Malignancy and the Small Intestinal Mucosa

SIR,—I was interested to read Dr. B. Creamer's article (5 December, p. 1435). My colleagues and I have studied, by jejunal biopsy, 16 cases of malignant disease not obviously affecting the small intestine and the results have been briefly reported.¹ Eight of the patients had leukaemia, three suffered from lymphosarcoma, and five had malignancy of the large bowel. No abnormality was found in any of the biopsy specimens.—I am, etc.,

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REFERENCE

- ¹ Girdwood, R. H., Dellipiani, A. W., McManus, J. P. A., and Delamore, I. W., *Scot. med. J.*, 1964, 9, 502.

Management of Respiratory Failure

SIR,—It is disappointing to find an authority as eminent as Dr. E. J. M. Campbell (21 November, p. 1328) seeming to suggest that Dr. Hutchison and his colleagues exaggerate the problems of respiratory failure. It is true that the majority of patients survive with low concentrations of oxygen, antibiotics, and a minimum of laboratory investigation but this is of no consolation and less help in the problem of a severely ill patient. If many hospitals cannot provide adequate laboratory support for the treatment of these patients, still more are unable to provide adequate facilities for treatment by tracheostomy and mechanical respiration—a method which has unsolved difficulties of its own.¹ This argument justified neither position but supports efforts like that of Hutchison and his colleagues to improve our understanding of the problems in the area of treatment that lies between these two extremes.

There seem to be three factors which are generally agreed to be of importance—namely, hypoxia, hypercapnia, and acidosis. Hypoxia was the first of these problems to receive attention, but we do not yet know at what critical level of oxygen pressure physiological mechanisms begin to fail. My own unpublished observations in 90 patients led me to accept tentatively an arterial P_{O_2} of 40 mm., as Dr. Campbell did, as the minimum "safe" level, but Hutchison and his co-workers' discussion of this question very clearly illustrates the point that this figure is purely arbitrary and based on an impression. Serious hypoxia produces a metabolic acidosis due to the accumulation of lactic acid. This is most clearly seen in circulatory arrest where the buffer base diminishes rapidly within minutes of the event. Patients with chronic hypercapnia develop a compensatory metabolic alkalosis, and the buffer base is normally elevated. This may often mean that a patient who has a normal buffer base when first seen in an exacerbation already has a concealed metabolic acidosis. Hypercapnia produces an acidosis with an additive effect to that of hypoxia. From some unpublished observations it seems that individuals respond differently at different times to the same high levels of CO_2 pressure and this appears to be explained on differences in the actual pH on the different occasions.

The metabolic component of the acidosis of respiratory failure has been largely ignored until the publication from Edinburgh. The next logical step in treatment seems to be a direct attack on this acidosis. Dr. Hutchison and his colleagues did this in their Case 7 but in view of their reference to Huckabee's work² it seems odd that they should have chosen to use sodium lactate in an attempt to buffer an acidosis due to lactic acid, and odder still that they should be disappointed with its poor effect. The blood buffer base that is most severely depleted in these situations is bicarbonate and it seems sensible to give this substance parenterally to make good the deficit.³ Relief of the acidosis in this way lightens the cortical depression and, like respiratory stimulants, improves ventilation, with a resulting steady fall in the PCO_2 .⁴

Experience of bicarbonate buffering in 10 patients with very severe respiratory acidosis suggests that this is a worth-while addition to treatment.⁵

In summary, the Edinburgh workers have made a valuable contribution to this difficult and confusing problem. I support their contention that frequent monitoring of the arterial P_{O_2} and acid-base studies is essential for adequate treatment in the patient with severe respiratory failure. I would urge them and Dr. Campbell, as well as any others interested in the problem, to try to assess the value of bicarbonate buffering when severe acidosis is present.—I am, etc.,

Glasgow W.2.

G. J. ADDIS.

REFERENCES

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² Huckabee, W. E., *J. clin. Invest.*, 1958, 37, 264.
³ Addis, G. J., Thomson, W. S. T., and Welch, J. D., *Lancet*, 1964, 2, 223.
⁴ Brooks, D. K., and Feldman, S. A., *Anaesthesia*, 1962, 17, 161.
⁵ Thomson, W. S. T., and Addis, G. J., *Proc. Assoc. clin. Biochem.*, in press.

Thyrotoxicosis in Childhood

SIR,—As the person who introduced serum protein-bound iodine estimations to the Staffordshire General Infirmary, I agree with Dr. F. J. Pick (21 November, p. 1329) when he says that this investigation should be more widely available. In a small way I have endeavoured to give a somewhat similar, though unofficial, service since I moved to the London area in 1963.

But I would disagree with him on two points in his letter. Firstly, the determination is of limited value in pregnancy. Whereas the occasional subnormal result suggests co-existent hypothyroidism, no significance can be attached to readings of from 7 to 10 $\mu g. %$, since figures in this range are commonplace in pregnancies uncomplicated by thyroid disease.

Secondly, after contrast radiography not all P.B.I. readings are so unusually high as to be obvious. The following are P.B.I. readings of blood specimens taken before, one month, and two months after cholecystography in three individuals with normal gall-bladder function.

Patient	Before (P.B.I.; $\mu g. %$)	1 Month After (P.B.I.; $\mu g. %$)	2 Months After (P.B.I.; $\mu g. %$)
1	4.7	8.4	5.1
2	4.7	14.3	7.4
3	4.7	9.9	6.6

Without knowledge of these cholecystograms having been carried out all three individuals after one month, and one individual after two months, would (biochemically) have been wrongly assessed as thyrotoxic.—I am, etc.,

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Aneurysm of the Hepatic Artery

SIR,—Aneurysms of the hepatic artery are rare.¹ They may produce a variety of effects which depends upon the situation of the aneurysm. This is an account of rupture of an aneurysm on the right branch of the hepatic artery.

A woman aged 77 was admitted because of severe intermittent pain in the back and abdomen which had been present for three days. Her urine had become dark in colour three weeks before admission when she had colicky pain in the right hypochondrium which lasted for seven days. She was jaundiced and febrile; the right hypochondrium and the lumbar regions were tender and Murphy's sign was positive. Abnormal findings on investigation were a plasma bilirubin of 8.8 mg./100 ml., serum alkaline phosphatase 25 King-Armstrong Units, and a serum glutamic pyruvic transaminase of 187 units.

On the morning on her fourth day in hospital she collapsed with a low blood-pressure and complained of severe upper abdominal pain. At laparotomy 3 litres of blood clot and fluid were found. This appeared to have arisen through a tear in the wall of a large subcapsular haematoma on the superior surface of the right lobe of the liver. The tear was stitched but bleeding continued until, finally, the hepatic artery was ligated. The gall-bladder was found to contain stones and pale green bile. Her blood-pressure fell again the next morning and she died.

Necropsy was performed 24 hours after death. The peritoneal cavity contained 600 ml. of fluid blood. The cut surface of the liver showed a fresh haematoma which was continuous with the subcapsular haematoma at the site of the tear. Adjacent to this an oval aneurysm (0.7 × 0.4 cm.) was found attached to the right main branch of the hepatic artery. Histologically the wall of the aneurysm consisted in some parts of arterial adventitia with blood clot separating it from the media. In other areas the wall consisted of full thickness of artery wall showing sharply defined areas of fibrinoid necrosis. There was moderate diffuse intimal fibroelastic thickening but no other evidence of arterial disease in this or adjacent vessels.

The rarity of aneurysms of the hepatic artery contrasts with the splenic artery, where aneurysms are common, and may partly be explained by the lack of surrounding support of the latter vessel.

In this case the histological appearance of segmental fibrinoid necrosis with adjacent, largely normal vessel wall, suggests that the artery first weakened, dilated, and then burst. The initiating factor is not clear. There was no evidence of inflammation in the wall of the aneurysm nor of medial damage in the surviving segments of artery.

The effects of rupture of such aneurysms are varied and often startling. Of Dwight and Ratcliffe's 70 cases 30 burst into the peritoneal cavity, and an almost equal number ruptured into the gall-bladder or bile ducts, producing intestinal haemorrhage. Patients often survive rupture of the aneurysm into the biliary system or gut, but

only one survivor has been reported from haemorrhage into the peritoneal cavity.

Several surgical operations have been tried for this condition,³ such as excision of the aneurysm followed either by end-to-end suture of the hepatic artery or by anastomosis of the proximal end of the splenic artery (after splenectomy) with the distal end of the hepatic artery.

We are grateful to Mr. J. Withycombe for permission to publish this case.

—We are, etc.,

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REFERENCES

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Atypical Responses to Nortriptyline

SIR,—We have now observed two patients suffering from anxiety-depressive reactions who, having been given nortriptyline medication, have rapidly developed acutely depressed and tense states with pressing ruminations on death in general and suicide in particular.

In the first case the nortriptyline was prescribed by the family doctor, with reassurance, and the patient was afterwards admitted to hospital. Cessation of nortriptyline medication produced rapid improvement. In the other case medication was changed from amitriptyline, and after an interval of five days nortriptyline (Aventyl) was prescribed, and a rapid onset of an intensely painful depressive swing with morbid preoccupation with death and suicide occurred. After her family doctor had returned her to amitriptyline medication these symptoms ceased abruptly.

The nortriptyline in both cases was prescribed with encouragement, and both doctors and patients expected a good outcome. It seems that these symptoms may well be atypical physiological responses to the drug.—We are, etc.,

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P. S. IRELAND.

Ampicillin for Typhoid Carriers

SIR,—Dr. A. B. Christie (3 October, p. 876) may be interested in our recent experiences with a typhoid carrier receiving ampicillin prior to cholecystectomy.

This lady, who had positive faecal cultures and a non-functioning gallbladder containing numerous calculi, received ampicillin 1 g. 6-hourly for three weeks before operation. During this period, her faecal cultures became negative and her serum ampicillin level was observed to be 5 µg./ml., 285 minutes after the last oral dose. A specimen of duodenal aspirate contained ampicillin in a concentration of 4 µg./ml. The minimal inhibitory concentration of ampicillin for the patient's strain of *Salmonella typhi* was 0.6 µg./ml. Bile from the excised gall-bladder contained ampicillin in a concentration of 16 µg./ml., and routine cultures of this and crushed calculi were negative. When these were repeated in the presence of 15,000 Levy units of penicillinase, *S. typhi* was recovered from all samples of bile and from numerous calculi. In an attempt to explore the effect of ampicillin on the patient's organism *in vitro*, 1.2×10^8 viable cells were added to sterile broth containing 20 µg./ml. ampicillin in a manner similar to that described

by Rolinson and Stevens.¹ At three hours the viable count was 7×10^4 , at seven hours 5×10^4 , and at twenty-four hours 3×10^4 .

This observation, together with the recovery of viable typhoid bacilli from bile containing high concentrations of ampicillin (and not merely from calculi), confirms the need for caution in assessing the value of this antibiotic in the treatment of chronic carriers.—I am, etc.,

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REFERENCE

- ¹ Rolinson, G. N., and Stevens, S., *Brit. med. J.*, 1961, 2, 191.

Treatment of Acute Poisoning

SIR,—Your recent article on Treatment of Acute Poisoning (10 October, p. 927) considers various measures to remove poison which has gained access to the body. There is considerable experimental evidence to suggest that spontaneous emesis is more effective in the removal of poison than gastric lavage.¹ The considerable experience with poisoning at the Boston Poison Information Center as well as elsewhere has convinced us that Syrup of Ipecac. is the most effective means of producing spontaneous emesis.² We now recommend that when the substance ingested is not a corrosive, hydrocarbon, or if the patient is not unconscious or convulsing, he be given 15 ml. of Syrup of Ipecac. (one tablespoon). The patient then is given something to drink, and vomiting occurs in the vast majority of cases within 15 to 20 minutes. This treatment can be given in the home if the doctor has prescribed a small bottle of Syrup of Ipecac. for the medicine cabinet, and by its prescription, we hope, has practised accident prevention. It is also our experience, and that reported recently by Dr. William Robertson, that mechanical attempts to produce vomiting are generally unsuccessful.

We also agree with your writer that emesis should be induced even if the substance was ingested as long as eight hours previously.—I am, etc.,

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REFERENCES

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- ² Robertson, W. O., *Amer. J. Dis. Child.*, 1962, 103, 136.

Safety with Parathion

SIR,—Parathion, an organophosphorus insecticide, has been used for the control of *Quelea quelea quelea* (the Sudan Dioch) for a number of years. It is important not only to have well-designed safety precautions but also to ensure that they are observed.

An anti-quelea campaign was started in the north-eastern area of Northern Nigeria using aerial spraying of parathion. The parathion used was 50% technical parathion diluted with diesel oil 1:1. Six weeks after the spraying started the aircraft crashed and the pilot was severely contaminated with parathion. The pilot was found within 20 minutes of the crash, and by that time he had stripped off his clothes and had washed himself in a small stream. One ampoule of atropine (1/100 gr.—0.65 mg.) was given

intramuscularly at the time he arrived at the base camp. The pulse rate at this time was 45 per minute. The pilot was apparently normal and made no complaint. He talked normally with the engineer about the crash and had coffee and his supper. Three hours after the crash he complained of pain in the eyes and some disturbance of vision and very soon after this began to perspire heavily and to vomit. Within 40 minutes the pilot began to have convulsions. His pulse was reported at this time as 30 per minute. His breathing stopped and artificial respiration was started and atropine (1/100 gr.) was given by intramuscular injection. The convulsions and paralysis of respiration continued and the pilot died five hours after the crash in spite of continuous artificial respiration. It was recorded that there was an excessive production of saliva and bronchial secretions at the time of the onset of the convulsions.

The safety regulations laid down that full protective clothing be worn by the pilot and by those handling insecticide and laid down the precautions to be taken in handling. The pilot was not allowed to fly through the insecticide spray mist on turning and was required to have eye protection (goggles or eye shield), and nose and throat protection from a mask made from several layers of gauze which were changed every second flying hour. It was further laid down that cholinesterase examinations for all staff handling or coming into contact in any way with parathion be made every two weeks, from four weeks before the start of the spraying operations to four weeks after the cessation of the spraying operations.

After the accident it was found that the standing orders had been followed with the exception of that part of the standing orders concerning the cholinesterase examinations. Only one cholinesterase examination was done and that four weeks after the start of the spraying and ten days before the fatal accident, when he was found to have a cholinesterase level of 50%, and 62.5% on retesting. If a level of between 75% and 50% was recorded and confirmed on retesting, the standing instructions laid down that overexposure was probable and suspension from work for two weeks should be made.

It seems likely that the crash was due to a minor acute intoxication with parathion superimposed on a chronic intoxication and that the resulting incoordination was responsible for the crash. The treatment given was not intensive enough and the dose of atropine was negligible. Organophosphorus insecticides are, like all pesticides, potentially dangerous if misused or handled carelessly. Some of this group, especially parathion, are extremely poisonous and are liable to be lethal if mishandled. Medical care should be immediately available—this is important in a field campaign in areas far away from a hospital or doctor. If poisoning occurs treatment must be prompt: the two specific antidotes, atropine and an oxime (such as pralidoxime) must be given and repeated until symptoms cease. The patient must be observed carefully for 48 hours. Evacuation by road is to be avoided until recovery is assured: this implies the ability for treatment to be completed on the spot. With the necessary drugs and a simple machine for achieving passive ventilation of the lungs and the requisite professional skill, this is not too difficult.

In this present case the degree of contamination was such as likely to be lethal in any case, except possibly if skilled professional attention had been available on the spot. However, inattention to standing orders with regard to the routine cholinesterase examinations occurred, and this was very probably a contributory factor. The practice of preventive medicine advances as