The outstanding and impressive feature in this series of cases is not the occurrence of reactions or anything that indicated ill effects as a result of transfusion, but the remarkable way in which the patients, whose conditions appeared hopeless, recovered.

The series of cases is admittedly small, but the conditions were such that if serum were toxic, one would have expected marked manifestations of toxicity.

An analysis of the results leads us to the conclusion that, so far as this series of cases is concerned, serum was non-toxic. This coincides with our previous clinical experiences of the previous two years when using serum in up to 1,000 c.cm. quantities.

SULPHONAMIDE AMBLYOPIA AND ITS TREATMENT WITH NICOTINIC ACID

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IN November 1943 an ophthalmologist was confronted with a case of total blindness in a girl following prolonged use of M&B 693. On my suggestion she was treated with nicotinic acid, which resulted in complete restoration of her sight. In March 1944 Hollis and Baty (New England) reported a case of a 6 weeks' old child treated with sulphathiazole for meningitis due to the colon bacillus. The drug sterilized the cerebro-spinal fluid in a week but left the child totally blind. The report of Hollis and Baty's case reached me by August 1944. In the same month another case of complete blindness of about four months' standing following the use of a sulphonamide given for puerperal sepsis was brought to my notice. This case is still under treatment with not much hope of success. In all the three cases the cause of amaurosis is optic atrophy of the toxic type. There is practically no mention of this manifestation of sulpha drug poisoning in the literature, though visual disturbances with optic neuritis due to sulphonamides have been recorded as early as 1937 (Bucy). This crippling toxic effect of so widely used drugs does not appear to be very uncommon. It fortunately appears to be amenable to nicotinic acid therapy if given in very early stages but is generally resistant to ordinary routine treatment in all stages and does not appear to yield even to nicotinic acid if its exhibition is delayed for a few months.

The data of the two cases that have come to my notice are given here:—

Case 1.—Muslim girl, aged 8 years, was operated on for mastoiditis; a sinus persisted. M&B 693, three tablets and sulphanilamide dressing locally, were given daily for about a month. The sinus did not heal but the girl developed a sudden loss of vision on 6th November, 1943. She was examined at the M. D. Eye Hospital, Allahabad.

11th November, 1943. 'Eyes: (1) no paralysis of any ocular muscle detectable; (2) pupil—somewhat dilated and inactive; (3) media—clear; (4) tension—18 mm.; (5) vision—R/E—no PL (perception of light), L/E—PL? No PR; (6) fundus—(*a*) optic disc—white; margins somewhat blurred; blood vessels near the disc narrow in calibre, otherwise normal. Lamina cribrosa—not obliterated; (*b*) general look of fundus—not much change; Kahn test—negative.'

Acetylcholine ½ c.cm., potassium iodide and sodium salicylate given internally, and oleate of mercury to temples. There was no improvement. I then advised nicotinic acid. The girl was given 50 mg. intramuscularly and 100 mg. twice a day orally. In eight days, PL and PR restored in both eyes. On the tenth day, vision—hand movements at 6 inches to 9 inches. On 1st December, 1943, finger counting at 6 inches. In twenty-five days, she could walk about easily and her disc assumed a very light pink colour. Injections of nicotinic acid were stopped but 100 mg. was given orally twice daily. In five weeks her optic disc became absolutely normal and her vision in both eyes was 6/12.

Case 2.—Muslim female, aged 28 years, had puerperal sepsis and was given a sulphonamide, 4 tablets a day for four days. On the fourth day she felt haziness of vision and in about ten days lost her sight completely. She tried various treatments and appeared at M. D. Eye Hospital, Allahabad, after 4½ months.

Examinations.—Eye: (1) tension—normal; (2) media—clear; (3) fundus—(*a*) optic atrophy (white disc with thin vessels, (*b*) lamina cribrosa—quite clear. No PL.

Treatment.—50 mg. intramuscularly (3 injections) and 300 mg. of nicotinic acid orally a day for one week. No improvement. She failed to attend for some time and is now under treatment again without any hope of success.

Discussion.—A careful study of the clinical nature of the toxic effects of sulphonamides shows a close resemblance to the clinical manifestations of the deficiency of vitamin B_2 group and especially that of nicotinic acid.

Depletion of nicotinic acid in the body damages the very same four systems—the gastro-intestinal, circulatory, dermal and nervous—as sulpha drug poisoning does. The nature of the lesions of both is also similar, being degenerative rather than inflammatory in type. I have also noticed that sulpha drugs produce more toxic effects in a patient who already shows nicotinic acid deficiency and that the exhibition of nicotinic acid does act as a preventive and curative to the toxic effects of M&B 693 and other members of sulpha group. Our American colleagues are also using it in increasing number of cases with encouraging results. Moreover, there is experimental evidence that sulpha drugs interfere with vitamin B synthesis that takes place in the intestines of animals. If this intestinal synthesis also occurs in man (of which we have no definite proof as yet) sulpha drugs may be causing definite interference to the process and thus giving a severe depletion of vitamin B complex which may cause an enhancement of the toxic reactions of sulphonamides. The increased liability of neurosis, mental states, and other damage to the nervous system now reported on the ingestion of sulphaguanidine or succinal-sulphathiazole may be due to this cause, as there is less absorption of these drugs from the gut and thus they have an increasing opportunity to interfere with the synthesis of vitamin

B complex in the intestine. However, it is evident through animal experimentations and human autopsies that sulpha drugs cause epithelial degeneration. It is, therefore, rational to believe that nicotinic acid which essentially nourishes epithelial tissues should be able to guard them against the destructive action of the drugs and restore them to normal if the damage has not proceeded to total destruction.

Summary

1. Two cases of optic atrophy with blindness due to M&B 693 are described.

2. The probable nature of the lesion in sulphonamide amblyopia and the rationale of its treatment with nicotinic acid are detailed.

3. Restoration of sight with nicotinic acid in one case and its failure in the other are recorded.

Acknowledgment

I have to thank Lieut.-Colonel F. E. R. Laborda, the Chief Medical Officer, East Indian Railway, for his permission to get the note published. I am indebted to Dr. M. U. Khan, Medical Officer in charge M. D. Eye Hospital, Allahabad, for the notes of the above two cases and for his special care and co-operation in noting the effects of nicotinic acid on the damaged nerves ophthalmoscopically and in other ways.

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TOLERANCE TO ENTEROVIOFORM TABLETS

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IN spite of the widespread and often indiscriminate use of enterovioform tablets there are very few case reports in the literature of enterovioform intolerance. In this country at least, enterovioform has rightly come to occupy a very prominent place in the armamentarium of the practitioner. In view of its immense popularity and widespread employment, it is indeed surprising that not a single case of fatal poisoning from enterovioform has ever been reported. Toxic symptoms have been noted with great rarity and have invariably been mild in nature.

The value of the drug enterovioform (or more correctly 'Vioform') was proved for the first time in the amœbiasis of monkeys by Anderson and Koch in 1931, but it is to David, Johnstone, Reed and Leake (1933) that we are really indebted for the introduction of this drug in the treatment of human amœbiasis.

Enterovioform, the active substance of which is iodochlorhydroxyquinoline, has been found to be of value not only in amœbic dysentery and amœbiasis but also in a host of other common and uncommon ailments such as bacillary dysentery, enterocolitis, summer diarrhœa, fermentative and putrefactive dyspepsias and even balantidial infections, lambliasis and ascariasis.

The great majority of workers agree on the low toxicity of enterovioform.

It is said that the rabbit will tolerate quite easily one gramme of enterovioform per kilogram body-weight, given orally or rectally; even when two grammes per kilogram are administered daily for fourteen days, no toxic symptoms are perceptible. Rabbits receiving 250 mg. in a single dose have shown fatty infiltration of the liver as well as damage to the renal tubules (Craig, 1934).

In man, David, Johnstone, Reed and Leake (1933) observed no signs of toxicity or unusual symptoms in any of their forty-seven cases of amœbiasis. In 1931, Anderson and Reed noted toxic symptoms in three out of sixty cases of amœbiasis treated with enterovioform. In one case there were reported palpitation, dyspnœa, headache and sense of fullness in the head. In the other two cases, there were gastro-intestinal symptoms like colic, flatulence and diarrhœa.

Excellent results have been reported in acute and chronic amœbiasis by a host of authors (Azmy Bey and Taha, 1934; Giordano, 1934; Lopez Ramirez and Galan, 1935; Ugrankar, 1938) with no toxic symptoms whatsoever. Even when administered by El-Biblawi (1936) to two pregnant patients, enterovioform caused no side effects.

The extremely low toxicity of enterovioform commented on by numerous workers in the past, is confirmed in full by the amazing degree of tolerance exhibited by my patient to the protracted administration of enterovioform.

Case report

A Bori patient, aged 35, was brought to me for examination on 14th August, 1944, for symptoms suggestive of cardiovascular disorder. In June 1944, the patient started noticing a gradually increasing lassitude and excessive fatigue on walking or climbing stairs. This was followed by frequent headaches, mainly frontal in type, mental depression and dyspnœa on effort.

There were no pains in the chest and no disturbance of bowel movements. On enquiry, he gave a most interesting history. In the middle of 1943, he had been examined for intestinal pains, diarrhœa and mucus in the stools by a consulting physician in Bombay who had prescribed enterovioform tablets by mouth, six tablets a day. The patient being relieved of all his intestinal symptoms within a fortnight of its administration was tempted into continuing these tablets without a break until August 1944, *i.e.* for a period of eleven months, during which time he finished, in all, one hundred bottles of enterovioform or two thousand tablets !

On examination, he was found to be a thin, undernourished individual of morose disposition. He showed signs of excessive nervous irritability and displayed a fine tremor of the outstretched hands. There was no pallor or cyanosis, no œdema, engorgement of veins or