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COMMUNICATIONS

THE AETIOLOGY OF CHRONIC PRIMARY
GLAUCOMA

BY

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IN a previous paper¹ I described primary glaucoma in association with epidemic dropsy. This interesting disease broke out again in parts of Bengal, Bihar, the United Provinces, Assam and Burma in 1934-35 and during this period 1,695 cases of this type of glaucoma came for treatment to the Eye Infirmary, Medical College Hospitals, Calcutta.

To-day most ophthalmologists regard the causation of primary glaucoma as evidence of a diseased state, not only of the eye but of the body in general.

With a view to the elucidation of the aetiology of primary glaucoma in general this disease provided a vast field for research. It is the only general disease at present known in which glaucoma forms an integral part and hence is the biggest clinical lead we have ever had in the pathogenesis of glaucoma, and places primary glaucoma in its proper environment, namely a symptom complex of a general disease.

It is now definitely recognised that epidemic dropsy is an entirely different disease from beri-beri and there are no points of similarity either in the symptomatology or the pathology between the disease that is now epidemic in Bengal and the beri-beri which has been claimed as the human counterpart of polyneuritis gallinarum of fowls. Although the aetiology of epidemic dropsy in

the present state of our knowledge is unknown, there is more justification in placing this disease amongst the bowel diseases rather than the food deficiency diseases, and it would perhaps be more satisfactory if the Bengal epidemic dropsy were classified amongst the diseases of uncertain aetiology, as having nothing whatsoever to do with the diseases caused by vitamin "B" deficiency. In the pathology of epidemic dropsy whether regarded from the general or the ophthalmological or the dermatological aspects, there is never to be found any evidence of inflammation and the two outstanding manifestations are the vaso-dilatation of the whole capillary system and an increased permeability of the capillary endothelium.

In the eye, microscopic examination of the filtration angle shows that the canal of Schlemm and the tissues in the immediate vicinity do not show any abnormalities either in cellularity or increased fibrosis. The epithelium of the ciliary processes also does not show any change. Increased dilatation of the blood tissues is seen in the sub-epithelial connective tissue of these processes. There is also an enormous dilatation of the capillaries of the choroid, but there is no evidence of any inflammatory process to be found in the whole of the uveal tract. (See Figs. 1 to 4 and Plate I).

FIG. 1.

Photomicrograph of the filtration angle of the eye from a case of epidemic dropsy. The channels of absorption (canal of Schlemm and tissues around) do not show any abnormalities either in cellularity or increased fibrosis.

FIG. 2.

FIG. 3.

Figs. 2 and 3 show different parts of the ciliary body. The epithelium of the ciliary processes does not show any change. Marked vascular dilatation is present in the sub-epithelial connective tissues. There is no evidence of any inflammatory process.

FIG. 4.

Photomicrograph of the choroid from a case of epidemic dropsy showing enormous dilatation of the capillaries. Such a vascular change in the choroid coat often gives an impression of haemorrhage although actual extravasation of blood in the tissues does not take place. The wide gap between the vascular and pigmented layer has been apparently caused during the preparation of the specimen.

In the present state of our knowledge the prevalent opinion is that the disease is associated with the ingestion of diseased, stored, par-boiled rice as patients recover quickly after a stoppage of rice in early cases: more advanced and late cases take a much longer period to recover according to the duration of the disease. Relapses invariably occur if the rice is resumed too early. These are liable to occur even when healthy rice is eaten suggesting that infection of the rice occurs in the intestines of the patient. Gram-positive organisms with certain special characteristics are frequently found in the stools of cases of epidemic dropsy and similar organisms have been recovered from diseased rice. In the Tropical School of Medicine, Calcutta, the blood and urine of a large number of epidemic dropsy cases have been examined during the different stages of the disease but no organisms have been found. From the stools of patients and from the infected rice some two hundred strains of Gram-positive spore-forming bacilli have been isolated and tested for agglutination with the sera of convalescent patients. Eight strains, four from actual patients, and four from

IRIS

in Epidemic Dropsy Glaucoma

Magnification X 44

PLATE I.

Section of iris in epidemic dropsy glaucoma showing marked dilatation and engorgement of capillaries. Total absence of any sign of inflammation.

rice were found to agglutinate in a high dilution with the sera of convalescent patients and not with the sera of normal persons. These observations are of importance in establishing the causation of the disease. The results so far obtained indicate that an organism of the genus *Bacillus* infects the rice and the ingestion of this rice leads to the development of the disease. Further, that the toxic or other products are elaborated mainly in the rice or in the presence of rice in the intestinal canal, and these toxins resemble a substance allied to an "H" substance or histamine in their action.

As pointed out before, glaucoma associated with epidemic dropsy is characterised by very high tensions occurring in both eyes at the same time, no lowering of the tension by miotics, the presence of a normal or deep anterior chamber, the absence of any inflammation or external signs of congestion, the occurrence of glaucoma in persons irrespective of age, and glaucoma may be the first manifestation of the toxæmia.

Recently I have been able to examine the aqueous humour in a limited number of cases of glaucoma associated with epidemic dropsy. Unfortunately from a therapeutic point of view an anterior sclerotomy is of very little practical use as a means of treatment, as in all the cases in which "tapping" of the anterior chamber was carried out, sclero-corneal trephining had to be subsequently performed. Consequently one was not justified in "tapping" the anterior chamber in more cases. In some eyes this was performed under local anaesthesia with cocaine and in others it was done under general anaesthesia with sodium evipan. Altogether 23 cases were examined. Out of these, seven cases showed a well-marked histamine reaction. (See Fig. 5 and Table I). Sixteen cases failed to show any reaction whatsoever. Controls of 6 normal cases were also examined but failed to show any histamine reaction in the aqueous humour.

The protein fractions of the aqueous humour in eight cases of epidemic dropsy glaucoma were also examined by the refractometric method. The results of which are shown in Table II. Controls for the examination of protein fractions in the aqueous humour of 6 normal cases were also carried out, the results of which are shown in Table III. Examination of the aqueous humour in epidemic dropsy glaucoma shows that the percentage of albumen is greatly increased while the globulin remains the same; the normal ratio of albumen to globulin is 0.44 to 1.0 whereas in the aqueous humour of epidemic dropsy glaucoma, the albumen is more than the globulin in the ratio of 2.3 of albumen to 1.0 of globulin. Examination of the crystalloids in the aqueous humour shows no deviation from the normal. Examination of the aqueous humour in epidemic dropsy glaucoma for agglutinins was carried

FIG. 5.

Kymograph record of the uterus of a white mouse showing a definite relaxation with the aqueous humour of Epidemic Dropsy Glaucoma and the relaxation with Histamine in 1/50,000 dilution.

out in 8 cases. Specific agglutinins were found present in the blood serum but in no case were specific agglutinins found in the aqueous humour. This is of great interest as it is known that agglutinins are fastened to the globulins and not to the albumens in the blood serum. The results of these are shown in Table IV.

Examination of the blood sera of patients suffering from epidemic dropsy glaucoma shows that the total proteins have diminished and that this diminution is due to a considerable decrease in the albumen content. At the same time pseudo-globulin and eu-globulin have increased but not to such an extent as to compensate for the reduction of albumen. As the protein content of the serum is responsible for the physical state of the blood so these changes must necessarily have a great influence on the various physical and chemical properties of the serum.

Chopra and his co-workers² have proved in the sera of patients suffering from epidemic dropsy that the relative viscosity and surface tension are below normal values. The pH remains unaltered while the buffer action is also below normal. The higher viscosity value rests upon the constituent proteins. Of the three proteins that contribute to the viscosity of the serum, eu-globulin stands first in order, then comes pseudo-globulin and last of all comes the albumen fraction. Although there is a fair increase of pseudo-globulin and a small increase of eu-globulin in these cases they cannot in all probability counterbalance the effects produced by the decrease in the albumen fraction. The lowering of surface tension together with the diminution of the viscosity is unusual as a fall in viscosity is generally attended by a rise in surface tension.

TABLE I
PRESENCE OF "H" SUBSTANCE IN THE AQUEOUS HUMOUR OF EPIDEMIC DROPSY GLAUCOMA CASES

Serial No.	Name	Age	Sex and Caste	Eye operated	Tension	Vision	Date of operation	Operation	Anaesthesia	Quantity of "H" substance	Remarks
1	A.D.	18	H.F.	L.E.	67	3/60	23/5/34	A.C. tapped	Local—cocaine drops	Histamine + +	1st attack—3 years ago; duration 6 months. 2nd attack—4 months' duration
2	G.B.S.	22	H.M.	R.E.	57	6/36	20/8/34	A.C. tapped	Local—cocaine drops	Histamine + +	E. D. duration 3 months
3	R.B.	16	H.M.	R.E.	36	6/9	7/9/34	A.C. tapped	Sodium evipan	Histamine + +	1st attack—5 years ago 2nd attack—1 month duration
4	A.K.	52	M.F.	L.E.	57	6/24	29/9/34	A.C. tapped	Sodium evipan	Histamine + +	1st attack—duration 2 months
5	R.D.	21	H.F.	R.E.	77	6/9	13/12/34	A.C. tapped	Sodium evipan	Histamine + +	E. D. duration 4 months
6	T.D.	45	H.M.	R.E.	41	F.M.	28/1/35	A.C. tapped	Sodium evipan	Histamine + +	1st attack—4 years ago. 2nd attack—1 year duration
7	J.B.	28	H.F.	L.E.	53	6/6	1/2/35	A.C. tapped	Sodium evipan	Histamine + +	E. D. duration 5 months

TABLE II
PROTEIN FRACTIONS IN AQUEOUS HUMOUR IN EPIDEMIC
DROPSY CASES

	Albumen in gms. %	Globulin in gms. %	Total proteins in gms. %	Globulin to albumin ratio	Non- proteins in gms. %
Case I - - - -	—	—	0·0204	—	—
Case II - - - -	0·011	0·0044	0·0154	0·408	1·27
Case III - - - -	0·028	0·0130	0·0410	0·464	0·90
Case IV - - - -	0·021	0·0089	0·0299	0·420	1·13
Case V - - - -	0·028	0·0090	0·0370	0·400	1·15
Case VI - - - -	0·016	0·0090	0·0250	0·550	1·00
Case VII - - - -	0·022	0·0089	0·0309	0·410	1·04
Case VIII - - - -	0·038	0·0190	0·0570	0·500	1·11
Average for aqueous hu- mour of E.D. cases -	0·023	0·010	0·0310	0·450	—
Average for the blood sera of E.D. cases -	3·74	3·39	7·23	0·90	1·25
Average for the blood sera of normal man .	4·61	2·83	7·44	0·611	1·30

TABLE III
PROTEIN FRACTIONS IN AQUEOUS HUMOUR IN NORMAL CASES

Case No.	Disease	Albumen in gms. %	Globulin in gms. %	Total proteins in gms. %	Globulin to albumen ratio
I - -	Cataract	0·008	0·012	0·020	1·500
II - -	Cataract	0·005	0·015	0·020	3·000
III -	Cataract	0·003	0·011	0·014	3·666
IV - -	Cataract	0·0038	0·009	0·0128	2·368
V - -	After cataract	0·0041	0·0096	0·0137	2·341
VI - -	After cataract	0·0012	0·004	0·0052	3·333

TABLE IV
LIST OF CASES OF EPIDEMIC DROPSY GLAUCOMA IN WHICH AGGLUTININS WERE TESTED

Serial No.	Name	Age	Sex and Caste	Eye operated	Tension	Vision	A.C. tapped under sodium evipan	History of epidemic dropsy glaucoma	Agglutinins			Remarks
									Blood serum	Aqueous humour	Against	
1	H.C.G.	48	H.M.	L.E.	67 mm. Hg	F.m.	"	6 months' duration		Absent	T.A.B. vaccine	Advanced case
2	S.D.B.	35	H.F.	R.E.	57 mm. Hg R.E.	R.E. 6/12	"	3 months' duration		Absent	"	
3	P.B.	26	H.F.	L.E.	R.E. 67 mm. L.E. 77 mm.	R.E. 1/60 L.E. F.m.	"	6 months' duration	+ in 1/250	Absent	Rice bacilli	Advanced case
4	P.L.P.	36	H.M.	R.E.	B.E. 67 mm.	R.E. 6/24 L.E. 6/6	"	2½ months' duration	+ in 1/250	Absent	"	
5	D.C.S.	25	H.M.	R.E.	R.E. 70 L.E. 60	R.E. 2/60 L.E. 6/6	"	1 month's duration		Absent	"	
6	K.G.	44	H.F.	R.E.	R.E. 57 mm. Hg L.E. 67 mm. Hg	R.E. P.L. L.E. 6/18	"	3 months' duration	+ in 1/125 + 1/25	Absent	"	Advanced case
7	S.J.	56	H.F.	R.E.	R.E. 50 L.E. 40	R.E. F.m. no imp. L.E. c + 11'0 D.S. = 6/9	"	3 months' duration	+ in 1/250 and 1/50	Absent	"	2 years back B.E. operated for cataract
8	M.M.	20	H.F.	R.E.	R.E. 60 mm. L.E. 55 mm.	R.E. 6/12 L.E. 6/9	"	3 months' duration	+ in 1/125 and 1/50	Absent	"	

The primary factors in the production of an increased amount of aqueous humour in the eye-ball are :—

(1) Decrease in the colloid osmotic pressure of the serum.

(2) Increase in the permeability of the capillary wall so that the albumen molecules can pass through from the capillaries into the aqueous humour. The albumen molecules are much smaller than those of other proteins in the blood and can pass out more easily than others into the aqueous. The change in the surface tension is closely associated with the change in permeability. It is probable that the histamine-like body which has been proved to be present in some cases associated with epidemic dropsy produces similar reactions. The colloid osmotic pressure exerted by a certain percentage of albumen is much higher than that of an equal percentage of globulin and as albumen is composed of smaller molecules than globulin a given concentration of albumen therefore contains more molecules than the same percentage of globulin and has a higher actual osmotic pressure, due to the protein molecules. The increased permeability of the capillary walls causes a lower colloid osmotic pressure and the greater the permeability of the membrane, the lower the pressure.

(3) Increase in the hydrostatic pressure in the blood capillaries.

It is obvious that the operation of these three factors serves to aid the transudation from the capillaries into the aqueous humour in the eye-ball and to hinder reabsorption from the latter, thereby causing an increased amount of aqueous humour.

Summary

In the sera of patients suffering from epidemic dropsy the relative viscosity and the surface tension are lowered below normal. The pH remains unaltered while the buffer action is also below normal. The protein fractions show a considerable reduction in albumen while the globulins are found to be increased. The increase of pseudo-globulin is more marked than that of eu-globulin. In the aqueous humour of patients suffering from epidemic dropsy glaucoma there is a marked increase of the albumens while the globulins remain the same. The normal ratio of albumen to globulin is 0.44 to 1.0 whereas in the aqueous humour of epidemic dropsy glaucoma, the albumen is more than the globulin in the ratio of 2.3 of albumen to 1.0 of globulin. In a certain number of patients suffering from epidemic dropsy glaucoma, a histamine-like body has been proved to be present in the aqueous humour. The whole uveal tract shows a marked dilatation of the capillaries, and there is no evidence of any inflammatory process.

My thanks are due to Colonel R. N. Chopra and his co-workers in the Tropical School of Medicine, Calcutta, for their assistance in the examination of the aqueous humour. I am also indebted to my House Surgeon, Dr. P. K. Biswas, for his valuable help in this research.

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1. Kirwan, E. O'G.—*Arch. of Ophthal.*, Vol. XII, No. 1, July, 1934.
2. Chopra, R. N., Mukerjee, S. N., and Gupta, J. C.—*Ind. J. of Med. Res.*, Vol. XXIII, p. 353, 1935.

INTENSITY OF LIGHT IN RELATION TO THE EXAMINATION OF THE EYE*

BY

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- I. In the Correction of Errors of Refraction.
 1. Myopia, hyperopia and astigmatism by the acuity method.
 2. Astigmatism by special tests.
 - (a) With the broken circle and the illumination scale.
 - (b) With the radial line type of test chart.
 3. The presbyopic eye for near seeing.
- II. In the Standard Rating of Acuity and Its Rating for Other Purposes.
- III. In the Determination of the Near Point of Vision and the Apparent Range of Accommodation.
- IV. In the Study of the Visual Field with the Tangent Screen and the Perimeter.

In July, 1934, we published the description of an instrument which provides a convenient means of varying the intensity of illumination over a wide range from zero to very high without change in the colour of light or in the size, shape and location of the illuminated field.¹ This instrument was devised as an aid to the practitioner in examining the eye as well as in caring for it by prescribing the amount of light needed by the patient under examination. The use of variable illumination in the correction

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