

### Massive Hepatic Necrosis after Cyclophosphamide

SIR,—Massive hepatic necrosis following cyclophosphamide therapy does not seem to have been reported previously, and therefore it would appear worthwhile to record the present case.

In July 1969 a 61-year-old woman presented with a left mammary tumour, which she had noticed two weeks previously. Apart from an appendectomy (in 1923) and an artificial left pneumothorax (for tuberculosis—in 1929) she had otherwise been healthy. She habitually took no alcohol or drugs. The tumour was clinically confined to the breast, with no evidence of metastases, and there was no evidence of concurrent disease. The Hb was 97% and the W.B.C. count, 7,500/cu. mm.

On 30 June 1969 a left extended simple mastectomy was performed under general anaesthesia. The operation and recovery from anaesthesia were uneventful, and no blood trans-

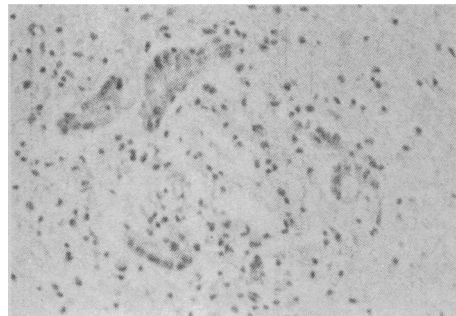


FIG. 1.—Microscopy of the liver, showing almost complete destruction of hepatic tissue and scanty lymphocytic infiltration ( $\times 130$ ).

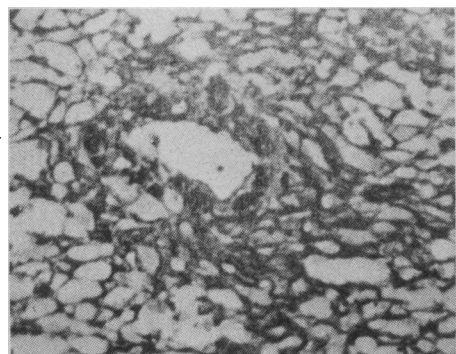


FIG. 2.—The liver silver-impregnated to show reticulin.

fusion was given. The resected tumour was an anaplastic scirrhous carcinoma, but the lymph nodes did not contain metastases. Postoperatively the Hb was 77% and the W.B.C. count 8,200/cu. mm. Immediately postoperatively treatment with cyclophosphamide was started—initially 50 mg. t.d.s. (for 14 days) and then 50 mg. daily. By 25 August the W.B.C. count had fallen to 3,900/cu. mm., and the patient was experiencing anorexia and nausea. Hence the cytotoxic agent was discontinued, a total dose of 2,800 mg. having been administered.

The patient was re-admitted on 2 September with a five-day history of general malaise, vomiting, and painless jaundice. The liver was clinically reduced in size, but there was no evidence of hepatic failure. The mastectomy wound was well healed and there was no evidence of metastatic disease. The investigations indicated a hepatocellular jaundice, and accordingly treatment with vitamin K, Parentrovite, ampicillin, oral neomycin, and a carbohydrate diet was instituted. However, the patient's condition steadily deteriorated, and signs of liver failure rapidly supervened. Death occurred on 5 September.

At necropsy the liver was shrunken (weight 430 g.). Its cut surface was pale and granular, and the normal lobular pattern was totally destroyed. Microscopically there was a complete absence of normal hepatic tissue, with only the reticulin framework of the hepatic cords and sinusoids remaining (Figures 1 and 2). There was a mild diffuse infiltration by mononuclears and lymphocytes, with occasional polymorphs. The only viable tissue was represented by clusters of small bile ducts around the sites of the portal tracts. There was no evidence of biliary obstruction, metastatic carcinoma, or any other lesion.

The only recognized hepatotoxic agent which the patient received was halothane; and this only on one occasion, so that it appears highly unlikely therefore that the hepatic necrosis was caused by it.<sup>1</sup> No blood transfusion had been given. The patient had not been in contact with infectious hepatitis and the histology of the liver did not support this diagnosis. By exclusion therefore, it seems probable that this was a cyclophosphamide-induced hepatic necrosis, a complication not previously attributed to this drug.—I am, etc.,

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#### REFERENCE

- <sup>1</sup> Mushin, W. W., Rosen, M., Bowen, D. J., and Campbell, H., *British Medical Journal*, 1964, 1, 329.

### Handicapped Children

SIR,—In your leading article (25 July, p. 179) you note parental "despair reinforces the recommendation in the Seebohm report . . . that social and family needs can be effectively met only through a compact social services department." I regret that I am filled with despair at your lack of appreciation of the consequences of the Seebohm report,<sup>1</sup> as well as that of the working party to which you refer.

In my borough, handicapped children are dealt with by two departments, the Education Department and a combined Health and Welfare Department. The consequence of the Seebohm report—that is, the Local Government Social Services Act—means that in future such children will be dealt with by three departments: the Education Department, Health Department, and Social Services Department.

I find it incomprehensible that the Government and public cannot appreciate the divisiveness of the Seebohm committee's recommendations, but are blindfolded into the illusion that there is a unification.—I am, etc.,

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Ilford, Essex.

#### REFERENCE

- <sup>1</sup> Local Authority and Allied Personal Social Services, *Report*, Cmnd., 3703, London, H.M.S.O., 1968.

### Cardiac Arrest and Bone Cement

SIR,—I read with interest the case report on cardiac arrest associated with bone cement (8 August, p. 326). The following case shows that a possible chemical effect is not the only risk associated with this useful material.

An active woman of 96 years had a Thompson femoral head prosthesis inserted following a subcapital fracture of the femoral neck. The prosthesis was embedded in "bone cement." As soon as this had hardened the head was placed in the acetabulum; at the same time her breathing became erratic and her heart stopped. She failed to respond to ventilation with oxygen and external heart massage. Necropsy revealed a large amount of fat in the pulmonary vessels.

It is a common practice to vent the medullary cavity while the cement is pressed into place and the prosthesis inserted, either by drilling the cortex at the lower limit of reaming or by inserting a stiff plastic tube. This precaution was not taken in this case, nor is it described by Dr. J. N. Powell and his colleagues.

The authors' comment on the rarity and possible toxic manifestations in total hip replacement using bone cement when compared with prosthetic replacement of the femoral head alone is interesting, as most techniques involve a larger quantity of cement and a larger bone/cement surface for possible noxious absorption.—I am, etc.,

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### G.P.s in the Hospital

SIR,—Entertaining though the discussion between Drs. "Apoth." "Admin." and "Phys." (8 August, p. 335) was, I feel it could have been more instructive if they had each done more homework before they started.

For example, to run away from the emigration problem by simply saying we "just don't know" the reasons for it is irresponsible. There is evidence that lack of hospital facilities and (or) beds is a factor in so far as general practitioners are concerned,<sup>1</sup> and having recently returned from a world tour I can confirm that this was mentioned by every general practitioner I met who had emigrated.

Secondly, the argument that the general-practitioner hospital is uneconomic seems to have been accepted without demur. At Tamworth, for example (13 June, p. 635), the patient not only has the advantage of the continuing interest of his family doctor when he has his hernia repaired, he also has the assurance that it will be done by a consultant surgeon, and at a cost to the State of considerably less than if the operation is done at the (more remote) district general hospital.

Thirdly, "Admin." continues to try and put across the notion that what is convenient (administratively, of course) is also necessarily right. Just how many patients currently being treated in hospitals really need "consultant-type" care must be a matter of opinion, but there can be no doubt that some do not. Traditionally in Britain the hospital gate has been the dividing line of responsibility, but the medical logic in this is unclear. Much serious illness can