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## PHRYNODERMA AND SOME ASSOCIATED CHANGES IN BLOOD LIPIDS\*

By K. RAJAGOPAL

and

S. R. CHOWDHURY

*Section of Biochemistry and Nutrition, All-India Institute of Hygiene and Public Health, Calcutta*

PHRYNODERMA is the name given by Nicholls (1933) to a hyperkeratosis occurring in malnourished individuals. This was attributed by him to vitamin A deficiency. Frazier and Hu (1931) had made observations on this condition in China and had recognized it as due to nutritional deficiency. This condition has been used as a convenient sign in routine nutritional surveys in India as an index of vitamin A deficiency. Rao (1937) has described the histopathology of phrynoderma and has brought out evidence that it is due to vitamin A deficiency. A nutritional survey carried out in Malabar (India) by Aykroyd and Rajagopal (1936), however, cast some doubt on the generally accepted aetiology of this condition. They described in their paper that there was little doubt that phrynoderma was associated with diet deficiency. But further work was required to establish the precise relationship. The amount of animal and vegetable fat (from fish and coconut) consumed by people in Malabar was relatively high, compared with other parts of the province where phrynoderma was common. They pointed out that phrynoderma may possibly be due to deficiency of fat in the diet, which prevents the normal lubrication of the skin. Another point to be considered is that inunction with vegetable oil is perhaps more commonly practised in Malabar and this would have kept the skin moist and glossy. Gopalan (1947) amplified this work and in controlled investigation of cases of phrynoderma found that linseed oil and yeast extract administered by mouth produced good recovery. The question now was whether the unsaturated fatty acids helped the cure of phrynoderma. Menon, Tulpule and Patwardhan (1950) continued the

investigation and they showed that phrynoderma is probably due to essential fatty acid deficiency. Marmite alone was found to be ineffective and also had no synergistic action with gingelly oil which was found to cure the skin condition. On analysing blood they showed that iodine number of plasma fatty acids was significantly less than that of normals and on oral administration of gingelly oil, good therapeutic results were noticed and the cure was accompanied by an increase in the unsaturation of plasma fatty acids.

### Experimental

Cases of phrynoderma were sent by the late Dr. L. M. Ghosh and by Dr. D. Panja, the dermatology specialist of the School of Tropical Medicine, Calcutta, for our observation and treatment. The patients had no preliminary medication of any kind before coming to us.

The history of the cases and the nature of skin lesions are presented in table I.

The level of the total fatty acids, cholesterol and iodine value of serum of the patients were estimated. These patients were administered three teaspoonfuls twice a day (total of  $\frac{3}{4}$  oz. a day) of raw linseed oil. The concentrations of different fatty acids in linseed oil were determined by the method of Mitchell, Kraybill and Zscheile (1943) and Beadle (1946) using alkali isomerization, followed by ultra-violet absorption measurement with a Beckman spectrophotometer. The concentrations of fatty acids in the linseed oil sample used were as follows:—

Linoleic acid	.. 7.6 per cent.
Linolenic acid	.. 44.1 „
Oleic acid ..	.. 21.6 „
Saturated acid	.. 26.7 „

The sample of linseed oil used for therapeutic purpose was tested for acid value and no sample having more than a value of 1.4 was used.

On the disappearance of the symptoms, the time taken for which varied from four weeks to twenty-four weeks, total fatty acids, cholesterol and iodine value of the fatty acids were estimated again. The estimations were also carried out in forty-five healthy normal individuals both men and women to obtain normal figures for these.

The iodine value was estimated by Yasuda's (1931) method and the cholesterol and total fatty acids were estimated by Bloor's (1928) method. In case of cholesterol estimation, the intensity of the colour was matched in a Pulfrich photometer using filter no. 11.

For the purpose of comparison, the results obtained by other workers engaged in similar work has been shown in table II.

The averages of blood lipid composition of phrynoderma cases in the present work and those obtained by other workers are shown in table III.

\* Preliminary results on the blood lipid analysis of twenty-two cases of phrynoderma and eight normal individuals were communicated in an Abstract to the Indian Science Congress Association, Poona, 1950.

TABLE I

Patient number	Age in years	Sex	Degree of skin lesions*	Duration	Other associated deficiencies	Complaints for which the patient sought relief
1	10	F.	A	6 months	Angular stomatitis. Glossitis.	Hemeralopia. Burning sensation of the tongue.
2	6	F.	A	1 year	..	Slight itching.
3	6	M.	B	6 months	..	..
4	13	M.	B	3 years with exacerbation in winter.	Angular stomatitis	..
5	4	M.	B	6 months	..	..
6	13	M.	B	8 "	..	..
7	15	M.	B	3 years with exacerbation in winter.	..	Slight itching.
8	12	F.	C	3 months	..	..
9	12	M.	C	1 year	Angular stomatitis	..
10	12	F.	C	4 months	..	..
11	8	M.	C	7 "	..	..
12	12	M.	D	10 "	..	..
13	12	M.	D	2 "	..	..
14	30	M.	B	6 "	..	..
15	35	M.	B	1 month	Bitot's spots	Slight itching.
16	20	M.	B	1½ years	Angular stomatitis. Glossitis. Inflammation on the margin of the eyelids and slight conjunctivitis.	Slight itching. Burning sensation of the tongue. Blepharitis.
17	25	M.	B	2 months	..	..
18	16	F.	B	3 years with exacerbation in winter.	Angular stomatitis. Glossitis.	Weakness. Burning sensation of the tongue.
19	16	M.	B	6 months	Brownish pigmentation on the sclera, conjunctivitis.	..
20	21	M.	B	11 "	..	Slight itching.
21	20	M.	C	6 "	Bitot's spots	..
22	17	M.	C	2½ years with exacerbation in winter.	..	..
23	21	F.	C	9 months	Angular stomatitis	..
24	18	M.	D	..	Glossitis, depigmented patches on the face, dermatitis on the scrotum.	Slight itching.

\* A = Wide distribution on upper extremities, trunk and the lower extremities and densely packed papules with black pin head.  
 B = Wide distribution as in A, but the keratotic papules not so severe as in A.  
 C = Distribution and the lesion limited to either lower or upper extremities and papules marked.  
 D = Distribution as in C but the papules less marked than in C.

TABLE II

Group studied	Author	mg./100 cc. serum			
		Total lipids	Cholesterol	Total fatty acids	Iodine number of fatty acids
14 normal adults.	Hansen (1937)	645	228	417	129
3 normal adults.	Ginsberg and co-workers (1937).	575	189	386	116
10 normal adults.	Finnerud and co-workers (1941).	..	..	634	99
45 normal adults.	Present investigation.	485	156	329	114

TABLE III

Group studied	Author	mg./100 cc. serum			
		Total lipids	Cholesterol	Total fatty acids	Iodine number of fatty acids
10 children	Menon and co-workers.	in plasma			
		534	152	384	96
13 children	Present investigation.	in serum			
11 adults		409	146	263	92
		443	138	305	94

For want of space the tables showing the serum lipid values of normal individuals and of patients before and after treatment have been omitted.

### Discussion

The serum analysis of normal cases in this study shows that the figures for the forty-five individuals for total lipids, cholesterol and total fatty acids are 485, 156 and 329 mg. per 100 cc. serum respectively. Comparison of these figures with those obtained by other workers cited in table II shows that the average figures for total lipids and cholesterol in our hand was found to be lower than those reported by Hansen (*loc. cit.*). The total fatty acid value corresponds fairly well with those obtained by other workers excepting the figure found by Hansen which is higher.

In the case of iodine number of fatty acids, the average works out to 114 and the range is 107 to 121. The figure agrees well with that obtained by Ginsberg and co-workers (1937) and is higher than that obtained by Finnerud and co-workers (1941) and lower than that obtained by Hansen (*loc. cit.*).

Diet surveys carried out in West Bengal among the class of people from whom the cases in this study are drawn, show that the diet generally comprises :—

Carbohydrate	..	640 gm.
Protein	..	74 gm.
Fat	..	27 gm.
Calcium	..	0.58 gm.
Phosphorus	..	1.4 gm.
Iron	..	30 mg.
Vitamin A	..	2,500 I.U.
Vitamin B <sub>1</sub>	..	1.9 mg.
Vitamin B <sub>2</sub>	..	1.0 mg.
Nicotinic acid	..	30.0 mg.
Vitamin C	..	88 mg.

It will be seen that the fat intake is very low, of the order of 27 gm. per day. The diet is preponderatingly a vegetarian one and it is evident that it lacks in animal protein as well. The requirement of vitamins and minerals is seen to be adequate excepting riboflavin. This is also brought out clinically by a good number of the subjects exhibiting signs of riboflavin deficiency, namely, angular stomatitis. The discrepancies in the figures for the total fatty acids, cholesterol and other constituents mentioned previously, with the values quoted by other workers, might perhaps be largely due to the differences in the quality and quantity of fat intake among the subjects studied by the several workers.

The results obtained among the phrynoderma cases are broadly grouped into two age groups—5 to 15 years and 16 years and above. This would allow comparison with the results carried out by Menon and co-workers (*loc. cit.*). In the younger age groups the figures in the present series are—total lipids 409, cholesterol 146, total fatty acids 263 mg. per 100 cc. serum and the iodine number of fatty acids is 92. This compares favourably with the values of Menon

and co-workers (*loc. cit.*)—total lipids 534, cholesterol 152 and total fatty acids 384 mg. per 100 cc. plasma and the iodine number of fatty acids is 96.

In the case of adults no comparison is possible as the latter workers have not included an appreciable number in this age group. In the present study more than 40 per cent of phrynoderma cases had other signs of nutritional deficiency as shown in table I. The administration of raw linseed oil was carried out by one of us (S. R. C.) and it will be seen that in no case was there any gastro-intestinal upset. The periodical examination, at monthly intervals, revealed that there was a general improvement of other signs besides phrynoderma; for example, the depigmented patches on the face in case 24 disappeared. There was no improvement in angular stomatitis, glossitis and Bitot's spots. The latter point that Bitot's spots did not regress is in confirmation of the observation noticed earlier by Aykroyd and Rajagopal (*loc. cit.*), that there was no parallelism between the occurrence of phrynoderma and Bitot's spots, casting some doubt that vitamin A deficiency was the cause of phrynoderma.

A statistical evaluation of the figures for serum lipid analysis will not be without interest.

### Iodine number

1. Mean values of iodine number for the diseased group before and after treatment were 92.96 and 110.50 respectively. The mean increase was 17.54 during treatment. The rise in iodine number was statistically significant ( $t = 4.58$  with 23 degrees of freedom).

2. The difference between the average values of the iodine number of the normal group (113.89) and the diseased group before treatment (92.96) was statistically significant ( $t = 6.09$  with 67 degrees of freedom).

3. The difference between the average values of iodine number of the normal group (113.89) and the diseased group after treatment (110.50) is still significant at 5 per cent level ( $t = 2.39$  with 67 degrees of freedom).

4. Sex and the age groups involved in the study have no significant influence on the iodine number.

### Cholesterol

1. In the normal group sex was found to have a significant effect on the cholesterol, the female having higher values.

2. In the diseased group neither sex nor the age group involved was found to have any significant effect on the cholesterol.

3. Significant difference was noticed between the cholesterol values of the normal group and the diseased group before treatment, the diseased group having lower mean value.

4. No significant difference was noticed for the cholesterol values of the diseased group between before and after treatment.

*Fatty acids*

1. Sex has no significant effect on fatty acids.
2. In the diseased group higher age groups were associated with larger amount of fatty acids but no such relationship was seen in the normal group.
3. The diseased group had significantly lower average amount of fatty acids before treatment compared to normal.
4. Significant increase was noticed in the fatty acid contents of the diseased group between before and after treatment.
5. There was no significant difference in the average fatty acid contents between the diseased group after treatment and the normal group or, in other words, the treatment had the effect of raising the fatty acid content of the diseased group to the level of the normal group.

*Summary*

1. Serum lipid analyses of 45 normals and 24 phrynoderma cases, before and after treatment, were carried out.
2. The average values of total lipids, cholesterol, total fatty acids and iodine number of fatty acids of the serum of phrynoderma cases were found to be lower than those of normal subjects.

	mg./100 cc. serum			Iodine number of fatty acids
	Total lipids	Cholesterol	Total fatty acids	
Normal subjects ..	485	156	329	114
Phrynoderma cases ..	443	138	305	94

3. Oral administration of raw linseed oil in  $\frac{3}{4}$  oz. dose per day for a period extending up to 24 weeks was carried out with phrynoderma cases. Improvement was noticeable even as early as in two weeks and cure was achieved in 4 to 24 weeks. Simultaneously with the clinical cure, the serum lipid composition also tended to rise to the level found in normal subjects.
4. This investigation confirms the original idea postulated in 1936 by Aykroyd and Rajagopal that phrynoderma is in some way connected with fat metabolism. The figures obtained for the lipid analysis in blood serum and also the clinical findings in the present investigation show that the essential fatty acids have a causative effect in this condition.

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☒ A NOTE ON THE ASCARICIDAL VALUE OF HETRAZAN\*

BY JASWANT SINGH, M.B., Ch.B. (Edin.), D.P.H. (Eng.), D.T.M. & H. (Lond.)  
 LIEUTENANT-COLONEL  
 N. G. S. RAGHAVAN, B.A., M.B., B.S.  
 B. G. MISRA  
 A. K. KRISHNASWAMY, M.B., B.S.  
 (Malaria Institute of India, Delhi)  
 and  
 RADHAGOVINDA ROY, M.B., B.S.  
 (Filaria Control Unit, Indian Council of Medical Research)

IN the course of treatment of bancroftian filariasis with Hetrazan, massive expulsion of ascarids was reported by Briceno Rossi and Hewitt (1949) in Puerto Cabello, Venezuela, as well as Galliard and Mille (1949) in Tahiti, South Pacific. Hewitt *et al.* (1950) reported similar action of Hetrazan when the drug was used in the mass control of bancroftian filariasis in the field in St. Croix, Virgin Islands. Following these observations, Hetrazan was used as an

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