit to the child, but at the same time the bacilli producing the immunity may constitute a potential danger, threatening the child with tuberculous diseases of various kinds. Therefore it was a great advance when Calmette and Guerin managed to produce their BCG-strain of tubercle bacilli and showed that it could be used as an immunizing agent.

Many reports have been published which intend to show the efficiency of BCG-vaccination, but most of them are presented in such a way that their frequently very optimistic conclusions seem unwarranted. I will only quote a few of those which I regard as being reliable. The most recent study and, according to my opinion the best planned one, is that performed by the British Medical Research Council (1956). It concerns about 25,000 tuberculin-negative adolescent school-children, chosen at random, living in an ordinary environment, half of them were BCG-vaccinated, the other half having been left unvaccinated as controls. The two groups were subsequently examined carefully at regular intervals. A preliminary report was published when the study had run for $2\frac{1}{2}$ years. It was found that roughly 5 times as many clinical cases of tuberculosis had occurred in the unvaccinated group as in the vaccinated one. Of special interest is the fact that there were 6 cases of miliary tuberculosis and tuberculous meningitis in the unvaccinated group, as against no case in the vaccinated children. The report concludes that the *BCG-vaccination had produced a substantial protection against tuberculosis.*

The result of this study corresponds fairly well with the experiences reported by Aronson (1952) of vaccination among American Indians in U.S.A., with those of Hyge

* Report read at the VIIIth International Congress of Pediatrics, Copenhagen, July 1956.

(1956) regarding the effect of the vaccination upon acutely exposed adolescent girls in a school in Denmark, and with the study DAHLSTRÖM and DIFS (1956) of BCG-vaccination in the Swedish army during the war. I suppose that it might be said, that there is a rather unanimous agreement among those who have had experience with this prophylactic procedure ; an adequately made BCG-vaccination, that is, a vaccination that has had time to produce tuberculin sensitivity before exposure, undoubtedly provides fairly satisfactory protection against the immediate consequences of a tuberculous infection, against serious forms of primary tuberculosis, against the early postprimary diseases, miliary tuberculosis and tuberculous meningitis, as well as against pleurisy and early postprimary pulmonary tuberculosis. The protection against late postprimary types of tuberculosis seems to be slighter and more uncertain.

What has been said about the efficiency of BCG-vaccination may also be applied to the use of the vole bacillus as an immunizing agent, according to the experience of the British Medical Research Council (1956). There seems to be no reason to change over from BCG to the vole vaccine.

At present there are some other problems regarding BCG-vaccination that are more generally discussed, namely the duration of the immunity, the use of freeze-dried vaccine, the untoward effects of the vaccination and the general principles of the vaccination as a public health measure.

Regarding the first question, that of *the persistence of the immunity*, it is not possible to arrive at any definite conclusions, and we here meet another problem, that of the method of assessment of immunity. Usually the existence of immunity is measured by tuberculin tests. We must admit, however, that tuberculin sensitivity and specific immunity are not identical. Lacking other easily applied methods of assessment, we have to rely upon the tuberculin sensitivity, when we want to determine the existence of immunity. Another factor that may interfere is the occurrence of subclinical tuberculous infection, which may influence the persistence of the immunity. With these reservations in mind, it might be said that the immunity can disappear within one year, but on the other hand, according to our experience, it can last for as long as 7 - 10 years or perhaps more. The duration of the immunity thus varies considerably — and it is not possible in advance to tell how long it will last. In all events it will as a rule last sufficiently long to be of real benefit to an exposed child.

Regarding *the use of lyophilized BCG*, there are without doubt some advantages to be gained through facilitating storage and distribution of the vaccine and also making its potency more uniform. Researches now in progress have shown thus far that freeze-dried vaccine may be used effectively up to one year after production, but with a certain decrease of its potency. At present it would be premature to recommend its general use, at least in countries without transport difficulties.

In countries with a well developed public health service and very low tuberculosis morbidity rate, *vaccination of selected groups* of the population, especially those who run an evident risk of exposure, seems to be the principle of choice — if there is any need of vaccination at all. Such selected groups are family contacts, medical students, student nurses etc. In countries with a very high tuberculosis morbidity rate, the risk of exposure is very great and thus there is need of more *general vaccination*. The latter principle has been followed by the World Health Organisation (1954) in its campaign against tuberculosis in post-war Europe and in its present campaign in Eastern countries. Usually, when BCG-vaccination is introduced into a country where there is no previous experience of its efficiency, it is at first tentatively given to selected groups of the population. After its benefit has been demonstrated, it is extended to larger and larger groups. This seems to be a logical development of the vaccination in a country with high tuberculosis morbidity rate. The reverse development, diminishing the use of general vaccination and continuing with vaccination of only selected groups when the tuberculosis morbidity rate has decreased to a very low figure, should be logical too. When only a few percent. of children become infected at 15 years of age, as in Sweden, there seems to be little indication to continue with general vaccination, for instance, of newborns. Although the resistance is lowest in early infancy, the risk of exposure is so small that there is little need of vaccination of this age group. If a more general vaccination should be performed in such a country the policy recommended by the British Medical Research Council (1956) seems to be that which should be preferred, i.e. vaccination fo school-children at pre-puberty age.

Many reports have been published of *complications or untoward reactions* after BCG-vaccination. These reactions are usually local and have developed at the site of the administration of the vaccine, and in the regional lymphatic glands in the form of abscesses. Lymph-node abscesses are always to be regarded as abnormal reactions, but local skin abscesses only when they are large and persist for a long time. The incidence of such complications in adequately performed vaccinations varies considerably with the commercial origin of the vaccine used, with the dose and the mode of administration and with the degree of susceptibility of the child. We have had very little trouble in this respect with intradermal administration of an adequate dose of the Swedish vaccine.

In addition to these untoward local reactions there are a few reports on the development of lupus in the neighbourhood if the site of the vaccination.

Some words may be added about the occurrence of *systemic BCG-processes*. During the last 5 years a few cases of such an abnormal course of BCG-vaccination have been published from the Scandinavian countries. These cases have been carefully studied and, according to my opinion, it must be admitted that BCG-bacilli in extremely rare instances may give rise to chronic inflammatory processes by haematogenous spread of the bacilli. These cases have not been due to a too-potent vaccine, because the same sample has been used in other children without any complication at all, nor do they depend upon an error in the administration of the vaccine. It is probably unknown individual factors, causing an abnormal susceptibility, that are responsible. In relation to the many hundred thousands of vaccinations performed in Scandinavia and the great protective benefit derived from these vaccinations, the occurrence of such an abnormal susceptibility is extremely rare and its significance should not be exaggerated.

In *conclusion* it might be said that tuberculosis in infancy and childhood may be prevented by the application of general public health measures aiming at the enlightment of the population, satisfactory milk hygiene, control of the health of people who have professional contact with children and by adequately performed BCG-vaccination.

REFERENCES

Aronson, J. D. and Aronson, Ch. (1952). *J. Amer. med. Ass.*, **149**, 334. An appraisal of protective value of BCG vaccine.

British Medical Research Council (1956). *Brit. med. J.*, **1**, 413. First report by Tuberculosis Vaccines Clinical Trials Committee.

Dahlström, G. and Difs, H. (1951). *Acta. Tuberc. Scand.*, **25**, Suppl. 27. The efficacy of BCG vaccination.

Falkmer, S., Lind, A. and Ploman, L. (1955). *Acta paedict.*, **44**, 219. Fatal tuberculosis from BCG vaccination.

Hollström, E. and Hård, S. (1953). *Acta. dermat.-venercol.*, **33**, 159. A fatality from BCG vaccination.

Hyge, T. V. (1956). *Acta. tuberc. Scand.*, **32**, 89. The efficacy of BCG-vaccination.

Imerslund, O. and Jonsen, T. (1954). *Acta. tuberc. Scand.*, **30**, 116. Lupus vulgaris and multiple bone lesions caused by BCG.

Meyer, J. (1954). *Amer. Rev. Tuberc.*, **53**, 517. A fatal case of tuberculosis produced by BCG.

Thrap-Meyer, H. (1954). *Acta. tuberc. Scand.*, **29**, 173. Generalized BCG infection in man.

Wallgren, A. (1952). *Advances in Pediatrics*, **5**, 232. BCG-vaccination.

——— (1953). *Acta tuberc. Scand.*, **28**, 155. Immunity in tuberculosis.

——— (1955). *Acta paediat.*, **44**, 237. Should mass-vaccination with BCG be discontinued in Scandinavia ?

World Health Organisation Technical Report Series (1954) No. 88. Sixth Report of the Expert Committee on Tuberculosis : Vaccination against Tuberculosis.

EDITORIAL NOTICES

Papers submitted for publication in *The Journal of Tropical Pediatrics* should be sent to the Editor, Department of Tropical Medicine, Tulane University, New Orleans, La., U.S.A.

The submission of matter for publication will be understood to imply that it is offered to this Journal alone. If accepted for publication, the copyright of papers becomes the property of the Journal ; but they may be re-published by permission, provided due acknowledgement be made of their having appeared in *The Journal of Tropical Pediatrics*.

Papers should, if possible, be typewritten ; they should be concisely written with subject matter logically arranged and sub-divided ; with references and abbreviations in the approved form ; and with indications of the position, in the text, of illustrations, tables, maps, etc.

All papers should be carefully read over and checked before submission for publication, thus avoiding heavy author's corrections. It must be pointed out that author's corrections are expensive, and in cases where these are excessive, authors may be asked to pay for them.

TITLES should be as brief as consistent with clarity ; and in many cases the value of a paper is enhanced by a short SUMMARY at the end.

TEMPERATURE CHARTS, GRAPHS AND DRAWINGS should be, if possible, in Indian ink on white board ; with *detail and essential lettering large enough to be clearly legible after reduction if necessary.*

ILLUSTRATIONS — If the number sent in is considered excessive, the author may be informed and given the opportunity of contributing to the cost.

Authors of Papers published in *The Journal of Tropical Pediatrics* receive 10 copies of the Journal free. Reprints can be supplied on payment, and must be ordered when submitting the paper.

Published for *The Journal of Tropical Pediatrics* by J. M. P. PUBLISHING SERVICES, Effingham House, Arundel St., London, W.C.2, and printed in Great Britain by F. J. Parsons, Ltd.. London, Folkestone and Hastings.