The CYSTINE *and* METHIONINE *Content of the Hair of* MALNOURISHED CHILDREN

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THE EXTENSION of medical care and observation to primitive areas of the world has emphasized the importance of the striking human weanling disease described for western medicine by Williams[1] and called *kwashiorkor*. This name, a West African dialect word for "red boy," describes the characteristic reddening of the skin and hair seen in dark-skinned children.

Kwashiorkor has now been described in many parts of the world[2] and appears to be a common complication of that crucial dietary transition in a child's development from the mother's breast to solid food. The visceral complications of the disease and particularly the profound alterations of the liver structure are believed to contribute to serious chronic diseases of adult life such as cirrhosis and carcinoma of the liver.[4,5] This residual injury is in addition to the very large mortality occurring in children when the dramatic kwashiorkor syndrome is present.

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Considerable evidence now indicates that kwashiorkor is primarily a nutritional disease.[6] Assessment of previous dietaries and trials with protein supplements have indicated that an insufficient amount of adequate protein in the diet is of first importance in the etiology of kwashiorkor.

It is well known that the eukeratins, of which mammalian hair protein is a representative, contain relatively large amounts of sulfur. This element is largely present as a component of cystine[7] with methionine and perhaps cysteine present in much smaller amounts.[8] It has been shown by Heard and Lewis[9] that the dietary sulfur levels influence the sulfur content and distribution of hair in growing rats.

It occurred to us that the cystine and methionine content of hair from malnourished children might be a sensitive indicator of the presence of kwashiorkor or one of its variants. Aside from the significance such a demonstration would have in revealing the etiology of kwashiorkor, a sensitive hair indicator might also serve to detect the disease before irreparable structural damage had been done. These considerations led us to a study of the content of cystine and methionine in the hair of such malnourished children.

METHODS

During April and May of 1953 approximately 75 hair samples were collected in a number of clinics in Indonesia. The majority were taken in the hospital of the University of Indonesia, Djakarta, and consisted of 10–1000 mg. of head hair obtained from normal

and malnourished children. The nutritional status of the children was classified by the Indonesian physicians on the basis of dietary histories, clinical signs, and laboratory measurements of hemoglobin and serum proteins. The children ranged in age from 8 to 48 months. They were for the most part described as being of Indonesian parentage, but a few were of Chinese ancestry.

Analysis of Hair

When the hair samples were received in Boston, they were defatted, dried to a constant weight, hydrolyzed with hydrochloric acid, and analyzed for methionine and cystine.

Fat Extraction: Each sample was rolled into a circle of Whatman #1 filter paper and the ends secured by stapling. The package was immersed in Bloor's solution (ethanol-ethyl ether 3:1) for 48 hours at room temperature. The solvent was renewed at the end of the first 24 hours.

Drying: The samples were air-dried for 72 hours at about 60° C. They were then placed in loosely corked plastic tubes and stored in a desiccator over phosphorus pentoxide.

Weighing: The tubes were then tightly stoppered and removed for weighing on each of at least three consecutive days. When a constant weight was reached, the contents of the package were emptied into a hydrolyzing flask. This was done by cutting the ends of the paper tube and allowing the hair to slide into the flask. The paper and the cut ends were returned to the original drying tube and weighed immediately and on at least three successive days. The weight of the hair sample analyzed was thus obtained by difference.

Hydrolysis: The hair was placed in a flask fitted with an air condenser and containing a 1:1 mixture of 20% hydrochloric acid and 88% formic acid. The volume of acid used depended on the weight of sample, but varied from 6–20 ml. for sample sizes of 200–1000 mg. The hair was refluxed for approximately 12 hours at 120–125° C. The resulting hydrolysate was transferred quantitatively to a porcelain evaporating dish and concentrated to a thick syrup on a steam bath. This was taken up in water and filtered through paper. The filtrate and washings were brought to a convenient volume with 0.1 *N* hydrochloric acid. Aliquots of this material were used for analysis.

Cystine analysis was by the Block and Bolling adaptation of the Winterstein-Folin procedure[10] and methionine was measured by the method of Horn, Jones, and Blum.[11]

Results

The analyses were successfully completed on hair samples from 40 children. The remaining samples, thought to be from children who did not have the kwashiorkor syndrome, furnished too little material for analysis. Of the 40 samples considered here, seven were from normal Indonesian children and 33 were from children classified as having kwashiorkor. The data obtained are shown in Table I, which gives a statistical summary of the findings. Inspection of this table reveals that there was no significant difference between methionine and cystine content of hair from normal or malnourished children. While the variation of the methionine content among children was large, as is indicated by the standard deviations in Table I, inspection of the data of individuals failed to reveal evidence that the hair composition was related either to the clinical description or to the laboratory measurements of hemoglobin, serum total protein, albumin and globulin which had been carried out in the Indonesian hospitals.

Since kwashiorkor, like many other nutritional diseases, appears to be the consequence of long continued dietary inadequacies, it is

TABLE I

The Methionine and Cystine Content of the Hair of Normal and Malnourished Indonesian Children

	Age, months, mean and standard deviation	Methionine as % of dry hair weight ± standard deviation	Cystine as % of dry hair weight ± standard deviation
Normals (7 females)	19.4 ± 9.5	0.641 ± .141	15.27 ± .797
Kwashiorkor (22 females)	22.4 ± 9.0	0.784 ± .259	15.01 ± 1.92
Kwashiorkor (11 males)	22.4 ± 9.7	0.793 ± .289	15.08 ± 2.09

proposed that changes of hair composition might require long periods of malnutrition for development. Thus, older children with longer exposure to the adverse dietary might reveal hair changes not seen in the younger children. Charts relating the hair content of both cystine and methionine to the age of the sick children were made, but these failed to reveal a meaningful relationship. Thus, the older children showed no progressive deviation from the control levels. Neither could a sex difference be demonstrated in this respect.

We conclude that kwashiorkor is not characterized by an abnormality of hair content of cystine and methionine. The structural changes of hair observed in kwashiorkor would appear to represent either a total inhibition of growth or a deviation of some other constituent than the sulfur-containing amino acids.

The observations of Dean[6] which indicate that leguminous foods may have a curative action when administered to children ill with kwashiorkor also argue against the disease being a sulfur deficiency, for pea and soybean proteins are notably lacking in cystine and methionine.

Summary

Chemical analysis of hair samples of 33 Indonesian children with kwashiorkor failed to reveal alterations of the cystine or methionine content.

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Resumen

El contenido de cistina y metionina de los cabellos de niños malnutridos

El análisis químico de muestras de cabellos de 33 niños indonésicos con kwashiorkor no reveló ninguna alteración del contenido de cistina o metionina.