

Scrotal Carcinoma

SIR,—The incidence of scrotal carcinoma in workers exposed to mineral oil has recently been highlighted by a £10,000 award by Mr. Justice Swanwick.¹ Local inquiries in New South Wales by management, alerted to the possibility of danger of carcinogenesis, prompted me to look into the matter.

In 15 years I have not seen a single case of scrotal carcinoma in New South Wales, despite the fact that many thousands of workers are exposed to mineral oils. Two large insurance companies, which together handle over 50% of the workers' compensation insurance in this State, have never seen a case of scrotal carcinoma. (Squamous carcinoma is quite a common lesion in Australia, involving predominantly those sites exposed to strong sunshine.) Perhaps, in addition to providing impervious aprons for workers exposed to mineral oils, a daily shower at the end of the shift should be mandatory, and underwear and overalls should be laundered frequently. This procedure is voluntarily followed by the vast majority of workers in this State.

Most people would agree that scrotal carcinoma should be an entirely preventable injury.—I am, etc.,

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REFERENCE

- ¹ *The Times*, 5 October 1968.

Tryptophan and Oral Contraceptives

SIR,—Rose^{1,2} and Price³ have shown that women taking oestrogen-progestogen preparations for contraceptive purposes have greatly increased urinary levels of tryptophan metabolites following a 5 g. or 2 g. load. Price measured the spontaneous metabolite excretion in women taking Enovid-E (norethynodrel and mestranol), but did not detect any significant increase in the metabolites measured, although 3-hydroxyanthranilic acid (3HA) was not determined. In two subjects on oral contraceptives Rose and Toseland⁴ reported somewhat higher levels of 3HA in acid-hydrolysed urine without loading, but determinations were not carried out before administration of the hormones.

We report here the finding of high levels of 3HA, without tryptophan loading, in two women taking oral contraceptives, and significantly raised levels in two further women studied for the first four months of administration of the hormone, one of whom was investigated for the effect of pyridoxine administration.

Early morning urine specimens were collected from the five subjects taking contraceptive preparations, and 24-hour urine collections as well were made in 12 normal female controls. No tryptophan load was given to any subject. 3HA was extracted from unhydrolysed urine by the method of McMillan⁵ and determined fluorimetrically following thin-layer electrophoresis on cellulose.⁶ Triplicate determinations were made on each specimen, a standard amount of pure 3HA being added to the third sample. The results were expressed in terms of the subject's creatinine excretion.

Urinary levels of 3HA in the controls aged 22–50⁷ ranged from 0.10–1.00 mg./g. creatinine. These results agree with those obtained by Benassi,⁸ but are slightly lower than those of Schievelbein.⁹ In three women aged 21–26, with

no evidence of renal disease, who had already been taking oral contraceptives for 3–15 months, the urinary 3HA was 1.5, 0.2, and 1.3 mg./g. creatinine respectively. In two further women aged 18 and 25 studied progressively the values obtained were as follows:

In mg3HA/g. creatine			
Prior to taking Hormone	After 4 Weeks on Hormone	After 4 Months on Hormone	At 4 Months after 5 Days on Pyridoxine 20 mg./day
0.26 0.15	0.52 —	3.14 0.75	0.40 —

Three significant facts emerge from this finding: (i) increased values of 3HA can be detected without tryptophan loading; (ii) the increase rises progressively with the duration of the administration of oestrogen-progestogen compounds; and that (iii) the increase is apparently reversed in a subject given pyridoxine supplements.

The last finding adds further support to the suggestion of Rose² and Heeley¹⁰ that pyridoxine may influence the metabolic fate of 3HA in the tryptophan-niacin pathway. These cases were found in a larger group of healthy young women, used as controls, in a study of the increased excretion⁵ of 3HA in rheumatoid arthritis. In this context it is interesting to read the report from Ann Arbor¹¹ of the apparent increase in the incidence of rheumatoid symptoms associated with the use of oral contraceptives. We realize, of course, that two subjects do not provide sufficient evidence to test this hypothesis, and the work is therefore being extended to cover a wider range of steroid hormones used in conception control and to study further the effects of pyridoxine supplements.—We are, etc.,

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REFERENCES

- ¹ Rose, D. P. *Nature (Lond.)*, 1966, 210, 196.
- ² Rose, D. P. *Clin. Sci.*, 1966, 31, 265.
- ³ Price, J. M., Thornton, M. J., and Mueller, L. M. *Amer. J. Clin. Nutr.*, 1967, 20, 452.
- ⁴ Rose, D. P., and Toseland, P. A., *Clin. Chim. Acta.*, 1967, 17, 235.
- ⁵ McMillan, M. *J. Clin. Path.*, 1966, 13, 140.
- ⁶ Toseland, P. A., *Clin. Chem.*, 1968, 14, 808.
- ⁷ Rose, D. P., *Clin. Chim. Acta.*, 1967, 18, 221.
- ⁸ Benassi, C. A., Veronese, F. M., and De Antoni, A., *Clin. Chim. Acta.*, 1967, 17, 383.
- ⁹ Schievelbein, H., and Buchfink, E., *Clin. Chim. Acta.*, 1967, 18, 291.
- ¹⁰ Heeley, A. F., Pesowicz, A. T., and McCubbing, D. G., *Clin. Sci.*, 1968, 35, 381.
- ¹¹ Bole, G. G., Friedlaender, M. H., and Smith, C. K., *Lancet*, 1969, 1, 323.

Toxicity of Carbon Tetrachloride

SIR,—I was interested to read Dr. R. J. Weir's memorandum on carbon tetrachloride poisoning (22 February, p. 487). We have recently confirmed the view that the toxicity of carbon tetrachloride (CCl₄) is dependent upon the activity of the hepatic drug-metabolizing enzymes.¹ These enzymes are responsible for the breakdown of many substrates such as drugs and steroids, and their activity can be altered by dietary and nutritional factors, hormonal changes in the body, and the ingestion of foreign chemicals.²

We have developed a convenient method of increasing drug-metabolizing activity in

rats by administering oral phenobarbitone in the drinking-water.³ Although the daily dose of phenobarbitone exceeds 100 mg./kg., doses which can be related to those taken by humans therapeutically cause a significant increase in activity.

Pretreatment of rats with phenobarbitone causes the median lethal dose (LD₅₀) of CCl₄ to fall from 3.6 ml./kg. to 0.5 ml./kg. 0.25 ml. CCl₄/kg. produces severe liver damage in phenobarbitone pretreated rats as shown by high liver fat and water content and high plasma isocitrate dehydrogenase and bilirubin levels. This dose of CCl₄ produces only slight damage in control rats. The amount of CCl₄ metabolized in the first six hours after administration of 0.25 ml. CCl₄/kg. to phenobarbitone pretreated rats is the same as that of control rats given a tenfold larger dose. Previous work has shown that rats fed on a protein-depleted diet are much less susceptible to CCl₄ poisoning,⁴ and this has been shown to be due to a very low level of hepatic drug-metabolizing enzyme.⁵ These facts indicate that the toxicity of CCl₄ is closely linked to its metabolism.

Administration of phenobarbitone to man has been shown to produce an increase in the rate of metabolism of phenylbutazone.⁶ Although, for obvious reasons, no work has been done on the metabolism of CCl₄ in man, it is likely that its metabolism will also be accelerated leading to increased toxicity.

It cannot be overemphasized that carbon tetrachloride is a highly toxic substance in any circumstance, and that individuals who are on barbiturate therapy may have a greatly increased susceptibility.—I am, etc.,

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REFERENCES

- ¹ Garner, R. C., and McLean, A. E. M., *Biochem. Pharmacol.*, in press.
- ² Conney, A. H., *Pharmacol. Rev.*, 1967, 19, 317.
- ³ Marshall, W. J., and McLean, A. E. M., *Biochem. Pharmacol.*, 1969, 18, 153.
- ⁴ McLean, A. E. M., and McLean, E. K., *Biochem. J.*, 1966, 100, 564.
- ⁵ Seawright, A. A., and McLean, A. E. M., *Biochem. J.*, 1967, 105, 1055.
- ⁶ Levi, A. J., Sherlock, S., and Walker, D., *Lancet*, 1968, 1, 1275.

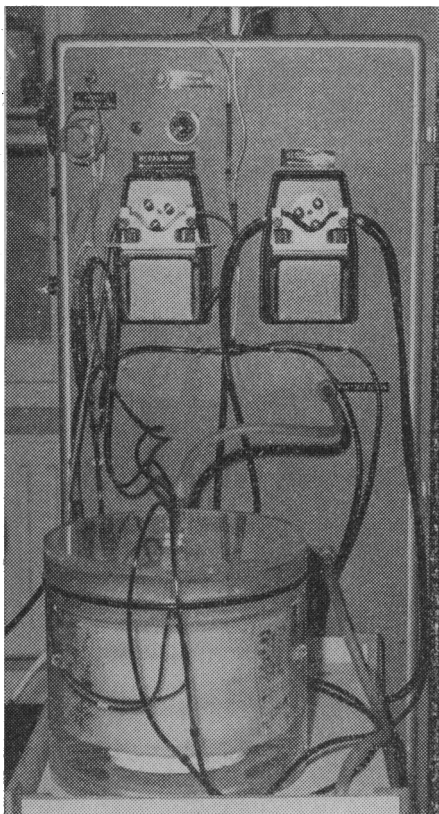
Economics of Dialysis

SIR,—The small but expanding group of doctors and nurses who man haemodialysis units throughout the country struggle daily with deficiencies of equipment, accommodation, and trained staff to the extent that these difficulties have become facts of life rather than limits. It is the time that it takes to dialyse a patient that is the real limitation to expansion of work, and the 14 hours' dialysis applied by a Kiil kidney is a full day's work for an installed mass of equipment worth probably £2,000. It also incurs the uncomfortable business of building the Kiil kidney and providing accommodation and staff for this wet performance. Money is important, and it is said that presterilized disposable coils are more expensive than Kiil boards. This has been debated too long and without a real, true costing on a basis of convenience, safety, and speed as well as cash.

The Capon-Heaton mini-coil (14 hours dialysis), costs £7; the Baxter "Ultraflo" coil costs £9 to dialyse adequately in seven hours. Our estimate of the cost of the 14 hours' dialysis, using the Kiil kidney, is a minimum of £5 each time and it is wet, messy, and often frustrating. From the bacterial point of view, the Kiil board

kidney is potentially dangerous, since the method of sterilization with 2% formalin does not reach any reasonable bacterial standard. The tendency of life today is to move towards the use of disposable equipment, and the Küll is really old-fashioned and clumsy.

We have had over a year's experience now with the Lucas monitor/dialysate proportioning system and been very pleased with its operation, granting, of course, that the machine is well and properly understood. Recently we have also been very pleased with the performance of the Baxter "Ultraflo" coil used in the newest model of the Travenol R.S.P. machine, and it seemed obvious to marry the two together. Thus we have built a container capable of holding the "Ultraflo" coil, providing a continuous flow of dialysate through the coil at high rates of flow and under an adjustable negative pressure so as to make use of the Lucas monitor system. This prototype canister, made of Perspex, is functioning well, producing perfectly normal dialyses with good end biochemical figures, and achieving these results within a period of between six and eight hours.



The present cost of such a dialysis is £9, but it is good economics to keep expensive equipment steadily employed, and the possibility of two, if not three, dialyses per 24 hours instead of one is surely an advance. Further development work is proceeding. The exciting prospect, of course, is that, without any increase of beds, we may accept more patients in permanent renal failure who nowadays see a future for themselves in the steadily increasing success of renal transplant work.—We are, etc.,

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Abortion Act in Practice

SIR,—Although I am not personally involved in applying the Abortion Act, may I be permitted to enlarge on one of Dr. J. H. Hughes's remarks (8 March, p. 637)? Dr. Hughes tells us that if all doctors "put their patient's welfare before their own religious and biased cobwebbed ideas on abortion" there would be no further problem. How delightfully simple! However, to reduce the matter to such a simple level one has to make a few assumptions:

- (1) that objections to a liberal interpretation of the Act are necessarily religious;
- (2) that being religious they are demonstrably irrelevant to our present situation (which is presumably what Dr. Hughes means by "cobwebbed");
- (3) that all doctors who don't think like Dr. Hughes are more concerned about the peace of their own consciences than about the welfare of their patients;
- (4) that any who doubt the wisdom of interpreting the Act liberally are biased, whereas its enthusiastic supporters and they alone are capable of unbiased judgement; and
- (5) that what is permitted by an Act of Parliament is *ipso facto* the best for all citizens.

No doubt others of your readers found these assumptions hard to swallow.—I am, etc.,

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SIR,—Dr. J. H. Hughes (8 March, p. 637) is timely in reminding us that without the "biased cobwebbed ideas on abortion" of many doctors "the new Act would present no problems at all." It certainly is amazing to see how much time is wasted by gynaecologists and psychiatrists on sorting out a problem which from the woman's point of view, and indeed in the view of a majority in this country, should present very few difficulties.

One of my patients, a highly strung mother of four children, was recommended by me for termination. She was involved in four consultations in three weeks at a local hospital only to be refused termination in the end. Worse things are happening in the country.

While this law is the envy of Europe and by far exceeds recent reform of the law on homosexuality and the proposed reform of the divorce law, there is one flaw in it: it does not set a time limit for termination. Experienced observers like the late Professor W. C. W. Nixon have always insisted on the 13 weeks' limit for termination, being well aware of the fact that by waiting longer a relatively simple operation, requiring no more than 20 minutes of a surgeon's time and about six hours in the hospital altogether, is turned into a hysterectomy with anything from 2 to 7 days in hospital. This quite unnecessary luxury is also unpleasant in other ways—for example, the viewing of the operation by doctors and nurses. There is little to be seen in the curettings of an 8/52 pregnancy, whereas beyond 14 weeks it does look rather ugly to some sensitive staff. It seems unnecessary to provoke their feelings. Complications, according to the Swedish statistics, are also higher in terminating the more advanced pregnancies.

Last but not least, the woman who comes late with her request for termination is more often than not also the woman who cannot

make up her mind and might therefore have psychiatric complications after termination. Granted there are the inexperienced children under 18 and there is the girl from darkest Ireland, but can we model medical procedure on them? Future policy should therefore be to leave this fine liberal law as it is, but with the insertion of a time limit of 13 weeks for termination.—I am, etc.,

London S.E.17.

E. F. RICHARD.

SIR,—To say that I was disgusted by Dr. J. H. Hughes's letter (8 March, p. 637) would be a masterpiece of understatement. Indeed, I find the trendy, assembly line philosophy of the whole letter so utterly repugnant that it would take up valuable space to itemize all my objections to it.

So, as we appear to be indulging in polemics, perhaps I may be allowed to spell out what I personally believe to be true. That an embryo implanted in the uterus is a potential human being. That an abortion destroys this potential human being. That it is the duty of the profession to preserve life, and that by destroying life it takes on itself the heaviest of responsibilities. These are not "religious and biased cobwebbed ideas"—these are surely the very stuff of medical ethics.

I also fully agree with Professor Keith Simpson (15 February, p. 436), and feel strongly that advertisements for establishments which appear to proclaim their main function as the destruction of life rather than its preservation are inappropriate to a respected medical journal, and leave a particularly nasty taste in the mouth.—I am, etc.,

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N. C. LEE.

Overinvestigation

SIR,—I would like to add two examples to the letter by Mr. A. Dickson Wright on overinvestigation (15 February, p. 440).

A previously healthy man of 42, who had sustained some superficial war injuries—for which he was in receipt of a pension—developed blueness of the fingers with early gangrene of finger tips in 1957. He was admitted urgently to hospital and somebody thought he saw splinter haemorrhages in the nails—rather difficult in blue-black nails. A diagnosis of subacute bacterial endocarditis was made and intravenous heparin and nicotinic acid given. This apparently produced some reaction—there is no record in the heavy dossier of the war pension reviews of the length of his stay in hospital. He was so depressed—or impressed—by the serious nature of his illness that treatment by E.C.T. was ordered. Investigations on the grand scale were repeatedly carried out, including repeat x-rays of the metallic fragments—all were normal. On one occasion the diagnosis of Raynaud's disease was put forward, but, possibly as the cold agglutinins did not match up to this, no decision was made. When seen recently he stated that he was attending hospital at intervals. Phenindione was prescribed and the prothrombin time estimated every 14 days. On examination the fingers were normal and there had been no further attacks. He had changed to an indoor occupation.

I suggest that if this man had been given a continuous hot bath for an hour, or put in a very warm bed with a few drinks of alcohol, this expensive and dangerous treatment and