FIG. 2—Electrophoretic patterns (on starch gel), reading from left to right: CC, CS, SS, SJ (patient), AH, AA. Application at arrow.

fast component in addition to haemoglobin S was found. The mobility of the component at pH 8.6 was about half way between A and H (Fig. 2). Blood samples were sent for reference purposes to Dr. Lehmann, of London, and to Mr. Robinson, of Detroit. They both reported that the fast-moving component was identical with haemoglobin J. Scanning showed that the composition of the patient's haemoglobin was about 40% S and 60% J.

Discussion

The episodes of jaundices was not thought to be a sickle-cell crisis clinically, and this view would seem to be justified. In fact, the patient suffers no disability attributable to his blood condition. He has a mild but well-compensated haemolytic anaemia, which is similar to some of our cases of sickle-cell/haemoglobin-C disease. In a series of 45 cases (MacIver and Went, 1958) of this latter condition a number were without any symptoms.

Investigation of the patient's family was interesting but disappointing. Both parents were stated to be dead, and the patient has no children and no full brothers or sisters. However, his mother, who was of negro stock, had six children by two other fathers, one of whom was Chinese. Both children by the latter and two of the other three children had the sickle-cell trait. The remaining child showed normal haemoglobin A only. It is justifiable to deduce from these findings that the mother carried an S gene. The father must therefore have contributed the J gene.

The patient stated that his mother "got him in Panama," and that his father was an American resident there. The predominantly Caucasian appearance of the patient, taking into account the negro mother, tends to support this possibility. To trace the father or his relatives would seem to be hopeless.

Summary

A case of sickle-cell/haemoglobin-J disease is reported. The interaction between the genes for haemoglobin S and J is not marked, resulting in a mild well-compensated haemolytic anaemia. Family studies suggest that the haemoglobin J was contributed by a Caucasian from North America.

We are grateful to Dr. E. S. Shoucair for referring the case to us, and to Drs. H. Lehmann, J. V. Neel, and A. R. Robinson for their kindness in comparing the characteristics of the fast haemoglobin in this case with other examples in their possession.

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ACETAZOLAMIDE IN SICKLE-CELL ANAEMIA

BY

W. D. dos SANTOS, M.A., M.B., Dip.Bact.

Department of Pathology, General Hospital,
Lagos, Nigeria

AND

H. LEHMANN, M.D., Sc.D., M.R.C.P., F.R.I.C.

Department of Pathology, St. Bartholomew's Hospital,
London

In 1957 Hilkevitz recommended acetazolamide ("diamox") for the treatment of patients with sickle-cell anaemia. Since then little has been reported on experiences with this drug in sickle-cell anaemia, although unpublished observations were said to be disappointing. However, there is at least one communication, by Charmot and Reynaud (1958), who found that sickle-cell crises were relieved by acetazolamide. The drug is a carbonhydrase inhibitor and, quite apart from any effect on the sickle cells, it would be expected to cause a metabolic acidosis. It is also known to produce a fall in serum potassium. Greenberg and Kass (1958) have laid emphasis on the importance of the blood pH in the causation or prevention of sickle-cell crises, and they produced crises by treating patients with ammonium chloride and acetazolamide, but not with acetazolamide alone. Tenney and Tschetter (1959) found that the metabolic acidosis caused by acetazolamide in rats was accompanied by a fall in oxygen consumption. It occurred to us that sickle-cell anaemia patients might have failed to respond to treatment with acetazolamide because of the associated acidosis.

Present Investigation

We decided to treat (at the General Hospital, Lagos, Nigeria) patients for two weeks with acetazolamide and, at the same time, to give them large amounts of sodium bicarbonate and potassium chloride to counteract the metabolic acidosis and hypokalaemia associated with prolonged acetazolamide therapy.

Table I summarizes the ages of the patients, their

TABLE I.—Patients Treated with Acetazolamide

Case No.	Age in Years	Weight (kg.)	Acetazolamide (mg./kg. Day)	Daily Supplement (g.)			
				NaHCO ₃		KCl	
				1st Week	2nd Week	1st Week	2nd Week
1	7/12	7.7	24	3	6	0.8	1.5
2	2	9.1	21	6	12	1.5	3
3	24	11.3	17	6	12	1.5	3
4	34	10.9	17	3	6	0.8	1.5
5	5	15.9	12	6	12	1.5	3
6	5	13.6	14	6	12	1.5	3
7	7	18.6	10	6	12	1.5	3
8	9	30.0	12	9	18	2.8	4.5
9	8	19.6	9	6	12	1.5	3
10	15	57.3	7	9	18	2.8	4.5
11	20	36.4	10	9	18	2.8	4.5

TABLE II.—Summary of Findings. In=before treatment; 1=after one week; 2=after two weeks of treatment.

Case No.	Haemoglobin (g./100 ml.)			Sickled Cells (%)			Reticulocytes (%)			Alkali Reserve (mEq/l.)			Serum Na (mEq/l.)			Serum K (mEq/l.)			Serum Cl (mEq/l.)	
	In	1	2	In	1	2	In	1	2	In	1	2	In	1	2	In	1	2	1	2
1*	7.4	6.2	6.7	13	10	6	6	4	7	—	—	—	—	—	—	—	—	—	—	130
2*	7.7	6.7	8.4	9	6	3	5	7	4	—	—	—	—	—	—	—	—	—	—	135
3*	6.4	6.7	6.7	5	3	3	14	6	6	—	—	—	—	—	—	—	—	—	—	130
4†	8.1	6.6	8.0	13	4	3	3	20	12	20	25	16	120	140	119	4.9	3.6	3.2	—	115
5†	4.9	8.8	7.2	13	9	10	10	35	3	26	23	20	130	130	129	4.2	3.5	3.4	—	110
6†	8.3	8.9	7.7	20	7	12	9	8	13	29	22	17	119	117	120	5.8	3.1	2.9	—	105
7	6.8	6.8	6.7	20	13	14.5	7	14	9	29	20	19	120	126	120	4.5	3.7	3.4	—	118
8	7.7	7.4	7.4	18	14	10	12	6	8	27	25	18	125	130	130	5.3	3.7	4.5	—	110
9†	6.5	8.0	7.5	14	12	14	25	28	5	26	23	20	134	130	129	4.0	3.0	3.1	—	115
10†	6.5	7.7	7.1	16	22	13	16	18	9	28	22	19	130	129	129	4.1	3.8	4.1	—	120
11‡	12.0	9.8	10.7	6	14	3	4	4	4	27	20	17	125	119	120	4.2	3.4	3.4	—	120

* Treated as out-patients. † Recovering from sickle-cell crisis. ‡ Developing crisis on admission to hospital.

weight, and the dosage of acetazolamide per kg. body weight. Their ages varied from 7 months to 20 years and the dosage of acetazolamide was varied from 7 to 24 mg. per kg. body weight per day. Ten of these patients (Cases 1 and 10) suffered from sickle-cell anaemia and one (Case 11) from sickle-cell haemoglobin C disease. Three had already been admitted to hospital (Cases 5, 9, and 10) and five (Cases 4, 6, 7, 8, and 11) were specially admitted for the purpose of this study. Cases 4 and 11 developed a crisis on the first day after admission to hospital. Cases 1, 2, and 3 were studied as out-patients, but they were children of educated parents with a special interest in the disease, and we felt confident that they were given their treatment regularly. Acetazolamide was given in three divided doses, and the general regime was as follows. All patients received a daily supplement of sodium bicarbonate and potassium chloride in three divided doses, and Table I shows the amounts given daily to each patient in the first and second weeks. All patients also received a high-protein diet and "casilan" as an additional source of protein. The daily amount of casilan was varied, according to body weight, from 50 to 150 g.

In view of the fact that megaloblastic anaemia can be associated with sickle-cell anaemia and sickle-cell haemoglobin C disease (Captain and Dr. J. Watson-Williams, personal communication), we gave all patients "prenatal," a vitamin preparation which contains vitamins A, D, B₁, B₂, nicotinamide, B₁₂, K, C, and folic acid, as well as a generous supplement of calcium, phosphorus, iron, and manganese.

Table II shows the changes in haemoglobin level after one and two weeks. It will be seen that in Cases 5, 9, and 10 there was an increase of haemoglobin concentration after the first week, but these patients were recovering from sickle-cell crises. Patients 4 and 11, who developed a crisis on admission to hospital, showed a fall in haemoglobin level after the first week, but the other subjects showed no appreciable change. There was a tendency for the percentage of sickled cells to fall during the two weeks of treatment with acetazolamide. The reticulocyte count was particularly high in the three children recovering from crises, but was high also in two others. At the beginning of the experiment there was a tendency for the reticulocyte count to fall in all subjects.

The alkali reserve was determined only in the eight in-patients; there was a fall in alkali reserves in all, and in one (Case 4) it had fallen to the dangerous level of 16 mEq/l. at the end of two weeks. The day after the treatment finished, this child experienced a severe crisis. The sodium level was low to begin with in all

of the eight patients examined, but there was no conspicuous fall in the course of the treatment. The potassium level was normal to begin with, but fell in the eight patients whose serum potassium was measured, and in six of them to below the normal level of 3.8 mEq/l. Even after the end of the second week, when the daily supplement of NaHCO₃ had been doubled, the serum chloride was high in all cases. Unfortunately, it had not been measured at the beginning of the trial, but had been determined at the end of the first week in five and at the end of the second week in all subjects. The serum bilirubin level was within normal limits in 7 of the 11 patients, and was above normal throughout the trial in the older children with sickle-cell anaemia (Cases 7, 8, 9, and 10).

Conclusion

The impression we gained from the two-weeks' observation of 11 patients with sickle-cell disease was that acetazolamide had little influence on the course of their anaemia. The observation extended over only a short period of time, but it was felt that if acetazolamide was inhibiting intravascular haemolysis significantly an effect on the haemoglobin level should have become noticeable. Obviously the metabolic acidosis caused by acetazolamide could not be counteracted by the sodium bicarbonate supplements. Neither was it possible to prevent the hypokalaemia by potassium chloride supplements. We considered a further increase in the supplements above the amount given during the second week as not practicable.

We thank Dr. G. Skinner for permission to study Cases 1 and 9, and Dr. J. D. Mabayoje for permission to study Case 10. These patients had already been admitted to the General Hospital, Lagos, under their care. The remainder of the subjects were all members of Dr. Mabayoje's panel of sickle-cell disease patients and were asked by him to take part in this trial. We also thank Dr. B. Gans for giving us the facilities of his wards. In addition we thank the medical and technical staff of the pathology department, particularly Mr. J. S. Ajayi, for their help with the laboratory work. One of us (W. D. d. S.) acknowledges permission to publish by the Minister of Health, Federal Government, Nigeria and the other (H. L.) would like to thank the Federal and Eastern Region Governments, Nigeria, for defraying the expenses of his visit to Nigeria.

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