in this country due to prolonged ingestion of phenacetin.² Shortly afterwards, a second case was described by Jacobs in May 1964.³ Sanerkin and Weaver suggested that serious phenacetin nephropathy might be more common than is generally supposed, and their view is amply justified by the fact that I have found three cases of death due to chronic necrosis of the renal papillae within the space of four months from February 1965 to June 1965. Each of these three cases was associated with a history of prolonged ingestion of an analgesic compound containing phenacetin, and each case has shown no evidence of diabetes mellitus and no evidence of obstruction in the urinary tract.

Case 1.—On 22 February 1965 a young woman aged 35 was admitted to Southend General Hospital in coma and died before a clinical diagnosis could be made. At necropsy there was marked necrosis of the renal papillae. Histology confirmed chronic necrosis of the renal papillae, together with chronic interstitial nephritis. I recalled the observation of Sanerkin and Weaver that inquiries should be made in such cases regarding the ingestion of phenacetin, and the inquiries of the Coroner's Officer revealed that the deceased had taken approximately 16 tablets of Veganin (each tablet containing 250 mg. of phenacetin) each day over a period of six years.

Case 2.—Shortly after I had reported the first case described I received the histological sections of bilateral granular kidneys from a woman, aged 60 years, on whom I performed a necropsy on 2 February 1965. The kidneys showed chronic necrosis of the renal papillae and chronic interstitial nephritis. Macroscopically, the kidneys were uniformly grossly contracted and each weighed 40 g. Re-examination of the kidney fragments taken for histology showed naked-eye papillary necrosis. The cause of death was uraemia, and I subsequently questioned the patient's daughter, who told me that her mother had taken about 15 tablets of Codis (each tablet containing 4 grains (260 mg.) of phenacetin) each day over about six years.

Case 3.—In April 1965 a man aged 68 years was admitted to Southend General Hospital with anaemia and a high blood urea. Since he had a painful hip, I suggested that inquiries should be made regarding the taking of analgesics. Although the man was confused, he did admit to taking Codis every night for a long time. This patient died on 6 June. The Coroner's Officer found 120 Codis tablets in the deceased's home and ascertained that the man had obtained Codis tablets in consignments of 400 at one time. The acquaintances of the deceased knew that he had taken tablets regularly, but they were not aware of the nature of these tablets.

Sanerkin and Weaver reported Aschoff bodies in the myocardium of their case, and it is of great interest to note that the young woman aged 36 showed an acute myocarditis on histological examination.

A complete description of these three cases will be incorporated in a paper, but I think it is desirable to report as quickly as possible the occurrence of three deaths associated with the prolonged ingestion of phenacetin which have been seen within the space of four months in one hospital.

The present knowledge regarding phenacetin nephropathy has been reviewed recently in the *B.M.J.* (13 March, p. 673), and though there may be some doubt as to whether phenacetin itself is the active principle producing nephropathy, the circumstantial evidence is surely now strong enough to make it essential that Great Britain should follow the example of Sweden, where the sale of phenacetin has been restricted to medical prescription since February 1961.

I thank Mr. G. Y. Jerman, H.M. Coroner for the County Borough of Southend-on-Sea, for permission to publish the details of the first and third cases.

—I am, etc.,

Department of Pathology,
Southend General Hospital.

S. J. BEALES.

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- 2 Sanerkin, N. G., and Weaver, Corinna M., *Brit. med. J.*, 1964, 1, 288.
- 3 Jacobs, H. S., *ibid.*, 1964, 1, 1381.

Abuse of Digitalis

SIR,—I should like to comment on one point of Dr. H. D. Friedberg's letter (19 June, p. 1611) in which he warns against the indiscriminate giving of potassium to patients with digitalis intoxication. Amongst the evidence of potassium loss, which he postulates as a prerequisite for giving potassium, he includes estimation of serum levels. It should be appreciated, however, that potassium loss need not be reflected in a lowered serum level. Electrocardiographic features suggesting hypo- or hyperkalaemia agree well with serum-potassium concentrations only if the latter are markedly abnormal (below 2.3 or over 6.7 mEq/litre).¹ Whether the clinically relevant factor is the intracellular potassium concentration or the intra/extracellular gradient seems still controversial.² From the practical point of view the salient consideration is that a normal serum-potassium level should not be regarded as a contraindication to the exhibition of potassium, which may be life-saving, provided there are other reasons to assume potassium depletion and the compound is given with the necessary precautions.—I am, etc.,

London W.1.

A. SCHOTT.

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- 2 Holzmänn, M., *Klinische Elektrokardiographie*, pp. 390 seq., 4th ed., 1961. Thieme, Stuttgart.

Carcinogenesis of Isoniazid in Mice

SIR,—Your editorial (12 June, p. 1508) on the carcinogenic action of isoniazid in mice and its "apparent" lack of effect in man treads dangerous ground. Similar special pleading could be used to ensure that no chemical (drug, food additive, or pesticide) was withheld from the environment until there was substantial evidence that it induced cancer in man. Results in animals are certainly not proof of carcinogenicity in man. However, experience tells us that (with one possible exception) every chemical known to induce cancer in man also gives rise to tumours in one or more species of experimental animal. It would seem prudent, therefore, in our present state of knowledge to regard all animal carcinogens as potentially dangerous to man.

The suggestion that "it seems highly improbable that so striking a sequel would not have been recorded" may be grossly misleading. Environmental carcinogens have a habit of remaining hidden unless they are actively sought out. The position is further complicated by the fact that the same

chemical effects different tissues in different species.¹ There is no certainty that if isoniazid induces tumours in man these will be leukaemias or carcinomas of the lung as in mice.

The clinician prescribing isoniazid has to balance the manifest value of the drug in combating tuberculosis against the possible danger. Nobody wishes such a valuable drug to be withheld, but until a careful and controlled analysis of the causes of death of patients treated with isoniazid is made² a rational assessment of the risk, if any, is impossible.—I am, etc.,

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Pathology and Cancer Research,
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Leeds 2.

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- 2 Roe, F. J. C., Boyland, E., and Haddow, A., *Brit. med. J.*, 1965, 1, 1550.

Transferable Antibiotic Resistance

SIR,—Your leading article under this heading (22 May, p. 1325) indicates that a new aspect of resistance to antibiotics could now be important, and although its implications have only so far been demonstrated in the laboratory, its relationship to clinical and field experience must be followed up.

There is one aspect of salmonella infection in calves in particular which could indicate that therapy in these animals is unlikely to have an effect on the human population. Infection of the calf with salmonella can occur in a number of ways—they can be infected by an excretor cow, infection can be transmitted through the faeces of another calf by contact with contaminated food or drinking-water, or even the milk fed to calves may contain the organisms. Although infection in calves can be a serious clinical entity, it has been found that the majority of recovered calves clear themselves completely of infection, so that after 12 weeks of age few of the original infected group remain carriers of the organisms.

Field¹ and his colleagues examined over 2,000 healthy cattle entering various abattoirs for slaughter, and salmonella organisms were isolated from 18 (0.8%). It seems likely, therefore, that, although young calves may develop clinical signs of salmonellosis and receive antibiotic therapy during the early stages of life, the number of those treated calves which will show evidence of salmonella when they go for slaughter at nine to ten months or later will be very small. It would appear, therefore, that the therapy of calves could reduce rather than increase the salmonella risk to human beings.

In the case referred to by Dr. Anderson where resistance was encountered following the use of ampicillin in the treatment of calves suffering from *Salmonella typhimurium*, 80 out of 130 calves in one house were passing the organisms, so that a very heavy infection was encountered. All 130 calves were treated with ampicillin at a therapeutic level of 8 mg./kg. for five days, and a dramatic response was obtained to therapy. In addition there was a marked reduction in the number of calves which were found to be passing salmonella organisms. Despite this

very concentrated therapy only two out of 40 strains of phage type 29 *S. typhi-murium* were found to be resistant to ampicillin after treatment.

It has been our experience that each calf unit, rather like a hospital ward, has its own specific bacterial and antibiotic problem, and one cannot say that the findings in one situation are indicative of the situation in the country as a whole.

The effect of a bacterial population in a calf unit depends very much on the system of management employed, the size of the pens, and the number of calves kept.—I am, etc.,

G. C. BRANDER.

Beecham Research Laboratory,
Brentford, Middlesex.

REFERENCE

- ¹ Field, H. I., *Spec. Rep. Min. Agr. Fish.*, 1954 (unpublished).

Abortion Law

SIR,—When a letter bears the signatures of eleven consultants it is perhaps natural to assume that it has unusual weight or even incontrovertible content, but on this occasion (Dr. H. R. Rollin and his colleagues, 5 June, p. 1497) I do not find it so. Your correspondents raise objection to opinions based "not on clinical grounds, but because of the admitted religious scruples" of consultant gynaecologists. In a problem which involves the destruction of the human embryo, do they really think that the term "scruple" is appropriate? Even if "belief" is substituted, the picture is still an inaccurate one. When I, a Catholic gynaecologist, give an opinion I give it as an integral person and it springs from my basic beliefs (by the sanctity of life, the dignity of man) and my clinical experience. It is surely the task of a consultant to recommend what seems to him in the best interests of the patient, and to explain his decision and the reasons for it to the patient and her doctor. They may then accept or reject it.

I am left wondering what else your correspondents would have me do. I do not agree that I am not entitled to an opinion on a point as basic as this. They must surely be aware of the different opinions which exist among psychiatrists¹; and gynaecologists also are acquainted with the problem, as seen recently in a masterly summary by Jeffcoate.²

Perhaps (if you will forgive the play on words, Sir) what is needed is an "unscrupulous gynaecologist." More seriously, in such cases what is surely required is a further opinion. You will perhaps forgive me for suggesting that in these circumstances I would recommend a second psychiatric opinion.—I am, etc.,

R. B. PARKER.

Birmingham 16.

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- ¹ Sim, M., *Brit. med. J.*, 1963, 2, 145.
² Jeffcoate, T. N. A., *ibid.*, 1960, 1, 581.

SIR,—Permit me to express regret at the tone which has crept into this correspondence. That men acting conscientiously and in good faith on behalf of their patients should be accused of perverted ethics and

"getting away with it" is, frankly, intolerable.—I am, etc.,

London S.W.13.

ELIOT SLATER.

SIR,—The apparent impasse between the opinions of Dr. H. R. Rollin and his colleagues (5 June, p. 1497) and those of Dr. M. Sim (19 June, p. 1612) is unlikely to be resolved by merely reforming the existing law.

In every mental hospital where I have worked one encounters consultant psychiatrists who hold differing views on the psychiatric indications for terminating pregnancy. For some time I have been interested in the reasons underlying such variations of informed opinion. Some views are perhaps biased through religious prejudice or reflect individual beliefs which are consciously or unconsciously determined, whereas others may be derived from early training in medicine and psychiatry. I regard my own orientation as largely dependent upon personal clinical experience, for I never remember receiving any detailed instruction on this vitally important topic when I was a student.

The findings and conclusions of Dr. Sim are undoubtedly impressive,¹ and I have yet to see them seriously challenged by protagonists from the opposite school. Dr. Rollin and his colleagues seem to be exaggerating the problem when they state that "whole sections of the community may be denied a service which is recognized as both legal and ethical" by a gynaecologist whose religious scruples preclude termination of pregnancy, for I have rarely found it difficult to find another gynaecologist with opposing views if one wants one.

Elsewhere, I have intimated that the establishment of a "termination board" may help to provide a practical solution to this complex problem.² Such a panel has successfully operated in Dorchester, Dorset, for three years and we are hoping to introduce one in this area shortly, possibly constructed along similar lines.³ Dr. Joyston-Bechal³ succinctly affirmed that a collective decision, rather than one made by "individual experts, would help to overcome the well-recognized discrepancies in psychiatric assessment and set the stage for future research and legislation by objectively considering the criteria for termination."

Apart from its service to the public the "termination board" could also function as a useful research tool. Cases presented to it would require to be adequately documented at the time, and subsequent follow-up analysis would confirm or refute the wisdom of decisions formulated by the panel, thereby enlarging its experience.

At present perhaps the most frequent decision before the clinician is either to sacrifice a life or allow a pregnancy to proceed which may possibly be detrimental to maternal health in some instances. The doctor, acting in good faith, may frequently be subjected to intolerable social pressures, which at times can be very alarming and occasionally quite overwhelming. It is therefore understandable that some psychiatrists should wish to share one of the most difficult and important decisions they are ever required to make with their colleagues. Under these circumstances, experience with "termination boards," perhaps organized on a regional basis, might surely

prove to be a valuable alternative to any precipitate amendments to the abortion law.—I am, etc.,

J. C. BARKER.

Shelton Hospital,
Shrewsbury, Shropshire.

REFERENCES

- ¹ Sim, M., *Brit. med. J.*, 1963, 2, 145.
² Barker, J. C., *Lancet*, 1965, 1, 708.
³ Joyston-Bechal, M. P., *ibid.*, 1965, 1, 219.

Porridge Test Meals

SIR,—We have recently had the opportunity to read the excellent paper by Dr. Flavell Mafts and his co-workers (20 March, p. 753) and wish to comment briefly on one of the methods used—viz., the use of an 8 g. porridge test meal as a quantitative test of gastric secretion.

Porridge is given in this test as a stimulus to the gastric phase of gastric secretion which depends on release of antral gastrin. It provides neither a reproducible nor a maximal estimate of gastric secretion,^{1,2} and the use of test meals in this type of work should have ceased following Kay's important paper in 1953.³ A test meal is useless for comparative purposes where secretion of acid is the parameter under study. Modern technique would indicate use of histamine, betazole hydrochloride (Histalog),⁴ or of the synthetic tetrapeptide gastrin⁵ for quantitative sequential studies on gastric secretion.

We acknowledge that the gastric-secretory study was a minor facet of the paper and have no wish to criticize other aspects of this most worth-while contribution.—We are, etc.,

P. E. BAUME.

D. W. PIPER.

The Royal North Shore Hospital
of Sydney,
Sydney, N.S.W., Australia.

REFERENCES

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² Sparberg, M., and Kirsner, J. B., *Amer. J. dig. Dis.*, 1964, 9, 567.
³ Kay, A. W., *Brit. med. J.*, 1953, 2, 77.
⁴ Zaterka, S., and Neves, D. P., *Gastroenterology*, 1964, 47, 251.
⁵ Makhlof, G. M., McManus, J. P. A., and Card, W. I., *Gut*, 1964, 5, 379.

Acute Osteitis in Childhood

SIR,—I was interested to read the report by Dr. G. A. Neligan and Dr. F. M. Elderkin (22 May, p. 1349) of the excellent results obtained in acute osteitis in children by the early administration of antibiotics and aspiration of sub-periosteal pus as soon as the indication arose.

All would agree with the authors' emphasis on the importance of early diagnosis and referral to hospital, but, in spite of previous evidence of the efficacy of aspiration as compared with other methods,² I would still question whether aspiration is always adequate to achieve the object of releasing pus under tension with minimum delay. In the last four years 17 children with acute osteitis affecting 20 bones have been treated at Odstock Hospital, Salisbury. The duration of symptoms was from one to seven days. Apart from two cases, whose symptoms were mild and who responded rapidly to antibiotics, all were explored within 48 hours, the periosteum being incised and the bone drilled.