# Infection and Nutritional Status

## I. The Effect of Chicken Pox on Nitrogen Metabolism in Children

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THE intense interest in the metabolic effects of severe infections during the early part of the century resulted in studies which clearly established the profound adverse effect of bacterial infections on nitrogen balance. A recent review of available reports on interrelationships between infection and nutrition[1] confirmed the impression that relatively little attention has been paid in recent years to the effect of infection on nutritional status in general and on protein metabolism in particular.

An exception has been the growing recognition that severe protein malnutrition in children, kwashiorkor, is frequently precipitated by an acute infectious episode.[2-8] There are no published studies of the effect of viral infections on nitrogen metabolism, but epidemiologic evidence[9-12] indicates that not only are bacterial infections such as bacillary dysentery important in this regard, but also measles, chicken pox and other diseases of viral origin.

The present study reports the effect of chicken pox on the nitrogen metabolism of children hospitalized in the metabolic unit of the Institute of Nutrition of Central America and Panama (INCAP). Since nitrogen balance studies were already in progress in two of these children, there was an opportunity to determine the metabolic effect of the prodromal as well as the acute phase of the disease.

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### MATERIAL

Six young boys in different stages of recovery from kwashiorkor were studied. All of them had passed the acute phase and were in the long period of recuperation. Having participated in previous balance studies, the subjects were accustomed to the procedure. Two of them (PC-91 and PC-98) were in a study at the time the first clinical signs of chicken pox appeared. All, except one (PC-98), had relatively severe skin lesions and were febrile during the first three to five days after appearance of the exanthem; the temperature of this patient (PC-98) never exceeded 37.9°c.

In order to obtain complete collections of urine and feces, the children were placed in a bed with a plastic container for the collection of feces protruding through a hole in the mattress, and a funnel of dental plate material was placed around the penis for the collection of urine. Since these were fastened directly to the patient, he could sit up and move about the bed with considerable freedom. Urine and fecal samples were maintained under refrigeration and pooled for each three-day period. Although the frequency of the balance periods varied somewhat from case to case, they generally involved three days on balance and three off. In some cases, observations were continued with diminished frequency of balance periods for three to four weeks after the appearance of the exanthem.

The diet was generally that fed the patient at the time his illness developed, and varied, therefore, from 2 to 5 gm. of protein per kg. of

TABLE I
Subjects Studied

| Subject | Age | Weight (kg.) |
|---|---|---|
| PC-82 | 2 yr.-9 mo. | 13.8 |
| PC-91 | 6 yr.-5 mo. | 16.3 |
| PC-92 | 3 yr.-3 mo. | 13.4 |
| PC-97 | 3 yr.-7 mo. | 14.3 |
| PC-98 | 2 yr.-4 mo. | 9.8 |
| PC-102 | 4 yr.-9 mo. | 13.8 |

body weight per day and 90 to 120 cal. Milk was the source of protein in all the patients but one (PC-98) who received Incaparina, a vegetable mixture of comparable protein quality.[13] All received supplementary carbohydrate and fat as calorie sources as well as adequate vitamins and minerals.

An aliquot of each component of the diet was set aside for analysis, and food not consumed or lost due to vomiting was deducted from the calculated intake. Nitrogen content of food and excreta was determined by the Kjeldahl method and the calculated nitrogen intake was based on actual analysis of the diet aliquots.

The weights and ages of the children appear in Table I.

## RESULTS

In the first three cases illustrated in Figure 1, net nitrogen retention decreased in the period immediately following the appearance of the exanthem, although previous balance periods were available in only one (PC-91) of the three to confirm that the drop did not begin at an earlier stage of the disease. In the next two cases (PC-92 and PC-102), the drop in nitrogen retention was delayed until the second balance period after the appearance of the exanthem.

The effect of the infection on three boys (PC-82, PC-91 and PC-97) was of relatively short duration. In two (PC-92 and PC-102) the adverse effect on nitrogen retention persisted for at least two weeks. No systematic differences in the temperature curve or other clinical aspects of these children were noted which might explain the differences in the duration of the effect.

The last case in Figure 1 (PC-98) is more difficult to interpret since a period of low retention was observed five days prior to the appearance of the skin manifestations and again seven days afterwards. It is not certain that these drops in retention were due exclusively to the chicken pox, since the child had only recently recovered from a prolonged period of diarrhea and furunculosis developed soon after the last balance period illustrated. There was, however, no overt evidence of these other disorders during the clinical episode of chicken pox. As noted previously, he remained essentially afebrile throughout, and the skin lesions, although typical, were less numerous than in the other children studied.

Another significant effect of the infection on net nitrogen metabolism (a reduction in intake) is concealed when the data are expressed as percentage of intake. The marked anorexia that developed in association with the infection made it almost impossible to maintain the nitrogen intake of children at predetermined levels, even with the efforts by a trained staff. All the children except one (PC-98), the very mild case, vomited frequently under these circumstances. Vomiting was not limited, however, to the balance periods with reduced retention. As shown in Table II, there is a tendency for nitrogen intake to drop during the acute phase of the disease, although the changes are not of large magnitude in most cases.

The intestinal absorption of nitrogen expressed as percentage of intake and urinary excretion as milligrams nitrogen per kilogram of body weight per day are also shown in Table II. Although the results are somewhat variable, there is no evidence that infection with chicken pox had any consistent effect on absorption. Since the decreased intake of nitrogen was not sufficient to account for the periods of decreased retention, the latter would of necessity have to be the result primarily of increased urinary excretion of nitrogen and the analytical figures for urinary nitrogen in Table II confirm this.

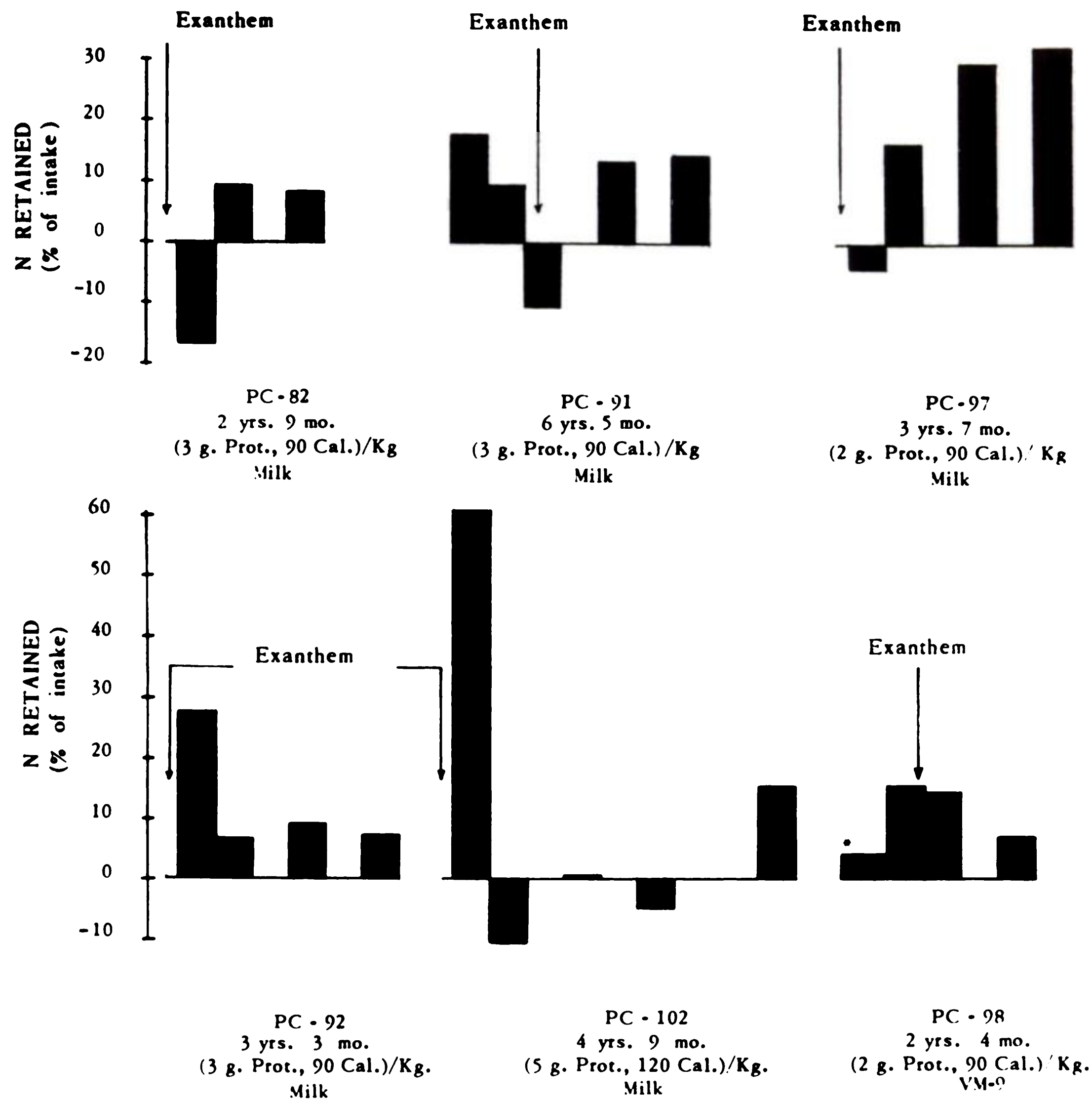


FIG. 1. Effect of chicken pox on nitrogen retention in children (three-day balance periods).

## COMMENTS

The results indicate that in each of the six cases studied the disease had an adverse effect on nitrogen metabolism although the timing appears to vary. That the variations observed are not likely to occur in children without an infection is seen in results obtained by us in several hundred other balance periods when infection was not present. In such children the maximum deviations observed over periods of a month or more were much lower than in the present study.

The results also show another common adverse consequence of infection, a reduction of food intake due to the child refusing to consume the same quantity as before the illness developed. Under prevailing practices in areas in which malnutrition is common, this effect could be aggravated by the tendency of parents and physicians alike to reduce the consumption of protein-rich foods during an acute infectious episode.

Another possible effect of infection could be a reduced absorption of nitrogen due to increased gastric motility or interference with biochemical processes involved in absorption at the cellular

**Table II**
Effect of Chicken Pox on Nitrogen Metabolism in Children
(Three-Day Study Periods)

| Subject | I | II | III | IV | V | VI | VII | VIII |
|---|---|---|---|---|---|---|---|---|
| *Nitrogen Intake (mg. N/kg./day)* | | | | | | | | |
| PC-82 | ↓305 | 425 | NC | 419 | ... | ... | ... | ... |
| PC-91 | 452 | 443 | ↓392 | NC | 437 | NC | 469 | ... |
| PC-97 | ↓251 | 268 | NC | 317 | NC | 242 | ... | 291 |
| PC-92 | ↓432 | 363 | NC | 446 | NC | 410 | ... | ... |
| PC-102 | ↓726 | 582 | NC | 685 | NC | 652 | NC* | 619 |
| PC-98 | 341† | 338 | 327 | ... | 309 | ... | ... | ... |
| *Nitrogen Absorption (% of intake)* | | | | | | | | |
| PC-82 | ↓89.4 | 89.7 | NC | 90.3 | ... | ... | ... | ... |
| PC-91 | 84.2 | 82.9 | ↓78.7 | NC | 81.9 | NC | 90.4 | ... |
| PC-97 | ↓71.1 | 76.9 | NC | 78.1 | NC | 80.7 | ... | ... |
| PC-92 | ↓87.4 | 84.3 | NC | 85.9 | NC | 83.2 | ... | ... |
| PC-102 | ↓80.2 | 79.6 | NC | 71.9 | NC | 70.7 | NC* | 78.9 |
| PC-98 | 52.3† | 68.7↓ | 60.9 | NC | 68.3 | ... | ... | ... |
| *Urinary Nitrogen Excretion (mg. N/kg./day)* | | | | | | | | |
| PC-82 | ↓324 | 341 | NC | 344 | ... | ... | ... | ... |
| PC-91 | 302 | 324 | ↓349 | NC | 298 | NC | 354 | ... |
| PC-97 | ↓188 | 161 | NC | 153 | NC | 146 | ... | 131 |
| PC-92 | ↓260 | 281 | NC | 343 | NC | 310 | ... | ... |
| PC-102 | ↓141 | 523 | NC | 484 | NC | 490 | NC* | 394 |
| PC-98 | 164† | 181 | 151 | ... | 189 | ... | ... | ... |

Note: ↓ Exanthem; NC = No collection.
* Seven days.
† Four days.

level in the intestinal wall. There is no evidence from the data presented that this is a factor of importance in chicken pox infections.

The principal effect of the infection seems definitely associated with an increased urinary nitrogen excretion which in turn may be explained by a loss of cell protein due to the infection of individual cells with the virus. An alternate possibility would be a direct interference of the infection with the normal growth and repair of tissue and hence a decrease in protein synthesis. Reiss,[14] on the basis of $N^{15}$ studies, concludes that both impaired synthesis and increased catabolism of protein occurred in the muscles of starved rats with streptococcal pneumonia, with the latter effect predominating.

Infection can also contribute to a lowered nitrogen balance by an increase in basal metabolic rate due to fever. It has been previously shown that the net effect of fever through such a mechanism is small compared to the total magnitude of the change observed, and that large nitrogen losses are often seen in afebrile infections.[15]

All but one of the children in the present study had already recovered from kwashiorkor, and all were receiving an apparently adequate protein intake. In children in lower socioeconomic groups the protein intake is markedly restricted in both quantity and quality, and the effect of an infection on nitrogen metabolism is likely to be more serious, although the absolute change as a result of the infection could be less.[16,17] The data presented help explain why an acute infection in a child who is already malnourished due to an inadequate protein intake is frequently followed by the development of kwashiorkor.


### SUMMARY

Nitrogen balance data were obtained for several three-day periods in each of six children with chicken pox. In all the children some degree of reduction in nitrogen retention was noted. In three of them, this occurred in the period immediately following the appearance of the exanthem, and in two, it was delayed for several more days. In the sixth child, a decrease occurred during the prodromal period. In two of the children the adverse effect lasted for as long as two weeks. Since the infection did not appear to influence nitrogen absorption, an increase in urinary nitrogen was obviously taking place. This was confirmed by direct measurement of urinary nitrogen. Despite efforts to maintain a constant dietary intake, the children consumed less food during the acute phase of infection. The results help explain the association between an epidemic of an acute infection and the subsequent appearance of an increased number of cases of kwashiorkor in children already suffering from underlying protein malnutrition.



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