AMNIOPLASTIN: A WARNING

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This note is intended as a warning against the clinical use of the membrane when improperly prepared. Amnioplastin, which was described in a recent number of the *Journal*,¹ is prepared from human amniotic membrane for the purpose of preventing adhesions between dura mater and lacerated brain. In the experiments described by these authors the membrane was soaked in alcohol, followed by boiling in distilled water for twenty minutes. An alternative method was proposed which substituted dry sterilization in the autoclave for the boiling. An unsatisfactory result with membrane prepared by this alternative method must now be reported.

Ineffectiveness of Dry Sterilization

Case A (Excision of brain scar; covering with amnioplastin; formation of adhesions; recurrence of epileptiform seizures).—This was the case of a boy who had received a depressed fracture of the skull at the age of 14 when struck by a baseball. When 16 he began to have epileptic seizures, which continued until he was admitted to our clinic at the age of 18, seven months ago. Craniotomy was carried out then and a meningo-cerebral scar was removed from the right frontal region at the site of the previous injury. After careful excision the bed of removal and neighbouring brain were covered with amnioplastin and the wound closed. The immediate result was good. He was attack-free for about four months; then his attacks recurred and became frequent and severe.

Because of the unsatisfactory post-operative course he was readmitted to hospital six months after the first operation and the wound reopened. Dense adhesions were found to have formed at the site of the removal and between the adjacent brain and dura. This was objectively a much worse result than would have been expected after simple excision without the use of amnioplastin. Careful dissection was carried out and a second excision performed. This has been followed by uncomplicated recovery up to the present time. Histological examination of the excised tissue showed that the membrane had disappeared but had been replaced by dense connective tissue. The amnioplastin used for this case had been prepared by cleaning the amniotic membrane in the usual way and by sterilization in the autoclave after immersion in alcohol, but without boiling.

Preparation of Amnioplastin

Subsequent study, largely carried out by Dr. Guy Odom in this clinic, indicates that if the amniotic membrane is boiled long enough in distilled water the major portion of the fat which such membranes contain is removed. It seems likely that this accounts for the favourable results obtained by Chao, Humphreys, and Penfield in their original animal experiments. It is now evident that if the membrane is to be used in man boiling should not be omitted.

Further experiments are being carried out with Dr. Odom upon the preparation and the use of amnioplastin. They will be reported as soon as the work is completed. The urgent need of a means of prevention of adhesions in war surgery prompted the early publication of the method and now makes it necessary to issue this warning without waiting for the completion of the study.

It may be stated at this time that excellent results have been obtained in animals when the membrane is boiled or

when the fatty material has been removed by adequate treatment in alcohol and ether. The membrane has been used in other human cases with apparently good results, but no other patient has been subjected to re-operation. We are not yet in a position fully to endorse its routine use in man. In the meantime we take this opportunity of advising against the use of unboiled membrane.

Clinical Memoranda

Agranulocytosis with Angina following Sulphonamide Treatment

The following interesting case seems to merit being placed on record.

CASE REPORT

The patient, a doctor aged 62, first consulted me in October, 1939, for a severe pustular infection of both feet which had been present since March of that year. In spite of it he had continued his work at high pressure, and had even played golf, until the day he saw me. Two examinations for fungus were negative. This, with a history of psoriasis and a residual patch on the left knee, justified the diagnosis of the pustular form of that disease. He declined in-patient treatment until a superadded *B. pyocyaneus* infection rendered it imperative.

He entered a nursing home on March 12, 1940, and a week later suddenly developed pain and swelling of the dorsum of the left foot and the characteristic lines of lymphangitis, extending as high as the middle third of the leg. His temperature, previously normal, rose to 102° F. the same day, and he was ordered three 0.2-gramme tablets of a well-known sulphonamide preparation at once, to be followed by two tablets two hours later. He had therefore received 1 gramme of the drug—that is, only half the recommended dose—on the first day of the complication. On the following day the temperature declined to 98.8° F., and the whole affected area was freely discharging and had begun to desquamate. The sulphonamide was continued, as advised by the makers, in diminishing doses; altogether thirty-eight tablets (7.6 grammes) were taken during ten days. On April 7 the patient complained of a sore mouth and felt and looked extremely ill, without any skin manifestations to account for his symptoms. Several necrotic ulcers were noted on the buccal mucous membrane, on the gums, and in the neighbourhood of the lower molar teeth on both sides. The three white cell counts (see table) indicate both the nature and the cause of the complication, and fully justified the serious prognosis given by the pathologist.

	10/4/40	12/4/40	16/4/40
Red cells	5,000,000	—	—
White cells	2,500	2,300	3,000
Colour index	0.9	—	—
Haemoglobin	95%	—	—
Polymorphs	2%	1%	16%
Lymphocytes	96%	93%	80%
Basophils	0	0	2%
Eosinophils	0	0	0
Monocytes	0	4%	2%
Megaloblasts	0	2%	0

The sulphonamide was stopped the day the buccal symptoms were observed (April 7), and from then onwards the clinical improvement was rapid as regards both the drug effects and the foot condition. It was not necessary to administer pentose nucleotide, the patient making a complete haematological recovery on small doses of anahaemin and benerva.

This case illustrates once again the peculiar liability of some individuals to lose their polymorphic cells after relatively small doses of this valuable medicament, for the total amount administered was moderate compared with the 28 grammes of sulphanilamide given in six days in a case of abortus fever without ill effect (Tatlow, 1940). Such discrepancy argues a specific idiosyncrasy on the part of the

¹ Chao, Humphreys, and Penfield, *British Medical Journal*, 1940, 1, 517.