Hepatitis B Antigen in V.D. Clinic Patients

SIR,—Mr. T. H. Bloomfield (30 June, p. 779) challenges the validity of using blood donors in comparative studies of the incidence of hepatitis b antigenaemia. The objection is that the exclusion of potential donors with a history of jaundice or of recent contract with a case of jaundice may reduce the proportion of subjects positive for hepatitis B antigen (HBAg) among those accepted for donation below the level in the general population. This contention is not necessarily correct.

Many of the rejected donors will have been exposed to the infective agent of viral hepatitis type A. In general, acute viral hepatitis type B is not followed by the persistence of HBAg in the serum, and there have been reports of almost identical carrier rates in adults with and without a past history of hepatitis.[1] Studies[2] of hepatitis B infection among volunteers and those naturally infected with the virus suggest that a greater proportion of individuals who have had a mild or inapparent infection than of those who have had a more severe illness become chronic carriers of HBAg.

A series of 5,640 volunteers with a history of either jaundice or of contact in the past six months with a case of jaundice have been tested for HBAg and hepatitis B antibody (HBAb). Four were HBAg positive and three HBAb positive, giving respective incidences of 1 in 1,410 for HBAg and 1 in 1,880 for HBAb. Using the same immunoelectro-osmophoretic technique to test for the first time 123,102 acceptable donors, 145 (1 in 849) were HBAg positive and 121 (1 in 1,017) were HBAb positive.

These findings by current methods of testing indicate that within the donor population of this region volunteers with a history of jaundice or of recent contact with a case of jaundice do not have a higher incidence of positivity for HBAg and HBAb than donors lacking this history. More sensitive methods of testing such as haemagglutination and radioimmunoassay might reveal a different picture.

However, Mr. Bloomfield draws attention to an important point. Blood donors are unrepresentative of the community as a whole, particularly in respect of age and sex. Even within a donor population there are subgroups with different incidences of HBAg positivity. For example, men prisoners have a higher incidence of HBAg positivity than non-institutionalized men, who in turn have a higher incidence of antigen than women[3].—I am, etc.,

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1 Cossart, Y. E., *British Medical Bulletin*, 1972, **28**, 156.
2 World Health Organization, *Viral Hepatitis*, Technical Report Series, No. 512. London, H.M.S.O., 1973.
3 Wallace, J., Milne, G. R., and Barr, A., *British Medical Journal*, 1972, **1**, 663.

Confidentiality

SIR,—The recent tape-recorded discussion on confidentiality and access to large amounts of data of a highly personal character (23 June, p. 700) and the subsequent correspondence have focused particularly on one issue—danger of recorded data being divulged—but left out almost entirely another aspect that seems to me no less important. The computer specialist, Mr. Barry Barber, who took part in your discussion came close to stating it when he said: "The key questions remain: (a) who may see what part of what record? (b) who may add to the record? (c) who may alter the record?"

What is recorded in medical data banks is not necessarily all, or even part, of what the subject of the record wished to be recorded. It is professional interpretation of that and of other assessments made by members of a profession—one of the oldest professions, it is true, but none the less interpretation of facts or believed facts.

With the rapid extension of nation-wide or even more comprehensive data banks facts are recorded also about credit-worthiness, alleged crimes, reliability, and all manner of personal information, by members of professions or quasi-professions who put down data they consider relevant, leaving out others, and often adding to them personal evaluations. Such information may then remain on the record for as long as the subject is alive, or even longer.

My point is that the general uneasiness about computer-aided information *processing* has given rise to a demand that the subject himself should have access to all that is recorded about him, question what he dislikes, and, if he so desires, have it removed from the record.

I am not at all convinced that what applies to, say, fiscal, criminal, or insurance records—where all medical doctors would no doubt agree—should not apply also to medical records. The possibility of dual loyalties, even among employed medical practitioners, is in fact alluded to in your discussion. It might be argued that a client, a tax payer, or an alleged criminal offender can assess a record but that a patient can not. It might be argued also that submarginal illiterate subjects would not understand the records or that seeing records might, in exceptional circumstances, aggravate the subject's condition.

It seems to me (as one concerned with studies bordering medicine and biology) that statutory or constitutional safeguards need to be provided, giving the individual person the right of access to all information stored about himself in data banks, and to have records altered. If this seems far-fetched in regard to medicine, look perhaps at the literally vital implications of psychosomatic "health" or "normality" under some Orwellian systems of government. We like to assume that data are recorded and seen only by reasonable individuals exclusively concerned with the subject's wellbeing and fair treatment. That may be so in some countries today. Can you guarantee that it will be so next year?—I am, etc.,

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Hazards of Laparoscopy

SIR,—I would like to comment on the excellent letters from Drs. M. McD. Usherwood and A. D. R. Ogborn (30 June, p. 773) and draw attention to certain relevant points.

It is wise to teach that all laparoscopic instruments require careful maintenance. They are not "nurse-proof," and every working part of each instrument should be checked at the beginning of each laparoscopy by the operator. I am surprised that Dr. Usherwood was unable to remove the detached part of his diathermy forceps, as foreign bodies in the pelvis and abdomen are usually removed readily at laparoscopy. I would recommend direct insertion of a long pair of artery forceps if there is difficulty in catching and holding a foreign body with either Palmer's forceps or Steptoe's grasping forceps.[1]

As regards the safety of introduction of the pneumoperitoneum needle to which Dr. Ogborn draws attention, it is well known that there are various sites which can be selected according to the obesity of the patient and the presence of abdominal scars.[1] However, the most important factor in safety is the actual technique of introduction of the needle. This should include two definite steps: (1) the insertion of the Verres or Palmer needle through the skin into the subdermal adipose layer of the abdominal wall *only*, using two hands on the needle, one at the cuff and one near the point; (2) the lifting up of the abdominal wall below the umbilicus, so that the needle can be advanced from the fatty layer through the fascia and peritoneum in a nearly horizontal direction. Adoption of this technique avoids altogether the hazard of damaging any retroperitoneal structure. The thinner the patient, the more horizontal should be the final thrust. Under no circumstances should the pneumoperitoneum needle be introduced with the gas source already attached and flowing, as I have seen some laparoscopists doing. The risk of puncturing a vessel of the abdominal wall, no matter which site is selected, is ever present, so that gas embolism could be caused.

The success of all techniques of laparoscopy depends not only on the skill of the operator, but also on good anaesthesia with relaxation of the abdominal wall, good instrumentation including maintenance, and constant attention to many minute details on the part of the laparoscopist. Gynaecological endoscopy is crying out for the establishment of special teaching centres so that the techniques of these most valuable procedures can be properly taught. Only in this way can fatalities be avoided.—I am, etc.,

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1 Steptoe, P. C., *Journal of Reproductive Medicine*, 1973, **10**, 221.

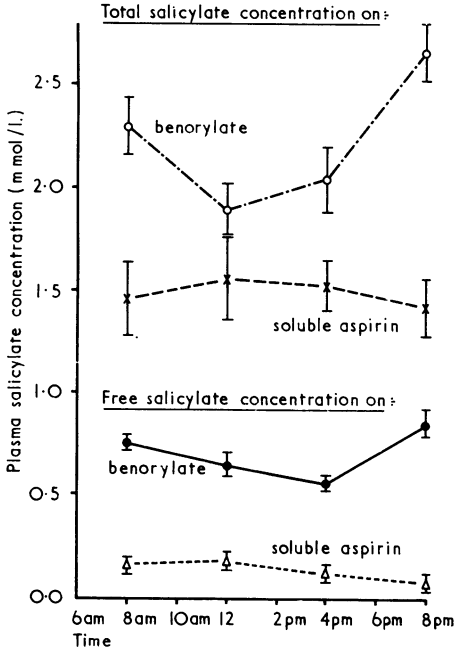
Toxicity of Benorylate

SIR,—The letter from Professor V. Wright and Dr. I. Haslock (26 May, p. 487) succinctly explains that the apparent increase in the overall incidence of tinnitus in patients receiving benorylate is most probably an indication that such patients are achieving therapeutic plasma salicylate levels for the first time. However, this logical explanation does not adequately explain the unexpectedly high concentrations of plasma salicylate in nine patients re-

ceiving 2·0 g of benorylate three times a day, which observations were the subject of my previous letter (14 April, p. 118).

Further measurements of plasma salicylate levels have been undertaken in the same nine patients and 12 randomly selected patients with active rheumatoid disease of the classic form. All patients were allocated seven days' treatment on benorylate 4·0 g (10 ml) twice daily followed by a further seven days during which soluble aspirin 1·2 g four times a day was substituted for benorylate. Venous blood was drawn at 8 a.m. and at four-hour intervals thereafter until 8 p.m. Total and free salicylate concentrations were measured in the separated plasma. Free, unbound, salicylate was separated by membrane ultrafiltration utilizing Centriflo ultrafilters.[1]

The mean total and free salicylate concentrations in the plasma of the nine patients who developed salicylism with benorylate are shown in the accompanying figure, which records the measurements



Mean plasma salicylate levels (± S.E.M.) at 4-hourly intervals, achieved with benorylate 4 g twice daily with soluble aspirin 1·2 g four times a day in nine patients with rheumatoid arthritis.

obtained on the third day of each regimen. In these patients plasma total salicylate concentrations were greater while they were taking benorylate than when taking soluble aspirin, the differences being statistically significant at 8 a.m. ($P = 0.02$) and 8 p.m. ($P < 0.01$). Free salicylate concentrations followed the same pattern except that the levels following benorylate were highly significantly greater than during aspirin administration at each sampling time ($P < 0.001$). When taking aspirin the relationship between plasma free and total salicylate concentrations was in keeping with data obtained in other studies.[2] However, during benorylate administration the concentration of free salicylate recorded was markedly greater than would be expected at the total plasma salicylate concentrations which were observed. Since toxicity rather than clinical effectiveness is associated with free salicylate concentrations greater than 0·6 mmol/l. in most individuals,[3] then it would seem that the increased incidence of salicylism in these nine patients, when on benorylate, as compared with aspirin treatment, is a reflection of the unexpectedly greater concentrations of unbound salicylate in their plasma during benorylate administration.

Considering the 12 other patients included in the study, the incidence of salicylism was the same on both treatment regimens, one patient developing the symptoms while receiving aspirin and one while taking benorylate. There were no significant differences between the plasma salicylate levels achieved when receiving benorylate and those obtained while taking aspirin, the mean values being 1·64 mmol/l. at 8 a.m. and 1·68 mmol/l. at 8 p.m. while taking aspirin, and 1·72 mmol/l. at 8 a.m. and 1·78 mmol/l. at 8 p.m. when taking benorylate. These plasma levels are similar to those achieved by Robertson et al.[4] when giving benorylate to normal volunteers.

Comparison of the two groups of patients revealed no significant differences in age, sex ratio, duration and severity of the disease process, or previous drug histories. Furthermore, there was no consistent quantitative differences between the plasma concentrations of albumin, alpha- and beta-globulins or IgM, IgA, and IgG. However, an in vitro study of the binding characteristics of the plasma of patients in the study indicated a difference between the two groups in that in the plasma of the patients who developed salicylism on benorylate the ratio of proteinbound to free salicylate was modified by the presence of benorylate at a concentration of 10 μg/ml. This modification manifested as a greater concentration of free salicylate at each total salicylate concentration than was obtained in the absence of the benorylate molecule. This phenomenon was not observed in plasma from those patients who showed tolerance of benorylate at the recommended dosages.

These results suggest that in certain individuals the benorylate molecule might interfere with the binding of salicylate to plasma proteins, but they do not explain the higher total salicylate concentrations which were observed while the patients were taking benorylate.—I am, etc.,

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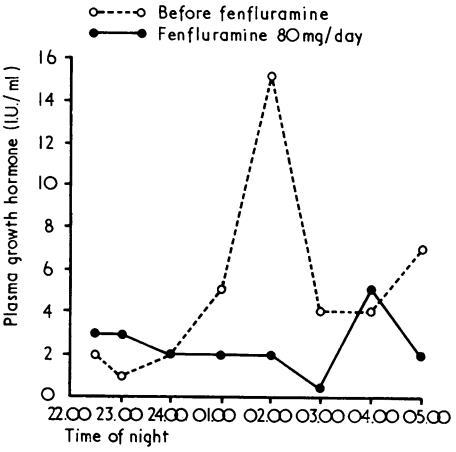
1 Blatt, W. F., Robinson, S. M., and Bixler, H. J., *Analytical Biochemistry*, 1968, **26**, 151.
2 Davison, C., and Smith, P. K., *Journal of Pharmacology and Experimental Therapeutics*, 1961, **133**, 161.
3 Smith, M. J. H., and Dawkins, P. D., *Journal of Pharmacy and Pharmacology*, 1971, **23**, 729.
4 Robertson, A., Glynn, J. P., and Watson, A. K., *Xenobiotica*, 1972, **2**, 339.

Fenfluramine and Growth Hormone Release

SIR,—Dr. D. L. F. Dunleavy and others (7 July, p. 48) describes increased nocturnal growth hormone secretion in a patient while on fenfluramine. An intermittent sampling method has the advantage of studying growth hormone secretion under conditions as near as possible to those under which fenfluramine is commonly used. Their findings might therefore have more clinical relevance than those of Mr. W. R. Sulaiman and Dr. R. H. Johnson (12 May, p. 329).

We, too, have studied overnight growth hormone secretion in a patient before and during treatment with fenfluramine, but by a continuous sampling method, estimating growth hormone in hourly collections. The patient was a 14-year-old girl weighing 95 kg. Overnight growth hormone secretion was studied on admission to hospital. She was then started on treatment with fenfluramine 40 mg twice daily and a further overnight study was carried out 48 hours later. Before and during the studies she was not dieting and lost no weight. Plasma fenfluramine levels during the second night of study were 144·2 ng/ml at 21·30 hours and 97·2 ng/ml at 06·00 hours. Growth hormone secretion for the two nights is shown in the figure. The result is inconclusive, but



certainly does not suggest increased growth hormone secretion when the girl was on fenfluramine. This is in contrast to the finding in Dr. Dunleavy's patient. We cannot account for this. However, Dr. Dunleavy and his colleagues do not mention whether there was any weight change in their patient between the two studies. Growth hormone secretion may be diminished in the obese patient, returning to more normal levels with weight reduction.[1]

The confusion in reports on the effect of fenfluramine on growth hormone levels[2 3] may only reflect the many independent pathways regulating secretion. It seems possible that different tests of growth hormone secretion may test the integrity of different pathways.[4] A drug acting on the central nervous system might stimulate some pathways and depress others, so that the recorded effect might depend on the particular test used. However, this would not explain the discrepancy between our result and that of Dr. Dunleavy and his colleagues. There is need for further study.

It remains questionable whether any change in growth hormone secretion in the patient on fenfluramine is of clinical importance. Growth hormone secretion and growth rate correlate only poorly. Without clinical evidence that fenfluramine does not depress growth rate—which may be difficult to demonstrate—paediatricians may be slightly concerned that they are causing