Correspondence

Correspondents are asked to be brief.

Athletes' Deaths

SIR,—In your leading article "Athletes' Deaths" (3 October, p. 4) you point out that heart failure in athletes may be due to coronary heart disease, or congenital abnormality of the coronary arteries, or chronic myocarditis, or a cardiac tumour. In this State we carry out coroner's necropsy examinations in the large majority of sudden or unexpected deaths and in the course of the years have seen almost 100 examples of sudden death in young adults. In many death had occurred while the individual was at rest or had undertaken mild physical activity. In none of our series of sudden death in young adults did we find any of the four conditions listed above, although we have seen viral myocarditis in young children. In the majority of our patients there was no disease of the coronary arteries but there was significant scarring of the myocardium, and in these individuals a consistent finding was hypoplasia of the aorta. A report on the earlier cases has been published.[1]

This finding has not been reported elsewhere and I suggest it be kept in mind as a possible cause of sudden death in young adults.—I am, etc.,

W. LAURIE.

Department of Health,
Government of Western Australia,
Perth,
Western Australia.

REFERENCE

1 Laurie, W., *Medical Journal of Australia*, 1968, 2, 710.

Hyperpyrexia after Anaesthesia

SIR,—The incidence of malignant hyperpyrexia[1 2] has brought a cloud to the sky of clinical anaesthesia. We report here a case which displayed two of the features of the recognized triad—hyperpyrexia and metabolic acidosis—without any apparent hypertonicity, and which had a history of uneventful anaesthesia a week previously.

A fit man of 59 underwent a laparotomy for large bowel neoplasm, and a left hemicolectomy was performed. Anaesthesia on this occasion was induced with thiopentone, tubocurarine, and phenoperidene, and was maintained with intermittent positive pressure ventilation, but no halothane was used. Two days postoperatively his temperature rose to 101°F. (38·5°C.) and remained around this level for a further five days, though his electrolytes and fluid balance were kept within normal limits. A diagnosis of ischaemic disease of the bowel was made, and it was decided to re-open his abdomen. Before coming to theatre his blood gas analysis was pH 7·39; P_{CO_2} 37; HCO_3 22·5; base equivalent -2·0; P_{O_2} 110 mm. Hg.

Anaesthesia was induced using thiopentone, pancuronium, phenazocine, and maintained with intermittent positive pressure ventilation; again no halothane was used. On re-opening the abdomen it was observed that perfusion of the tissues was poor, and the patient's temperature was found to be 105°F. (40·5°C.). Immediate steps to effect cooling were taken (jugular infusion of fluids through a coil placed in ice, and bags of ice on the patient's precordium) and 500 mg. of hydrocortisone were given. The temperature fell to 102°F. (39°C.) and an improvement in the perfusion of the gut was noticed by the surgeon. A small perforation was found at the site of the anastamosis which was undone and brought to the surface. A tracheal tug was evident on decurarization, and blood gas analysis showed a severe metabolic acidosis: pH 7·03; P_{CO_2} 72; $NaHCO_3$ 13·5; base equivalent -15. Ninety ml. of 5·6% sodium bicarbonate were given, and the patient was maintained on a Bird mark 8 respirator, using the patient triggering device. Temperature on returning to the ward was 102°F. (39°C.).

Three hours later his blood gas analysis was pH 7·18; P_{CO_2} 90; $NaHCO_3$ 26·4; B.E. -2·2. In view of the high P_{CO_2}, ventilation was then controlled using phenoperidene to depress his respiratory drive, and vigorous endobronchial suction was performed. Six hours later he recovered consciousness, and, as his blood gas analysis was found to be normal, he was extubated. His temperature was 101°F. (38·5°C.) but fell to normal within 24 hours.

In comparison with other cases reported, the pyrexia was moderate (105°F. (40·5°C.) was the highest observed) and there was no apparent muscle rigidity, but there was a severe metabolic acidosis and pyrexia, which can hardly be dissociated from the anaesthesia and surgery which the patient underwent. The possibility of bacteremic shock as a cause of the pyrexia would appear to be excluded by the fact that the blood pressure never fell below 100 mm.Hg during the operation.—We are, etc.,

SHEILA KENNY.
HUW ROLFE.

Adelaide Hospital,
Dublin 8.

REFERENCES

1 Murray, B. R. P., and Williams, P. A. D., *British Medical Journal*, 1969, 1, 488.
2 Isaacs, H., and Barlow, M. B., *British Medical Journal*, 1970, 1, 275.

Laparoscopy Hazard

SIR,—My attention has been drawn to an accident which occurred during gas insufflation of the abdomen for laparoscopy. Cardiac arrest was thought to have occurred as a result of overdistension of the peritoneal cavity with carbon dioxide, and the patient died three weeks later.

The technique of gas insufflation has been described by several authors, and the

importance of having a manometer or release valve incorporated in the circuit has been stressed. Seed, Shakespeare, and Muldoon[1] stated that the inflow pressure should not rise above 20 mm. Hg, a higher pressure usually indicating a blocked cannula. One of their patients suffered from tachycardia and a fall in blood pressure when the insufflation pressure rose above 40 mm. Hg for a short time, but recovery occurred immediately on decompression. These authors attributed the hypotension to compression of the vena cava, and suggested that it was more likely to occur earlier with a tense abdominal wall than with flaccid musculature. Splinting of the diaphragm will also embarrass respiration, and regurgitation of stomach contents may occur.

Once the dangers of overdistension are realized they can be easily avoided, but should this occur immediate release of pressure and raising the legs should quickly restore normal cardiac and respiratory function.—I am, etc.,

HUMPHREY ARTHURE.

London, W.1.

REFERENCE

1 Seed, R. F., Shakespeare, T. F., and Muldoon, M. J., *Anaesthesia*, 1970, **25**, 223.

Vasovagal Faint in the Supine Position

SIR,—The report by Drs. P. J. Verrill and W. H. Aellig (7 November, p. 348) of a severe faint in a dental patient given diazepam lying down is interesting and important. One can only speculate on whether he would have survived had he been sitting up and had the injected drug been a general anaesthetic, when loss of consciousness would have been expected and therefore the onset of the faint perhaps overlooked.

May I correct a small misrepresentation in their final sentence? They quote Weissler and Warren[1] as having stated that when fainting reactions occur in recumbent subjects they are particularly severe, often protracted, and associated with pronounced degrees of bradycardia. In fact what Weissler and Warren were referring to was not the faint itself, but the prodromal symptoms of fainting. It is not surprising that these are often severe and protracted in recumbent subjects, since it is extremely rare in that position for consciousness to be lost.—I am, etc.,

J. G. BOURNE.

Salisbury, Wilts.

REFERENCE

1 Weissler, M. W., and Warren, J. V., *American Heart Journal*, 1959, **57**, 786.

Phenacetin Nephropathy

SIR,—Dr. K. G. Koutsaimanis and Professor H. E. de Wardener (17 October, p. 131) give a timely reminder of the hazards of analgesic abuse, but their use of the term "phenacetin nephropathy" and their statements to the effect that it is only phenacetin which causes renal papillary necrosis cannot pass unchallenged. Although abuse of mixed analgesics is associated with papillary necrosis, it is most unlikely that phenacetin itself plays a major aetiological role. The salicylates and pyrazolones taken with it are much more likely to be the culprits. Let us re-examine the facts.

(1) Renal papillary necrosis has never been described in man in association with excessive consumption of phenacetin alone.

(2) Despite numerous determined efforts, it has proved virtually impossible to produce papillary lesions in experimental animals with phenacetin alone. Although Fordham *et al.*[1] succeeded in producing papillary lesions in three out of 39 rats, they had to work up to 3,000 mg./kg. of phenacetin daily. This dose actually exceeds the acute oral $L.D._{50}$. Compared with other drugs, phenacetin is remarkably non-toxic to the kidney.

(3) Phenacetin is invariably taken in combination with aspirin or pyrazolone derivatives such as antipyrine and amidopyrine. Unlike phenacetin, these anti-inflammatory drugs have consistently been shown to produce severe renal lesions including papillary necrosis in animals.[2-5]

(4) Renal papillary necrosis in man *has* been associated with heavy consumption of salicylates or pyrazolones.[6-9] There is also a very high incidence of non-obstructive pyelonephritis and papillary necrosis in patients with rheumatoid arthritis, a condition in which salicylates are usually given in high dosage.

I do not believe that phenacetin is entirely harmless, but I am very concerned that the current obsession with phenacetin will delay recognition of the greater nephrotoxicity of the drugs taken with it. Aspirin in particular seems to be a dangerous wolf in very familiar sheep's clothing. Its defenders point to the very high overall national consumption of aspirin as compared with phenacetin as an index of its safety. But analgesic abusers very rarely take plain aspirin. They prefer analgesic combinations (which until recently invariably contained phenacetin), believing them to be "better" or "stronger."

Dr. Koutsaimanis and Professor de Wardener are trying to have their cake and eat it in their interpretation of the experimental studies of phenacetin. They dismiss the negative findings as being "difficult to assess," and consider that the production of papillary necrosis in rats by combinations of phenacetin and aspirin is "not relevant to what happens in man." Their exclusive condemnation of phenacetin seems surprising. I take issue with Dr. Koutsaimanis and Professor de Wardener over another point. They quote me (and many other authors) incorrectly as having reported cases of "phenacetin nephritis." I have never seen a patient with this condition and neither, I suspect, have they. They also state that "phenacetin nephritis" was first described by Spühler and Zollinger.[10] In this article there is no mention of phenacetin (or acetophenetidin).—I am, etc.,

L. F. PRESCOTT.

University Department of Therapeutics,
Royal Infirmary,
Edinburgh.

REFERENCES

1 Fordham, C. C., Huffines, W. D., and Welt, L. G., *Annals of Internal Medicine*, 1965, **62**, 738.
2 Fellers, F. X., Pradilla, A., and Craig, J. M., in *Progress in Pyelonephritis*, ed. E. H. Kass, p. 337. Philadelphia, Davis, 1965.
3 Clausen, E., *Renal Damage Following Long-term Administration of Phenacetin and Acetylsalicylic Acid*. Copenhagen, Munksgaard, 1967.
4 Nanra, R. S., and Kincaid-Smith, P., *British Medical Journal*, 1970, **3**, 559.
5 Brown, D. M., and Hardy, T. L., *British Journal of Pharmacology and Chemotherapy*, 1968, **32**, 17.
6 Prescott, L. F., *Scottish Medical Journal*, 1969, **14**, 82.
7 Harvald, B., *American Journal of Medicine*, 1963, **35**, 481.
8 Ólafsson, Ó., Gudmundsson, K. R., and Brekkan, A., *Acta Medica Scandinavica*, 1966, **179**, 121.
9 Lawson, A. A. H., and Maclean, N., *Annals of the Rheumatic Diseases*, 1966, **25**, 441.
10 Spühler, O., and Zollinger, H. U., *Zeitschrift für klinische Medizin*, 1953, **151**, 1.

SIR,—Dr. K. G. Koutsaimanis and Professor H. E. de Wardener (17 October, p. 131) draw attention to apparent geographical differences in the incidence of renal papillary necrosis. Their estimate of the incidence of analgesic nephropathy in England and Wales is, however, much higher than that of Davies *et al.*,[1] who recently reviewed records of 18,866 adult necropsies in Liverpool covering a period of 5½ years. They found 31 cases of renal medullary necrosis, an incidence of 1·64 per 1,000 necropsies. The commonest aetiological factor was urinary tract obstruction or diabetes. Five patients had a history of analgesic abuse.

Phenacetin is a component of the analgesic compounds most commonly abused, but the question of whether it is phenacetin alone which produces nephropathy remains an open one. Work done recently in Australia and South Africa has emphasized the need for a closer examination of the effects of mixtures, particularly of aspirin, phenacetin, and caffeine. Abrahams and Levinson[2] in South Africa produced lesions of the renal papillae in rats fed with such mixtures. Kincaid-Smith and co-workers in Melbourne have reported a series of studies in which mixtures of analgesics, given at doses estimated to be equivalent to those consumed by some persons abusing analgesics, have produced renal damage. Drs. R. S. Nanra and P. Kincaid-Smith (5 September, p. 559) reported that nearly half their rats gavage-fed with aspirin and aspirin-containing mixtures developed papillary necrosis in 20 weeks. Aspirin alone produced necrosis in 36·8% of animals, whereas phenacetin in the same dose failed to cause any damage over 6 to 9 months. Brown and Hardy[3] studied the effects of large doses of phenacetin, phenazone, and amidopyrine on kidney function in rats. Phenazone caused a persistent celluria with evidence of slight kidney damage; amidopyrine caused papillary necrosis but little, if any, celluria. Phenacetin caused neither. Very little investigation appears to have been done into the possible part played by caffeine in the pathogenesis of analgesic nephropathy.

In including paracetamol in their recommendation that phenacetin be placed under stricter controls, the authors have not taken into account recent investigations into the metabolism of phenacetin. Paracetamol is indeed the principal metabolite in man but a number of others have now been identified.[4,5] There is some evidence that genetic factors may influence the route of metabolism.[6] Raaflaub and Dubach[7] have recently demonstrated a dose-dependent change in the pattern of metabolism of phenacetin in