OBSERVATIONS ON BLOOD COUNT AND BLOOD SUGAR IN CHOLERA

BY

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Cholera is a disease the very nature of which suggests that the adrenals may play an important part during the episode. In spite of Rogers's (1913) introduction of saline therapy to make up for the loss of fluid, death is not rare in cholera, and it is found impossible to restore and/or maintain the pulse in some of the cases in spite of prolonged infusion of saline. Lahiri (1945) treated a limited number of cholera cases with suprarenal extract and recorded encouraging results. Cholera is a disease with quite a short critical period, so it might well prove ideally suited to cortisone therapy. A few doses of cortisone might be enough to tide the patient over his crisis. In order to provide a rational basis for such therapy, the present study was undertaken to see if in cholera there is evidence of suprarenal activity as reflected by changes in the blood sugar and blood count. De *et al.* (1955) have already reported some histochemical changes in the gland in cholera.

Materials and Methods

Adult male patients admitted to the Nilratan Sircar Medical College Hospitals with signs and symptoms of cholera during the summer epidemic of 1954 were investigated. Immediately on admission and before starting treatment, about 3 ml. of blood was collected in an oxalated phial. We prepared 1 ml. of the specimen for estimating the sugar by immediate precipitation of the proteins and filtration. The remainder was used for estimating the haemoglobin (Sahli-Adams), and for total erythrocyte, leucocyte, and eosinophil cell (as quoted by Sevvit, 1954) counts and differential leucocyte count. The total number of neutrophils and lymphocytes per c.mm. and the total white cell to red cell ratio were calculated from the above data.

Rectal swabs were inoculated on taurocholate-agar plates for the growth of *Vibrio cholerae*, which was identified by slide agglutination with specific serum after taking representative colonies. The negative cases were re-examined with a fresh specimen, collected next day.

For control purposes, similar counts were done on members of the departmental staff, including domestic servants, the samples being collected between 11 a.m. and 12 noon.

Results and Comments

Eighteen cases admitted with signs and symptoms suggestive of cholera were bacteriologically positive (*V. cholerae*)

and 18 were negative. The same number (18) were available in the control group of apparently healthy persons. The mean values of the different observations from these three groups are summarized in the Table.

The average haemoglobin percentage was 95.28 (Sahli-Adams) in the control group, the lowest being 80 (one case) and the highest 100 (10 cases). The corresponding figures for culture-negative cases of non-choleric diarrhoea were 109.72, 70, and 130% respectively. Fourteen cases had a haemoglobin level of more than 100%. Among the culture-positive cases the average figure was 111.66%. The lowest was 95 and the highest 130. Fifteen out of the 18 cases of this group had a haemoglobin percentage over 100.

The average erythrocyte count in millions per c.mm. was 4.85 in the control group, the lowest was 4.1, and the highest 5.5 (one case). In eight cases the figure was lower than 5. In the cases of non-choleric diarrhoea the average figure was 5.56, the lowest 3.5, and the highest 6.5. Only one case had a red-cell count below 5 millions per c.mm., while seven other cases had a count below 5.5 millions. In the cholera cases the average value was 5.83, the lowest 4.1, and the highest 7.5. Three cases had counts below 5 millions, two others had an erythrocyte count below 5.5 millions, and 13 more cases had a count of 5.5 millions or above.

The total white-cell count in the control cases averaged 6,806 per c.mm. The lowest figure was 4,400, and the highest 9,500. In the cases of non-choleric diarrhoea the corresponding figures were 10,193, 3,500, and 16,000 respectively. Nine cases showed a leucocyte count above 10,000 per c.mm. In cases of cholera the average count was 12,638, the lowest 4,500, and the highest 25,000 per c.mm. A leucocyte count above 10,000 per c.mm. was found in 11 cases.

The W.B.C. (in thousands per c.mm.) to R.B.C. (in millions per c.mm.) ratio calculated from the average figures was 1.40 in the control group, 1.83 in the bacteriologically negative group, and 2.17 in the group of bacteriologically positive cases of cholera.

The average differential count of polymorphonuclear neutrophil leucocytes went up from 58% in the control group to 82.2% in the non-choleric group, and to 82.5% in the vibrio-positive group of cases. The corresponding figures for total polymorphonuclear cells calculated from the differential count and total leucocyte count were 3,957, 8,505, and 10,675 per c.mm. respectively.

The differential count of eosinophil cells was 5.39% in the control group, 1.17% in non-choleric diarrhoea, and 0.83% in cholera. The average total eosinophil counts (direct method) were 308.4, 105.5, and 94.5 per c.mm. respectively. There were no cases in the control group in which the eosinophils were completely absent, whereas in five vibrio-negative cases of diarrhoea and in six vibrio-positive cases no eosinophil cells were detected. Only 50 eosinophils per c.mm. were seen in four cases each of vibrio-positive and vibrio-negative diarrhoea, and only in one case of the control group. Sixteen cases of the latter group and six and eight cases respectively of the vibrio-positive and vibrio-negative groups had an eosinophil count of over 100 cells per c.mm.

The lymphocyte counts were 35.78% (calculated total count 2,405 per c.mm.) in the control group, 17.55% (calculated total, 1,469) in vibrio-negative diarrhoea, and 16.30% (calculated total 2,152) in the vibrio-positive cases. In the

Mean Values and Standard Errors of Haematological Findings and Blood Sugar in Control, Vibrio-positive, and Vibrio-negative Groups, Each of 18 Cases

	Hb % (Sahli-Adams)	R.B.C. ($\times 10^6$ /c.mm.)	W.B.C. $\times 10^3$ /c.mm.	W.B.C. R.B.C.	Neutrophils		Lymphocytes		Eosinophils		Sugar (mg./100 ml.)
					Diff. (%)	Total (%)	Diff. (%)	Total (per c.mm.)	Diff. (%)	Total (per c.mm.)	
Control	95.28 $\pm$ 1.78	4.85 $\pm$ 0.08	6.806 $\pm$ 0.28	1.40	58.00 $\pm$ 2.61	3,957 $\pm$ 140	35.78 $\pm$ 1.82	2,405 $\pm$ 117.4	5.39 $\pm$ 0.71	308.4 $\pm$ 33.7	100 (assumed)
Vibrio- positive	111.66 $\pm$ 3.10 t=5.28	5.83 $\pm$ 0.21 t=4.66	12.638 $\pm$ 1.25 t=4.66	2.17	82.50 $\pm$ 2.13 t=11.26	10,675 $\pm$ 983 t=6.83	14.60 $\pm$ 1.60 t=13.24	1,534 $\pm$ 196.9* t=4.93	0.83 $\pm$ 0.37 t=12.32	94.5 $\pm$ 17.2 t=12.43	88.17 $\pm$ 2.8 t=4.22
Vibrio- negative	109.72 $\pm$ 2.69 t=5.36	5.56 $\pm$ 0.16 t=4.42	10.193 $\pm$ 0.80 t=4.23	1.83	82.20 $\pm$ 3.40 t=7.12	8,505 $\pm$ 860 t=5.40	17.55 $\pm$ 2.92 t=6.24	1,469 $\pm$ 131.5 t=7.12	1.17 $\pm$ 0.34 t=12.41	105.5 $\pm$ 18.4 t=11.02	78.73 $\pm$ 3.27 t=6.50

* "t" for each value in the vibrio-positive and vibrio-negative groups is highly significant. * Two cases with lymphocytes above 6,000 per c.mm. excluded.

last-mentioned group, however, two cases had very high lymphocyte counts (6,120 and 6,500 per c.mm.), and if they are excluded the average differential count of lymphocytes comes down to 14.6%, the corresponding total count being 1,534 per c.mm.

Thus there has been on the whole a readjustment of the absolute and relative number of the different leucocytes, with polymorphonuclear leucocytosis, eosinopenia, and lymphopenia.

The blood sugar ranged from 110 to 130 mg. per 100 ml. in 4 cases, from 95 to 105 mg. in 4 cases, and from 55 to 85 mg. in 10 cases of the vibrio-positive group. The mean value was 88.17 mg. per 100 ml. In the vibrio-negative cases of diarrhoea the blood sugar was 120 to 130 mg. per 100 ml. in 3 cases, 95 mg. in 1 case, and 60 to 90 mg. in 14 cases, with a mean value of 78.73 mg. per 100 ml. The normal fasting level of blood has been assumed to be 100 mg. per 100 ml.

The patients had been admitted between 2 to 28 hours after the onset of symptoms, and they required from 2 to 20 pints (1.14 to 11.4 litres) of intravenous saline for maintenance of the pulse and blood pressure within normal limits. One patient in the vibrio-positive group died soon after admission, all the rest survived. No significant correlation could be found between any of the blood changes and the mortality, the amounts of saline needed, or the interval between onset and time of collection of blood. However, the two vibrio-positive cases with a high lymphocyte count (over 6,000 per c.mm.) required 18 to 20 pints (10.2 to 11.4 litres) of saline infusion before the pulse and blood pressure could be maintained, whereas no other case required more than 12 pints (6.8 litres).

Discussion

The rise in haemoglobin value and red-cell count may be taken as evidence of haemoconcentration induced chiefly by loss of fluid and partly by the addition of formed elements from splenic contraction. There was also an increase of the number of white cells per c.mm. Haemoconcentration is partly responsible for this change as well, but a rise in the white cell/red cell ratio in both groups of patients, indicating a disproportionate increase of the whites, suggests the occurrence of real leucocytosis.

In association with this leucocytosis the presence of neutrophilia, lymphopenia, and eosinopenia reflected in the total as well as differential counts indicates that increase in the number of neutrophils has been responsible for the leucocytosis. The blood changes are similar to what was observed by Selye (1950) in mice and rats exposed to various forms of alarming stimuli. The fall in eosinophils was most characteristic. Hills *et al.* (1948) have listed various clinical emergencies that bring about a striking fall in eosinophils in man. Cholera seems to be no exception, and is possibly related to increased liberation of cortical hormone. The lymphopenia in our cases was not, however, a relative one, but there was usually a decrease in the absolute number as well, unlike what Selye observed in his animals. Two vibrio-positive cases had a lymphocyte count of over 6,000 per c.mm. They required not less than 18 to 20 pints (10.2 to 11.4 litres) of saline to have their pulse restored, while the others, in which the lymphocytes numbered from 400 to 3,800 per c.mm., required only 2 to 12 pints (1.14 to 6.8 litres). Absence of a reduction in the lymphocyte count may be related to the relative severity of these two cases, but another case which proved fatal had only 1,600 lymphocytes with 200 eosinophils per c.mm.

Both vibrio-negative and vibrio-positive cases showed marked changes in the blood picture—namely, rise in haemoglobin percentage and in erythrocyte and leucocyte counts, neutrophilia, lymphopenia, and eosinopenia, together with a widely variable blood-sugar level. The average figures (see Table) indicate that these changes are similar in nature in the two groups of cases, although somewhat less marked in the former. The vibrio-negative cases are clinically indistinguishable from the vibrio-positive ones. They

are usually regarded as true cases of cholera (at least during epidemics), and lack of bacteriological confirmation is believed to be due to inadequacy of the cultural methods. It is possible that some of the vibrio-negative cases could be proved positive by using a large number and different types of media, and by a more frequent examination. But in view of the fact that De, Bhattacharya, and Sarkar (to be published) have, by inoculation into ligated loops of small intestine of rabbits, produced evidences of the pathogenicity of strains of *Bact. coli* isolated from many of these cases, it may not be unreasonable to think that not all these are cases of true cholera and that some at least are caused by pathogenic *Bact. coli*. It is interesting to note here that Rogers (1951) has recorded the occurrence of polymorphonuclear leucocytosis in acute gastro-enteritis due to sero-positive strains of *Bact. coli*.

Identical blood changes in both groups of cases point to the non-specific stimulation of the pituitary-adrenal axis by the associated dehydration, shock, and anoxia rather than by the products of *V. cholerae*.

While some of the cases had normal blood sugar, most of them exhibited definite hypoglycaemia. The blood-sugar level was not related to the duration of the disease during admission. As the patients cannot take anything by mouth during the earlier hours, the observed blood sugar can roughly be taken as the fasting value. Sayers (1950), in reviewing the literature, has remarked that one of the most characteristic actions of cortical hormone is to inhibit glucose utilization by the tissues. The relatively higher blood-sugar level in a minority of our cases may be due to an increase of cortical hormone or to reflex adrenaline discharge in shock. However, the observation of a low blood sugar in most of the cases is in keeping with the established fact that hypoglycaemia characterizes advanced shock (Sayers, 1950). In cholera this finding may perhaps be the result of deficiency of cortical hormone—an excess of which is known to decrease the glucose tolerance.

Conclusions and Summary

The occurrence of leucocytosis with neutrophilia, lymphopenia, and eosinopenia in cholera and non-choleric diarrhoea is related to increased suprarenal cortical activity under the stress of prevailing dehydration, shock, and anoxia. The significance of hypoglycaemia in most of the cases and of hyperglycaemia in a few is discussed.

We thank Dr. A. K. Duttgupta for permission to publish this paper. We are indebted to Dr. N. C. Ganguli and Dr. K. P. Sengupta for much help during the course of this work.

REFERENCES

- De, S. N., Sengupta, K. P., and Ganguli, N. C. (1955). *Lancet*, 1, 1043.
Hills, A. G., Forsham, P. H., and Finch, C. A. (1948). *Blood*, 3, 755.
Lahiri, S. C. (1945). *J. Indian med. Ass.*, 14, 113.
Rogers, K. B. (1951). *Proc. roy. Soc. Med.*, 44, 519.
Rogers, L. (1913). *Cholera and its Treatment*, p. 139. London.
Sayers, G. (1950). *Physiol. Rev.*, 30, 241.
Selye, H. (1950). *The Physiology and Pathology of Stress*. Montreal.
Sevitt, S. (1954). *British Medical Journal*, 1, 541.

Leeds has pioneered in the difficult field of dealing with back-to-back houses, said Mr. William Deedes, Parliamentary Secretary to the Ministry of Housing, speaking at Leeds Civic Hall in connexion with the "New Homes for Old" demonstration at Louis Street, on October 11. He pointed out that this problem bore heavily not only on Leeds but also on the surrounding towns. For two years the city had been carrying out tests, and experiments had shown that ventilation in these houses could be brought up to acceptable standards with very little cost. Grants would be approved for their improvement. While unfit ones would not be preserved, and many were included in the slum clearance programme, others had a lifetime of well over 15 years. Every house saved from decay meant one less new house to be built.