Three conclusions were drawn from this study: (1) That the risk of inducing bacteriuria at urological instrumentation under the conditions described is low ; (2) that this risk is not reduced by giving a single dose of a long-acting wide spectrum antibiotic ; (3) that many cases of bacteriuria induced by instrumentation are self-limiting and therefore presumably of no serious consequence.

A comparison of the results of this survey and of the results of other work in this field shows that conclusions regarding the risks of infection resulting from instrumentation in obstetric patients, or resulting from the presence of an indwelling catheter, cannot be applied to the risks of instrumentation in urological patients.

I would like to thank Mr. G. C. Tresidder, who allowed me to carry out this survey on his patients and who gave me great encouragement and assistance in its organization. I would also like to thank Professor M. W. Weatherall, who advised on the method of planning the trial, and Professor C. Barwell, in whose department the bacteriological work was performed. My thanks are also due to Lederle Laboratories for their co-operation and for the supply of demethylchlortetracycline tablets.

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Phrynoderma

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Brit. med. J., 1966, **1**, 29–30

In 1933 Nicholls coined the term " phrynoderma " to describe a particular type of follicular hyperkeratosis seen in tropical countries. The elbows, thighs, and buttocks are characteristically affected, the follicles contain large keratin plugs, and the adjacent skin is usually darker than normal. Most workers have come to the conclusion that it is a disease of malnutrition, though the precise deficiency is still in doubt. Frazier and Hu (1931) claimed that cod-liver oil produced improvement, and Loewenthal (1933) and Rao (1937) attributed this to an increased intake of vitamin A. Nicholls (1934), Aykroyd and Krishnan (1937), and Gopalan (1947), however, thought that vitamin-B deficiency was responsible, and Gopalan pointed out that xerophthalmia did not correlate with phrynoderma, as would be expected if vitamin-A deficiency was the cause. Finally, some evidence that deficiency of essential fatty acid might be the cause was produced by Ramalingaswami and Sinclair (1953).

The opportunity was taken to study this problem during a year (1962–3) as a lecturer at University College Hospital, Ibadan, Nigeria.

Method

All patients with follicular hyperkeratosis seen in the skin clinic at University College Hospital were studied and those with obvious phrynoderma were selected. A general examination was made, their diet assessed, and blood taken for estimation of haemoglobin, white-cell count, and serum vitamin-A level, the method of Paterson and Wiggins (1954) being used.

All cases were then given oral therapy, first riboflavin (20 mg. daily for a month), then aneurine hydrochloride (6 mg. daily for a month), and finally vitamin B co. forte *N.F.* (two tablets daily for a month ; each tablet contains riboflavin 2 mg., aneurine hydrochloride 5 mg., nicotinamide 20 mg., and pyridoxine hydrocloride 2 mg). Each patient was seen once a month.

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Results

Of 432 Nigerians seen in the skin clinic during December 1962 to July 1963 39 had follicular hyperkeratosis. All were children. Four had id eruptions (three due to tinea capitis (*Microsporon audouinii*) and one to ulcerating glandular tuberculosis), 11 had a bizarre dyskeratosis of a striking distribution which was probably due to an inherited keratin defect (Shrank, 1966), and two had keratosis pilaris. The remaining 22 (5% of all skin patients) had phrynoderma ; eight were boys and 14 were girls, with a mean age of 10 years (range 3 to 16).

The eruption had been present for a mean of eight months (range two weeks to one year) and involved the characteristic sites. There was no family history of a like eruption. All the children in this group seemed fit, with the exception of two who had stomatitis. Physical examination did not reveal any cause for the eruption, though three had palpable spleens due to chronic malaria.

Sixteen of the children were Yoruba and 23 were Ibo. Their diet was essentially the same and typical of the Western Region of Nigeria. It is composed mainly of the starchy roots—yam and cassava—supplemented with only small amounts of meat, beans, green vegetables, and fruit. Much of the food is cooked in red palm oil, which provides liberal amounts of linoleic acid (9.7% of the total fatty acids (Naismith, 1963)) and is the most potent natural source of carotene known (carotene content equivalent to 1,000–100,000 I.U. of vitamin A per 100 g. (Platt, 1962)). Evaluation of this

diet suggests that it will barely satisfy the requirements for protein and the B group of vitamins, particularly in the case of the younger children.

Haemoglobin and white-cell counts were within normal limits ; none had a haemoglobinopathy. Serum vitamin-A levels varied from 34 to 57 μg./100 ml. (mean 45 μg./100 ml.) ; these results are rather high, even for the Nigerian, as the normal range reported by Edozien (1960) is 11 to 40 μg./100 ml., with a mean of 26 μg./100 ml. This confirms that these children consumed large quantities of carotene ; this must have been in the form of red palm oil, as the only other source of carotene is red pepper, which provides a relatively small amount. It therefore follows that they also consumed a sufficient quantity of linoleic acid. The parallel relationship between the content of vitamin A and linoleic acid, dependent on the dietary use of red palm oil, is clearly shown in the composition of the breast milk of the Yoruba woman. It was found to contain twice as much linoleic acid and vitamin A as that of her European counterpart (vitamin A 112 μg./100 ml. ; linoleic acid 15% of the total fatty acids (Naismith, 1963)).

During treatment with riboflavin the stomatitis resolved. There was no apparent effect on the hyperkeratosis after the riboflavin or aneurine therapy, but after the month's treatment with vitamin B co. forte *N.F.* the keratin plugs fell out and the papules began to flatten, though the lesions still remained quite dark. In only one case, that of a girl aged 5, did the phrynoderma improve during the riboflavin therapy.

Discussion

These results exclude conclusively both a deficiency of vitamin A and of essential fatty acids as the cause of phrynoderma in Nigerian children.

The improvement after three months' therapy is not likely to have been spontaneous or attributable to the natural history of the disease, as patients had suffered from the disease for such varying lengths of time prior to treatment. Nor can the remission be a seasonal phenomenon, as new cases came to the clinic in both the wet and the dry seasons. The evidence presented in this paper in fact supports the view that vitamin-B therapy is an effective treatment for phrynoderma. Neither riboflavin nor aneurine hydrochloride on their own influenced the eruption, unless the remission obtained in the third month is regarded as a delayed effect ; this is unlikely, as Clarke and Okoro (1962), who treated 72 Nigerians in Lagos with combined oral and parenteral vitamin B, found that improvement was apparent within a month in 61 and within two weeks in 12. Gopalan (1947) had tried six therapies (vitamin A, niacin, riboflavin, yeast extract, linseed oil, and a mixture of the last two) and found that those with yeast extract produced the best improvement, while niacin alone was ineffective. All this evidence implies that treatment with several of the components of the B group of vitamins is effective when they are given together but not when given separately. Of all the drugs used pyridoxine was not administered separately, so it still may be the vital factor.

The doses given are a little greater than the therapeutic dose but are not excessive. Though it is most probable that this treatment corrects a deficiency of vitamin B, an unphysiological mechanism remains a possibility. Such a mechanism is postulated, for example, to explain the efficacy of massive doses of vitamin A in some cases of ichthyosis, a disorder which is not believed to be caused by a deficiency of vitamin A. If, however, vitamin-B deficiency was responsible for phrynoderma, and possibly solely responsible, a high family incidence, a more frequent occurrence in the community, and a close correlation with stomatitis would be expected. Alternatively, the deficiency may be the precipitating factor, while other factors determine the presentation as phrynoderma rather than stomatitis, and in one sibling rather than another.

The disease is found in many widely separated communities in Asia and Africa ; their customs differ, their racial constitution has no common denominator, and their climate is dissimilar, so these factors are unlikely to play a part in the disease. Uncleanliness can also be dismissed, as many of the communities are Moslem with strict ritual laws on washing ; certainly most Yoruba children, who are predominantly Moslem, are usually bathed twice a day. A high carotene content of the diet may be a factor in Nigeria, but it cannot be held responsible for phrynoderma in the Orient, as diets there are often deficient in this component. Keratosis pilaris is a possible factor, but sufferers from phrynoderma did not show evidence of keratosis pilaris when the phrynoderma had resolved.

It is difficult to understand the part played by vitamin B in this disorder. Histology shows the basic lesion to be a comedo, differing from that in acne vulgaris only in site (Loewenthal, 1933) ; ectopic comedones are known to be produced by exposure to mineral oils and chlorinated hydrocarbons but these are irrelevant to the Nigerian environment. The current hypothesis of comedo formation invokes two errors in the development of the pilosebaceous follicle ; first, the hair that normally keeps the follicle patent is either absent or in the resting phase and not growing, and, secondly, the sebaceous gland produces an altered secretion with more keratin and less lipid (Van Scott and MacCardle, 1956 ; Strauss and Kligman, 1960). The B group of vitamins could influence both these processes by their action on carbohydrate and lipid metabolism, but there is no evidence of a more direct effect on the pilosebaceous follicle.

Summary

A study was made of 22 Nigerian children with phrynoderma seen at University College Hospital, Ibadan.

Their high intake of red palm oil, which contains much carotene and linoleic acid, and their high serum levels of vitamin A, are strong evidence that deficiency of vitamin A and essential fatty acids is not responsible for phrynoderma in Nigerian children.

Remission of the dermatosis occurred with oral vitamin B co. forte *N.F.* but not with riboflavin or aneurine alone ; and, their diet being known to be low in the B group of vitamins, it is suggested that multiple deficiency of these nutrients is a major factor in producing phrynoderma.

Thanks are due to Professor J. C. Edozien for chemical estimations in his laboratory, and to Dr. D. J. Naismith for advice and help with the manuscript. This paper was part of a communication presented at the International Congress of Tropical Dermatology in June 1964.

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