TABLE I.—Case 2. Investigations

	Day 1	Day 2	Day 3	Day 4	Day 6	Day 8	Day 10	Day 18
Haemoglobin (g./100 ml.)	16.2			14.6			13.9	14.6
W.B.C./c.mm.	6,600			7,200			9,400	7,400
E.S.R.	2			2			6	6
Bilirubin (mg./100 ml.)		3.2	3.5	3.2	2.8	1.6	1.3	0.8
Alk. Phos. (K. A. units)		5.5	8.0	8.0	8.5	8.0	8.0	5.5
Thymol turbidity		0.5	1.0	1.0	1.0	1.8	4.5	0.8
S.G.O.T. (units/ml.)		840	2,000+	2,000+	168	129	70	20
Prothrombin activity (% average normal)		30	26	12	40	56	56	56

130/90. The urine contained 0.24 g./100 ml. protein, and the deposit showed a few leucocytes and large numbers of red cells. Platelets were 35,000/cu. mm., plasma urea 137 mEq/l.; bilirubin 5.5 mg./100 ml.; alkaline phosphatase 17 K.A. units; thymol turbidity 1.8. The plasma *p*-aminophenol level was not estimated.

On the third day he was drowsy and confused with facial oedema and conjunctival haemorrhages. The blood pressure fell terminally, being briefly maintained by the use of mephentermine, and the patient died of pulmonary oedema 80 hours after ingesting the tablets.

Case 2.—A 37-year-old male ingested 50 paracetamol tablets together with 200 mg. amylobarbitone sodium and a tot of whisky. He was admitted eight hours later and refused gastric lavage. He had received no other drugs. There was a confirmed history of drinking bouts but none of liver or kidney disease.

He appeared well and afebrile. The pulse was 90 and the blood pressure 145/90. There was no icterus, and the liver was not enlarged or tender. A diuresis was instituted using frusemide 40 mg. and 10% mannitol by intravenous infusion. A mean diuresis of 450 ml./hour was sustained for 60 hours.

Three hours after admission he complained of upper abdominal pain and vomited altered blood. On the second day he was icteric and drowsy. The liver was not enlarged, but there was excess urobilinogen in the urine. The patient complained of persistent epigastric discomfort and extreme lassitude, but these remitted progressively. He was mobilized on day 12 and discharged the 18th day after ingesting the tablets.

The plasma urea rose abruptly on the fourth day to 77 mg./100 ml., but otherwise the urea and electrolyte values were within the normal range throughout. The results of investigations are given in the Table.

This patient was reassessed four months later, at which time he was well. All liver function tests were repeated and showed only a lowered prothrombin activity at 56% of average normal. Bromsulphalein retention and liver biopsy were normal. Intravenous pycnography and glucose tolerance curve were performed with normal results.

Post-mortem Findings.—Case 1: The lungs displayed marked pulmonary oedema. The liver was congested, and it contained multiple areas of yellowish tissue which, on section, showed acute centrilobular necrosis extending through the mid zone. There was no evidence of a cholestatic lesion. The kidneys were soft, with pale, swollen cortices. Sections showed tubule degeneration seen maximally in the proximal convoluted tubules. There was some cast formation also seen in the collecting tubules. The features seen represent acute tubular necrosis associated with massive liver necrosis.

The necropsy findings are similar to those recorded by Davidson and Eastham.² Other than the small amount of alcohol taken by the survivor, neither case described here had received drugs known to have hepatotoxic effects. A direct toxic effect of paracetamol on the liver is inferred.

Prescott⁴ records significant increases in human tubule cell excretion rates following paracetamol ingestion, and the rat experiments of Boyd and Berczky¹ also revealed

acute toxic effects on the tubules. A direct toxic effect of paracetamol on the renal tubules cannot be dismissed.

The clinical features of both cases during the first 48 hours are very similar. The danger of liver damage occurring after a symptom-free interval following self-poisoning with paracetamol requires that observation be maintained for at least this length of time. The development of upper abdominal pain without pyrexia should be regarded with suspicion. Limited experience suggests that a diuresis induced by intravenous infusion is more hazardous in paracetamol poisoning, since acute tubular necrosis may occur without preceding hypotension (Case 1).

I wish to thank Dr. F. I. Lee and Dr. I. Weinbren for permission to publish the details of these cases. Dr. S. M. Murray kindly assisted with detailed reports on the pathological material of Case 1.

—I am, etc.,

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Another Side-effect of the "Pill" ?

SIR,—Dr. D. N. Barber (9 November, p. 390) refers to his earliest report¹ of the effect of an oral contraceptive on tissues supporting the teeth, and relates this action to the relaxation of the pelvic joints during pregnancy. In this connexion I wish to report an instance in which there appeared to be suggestive evidence of association of a drug of this sort with a very unusual type of ligament relaxation.

The patient, a 31-year-old lady, came with the complaint that when she sat up, or turned over in bed, or sneezed she could both feel and hear something "cracking in the upper part of the front of my chest." Moderate, localized, momentary pain was said to be associated with this sensation. Both physical and x-ray examinations revealed no pertinent findings other than considerable tenderness with crepitation and abnormal mobility at the junction of the manubrium with the body of the sternum—that is, a subluxation at this site.

The patient stated that she had been a regular user of the contraceptive pill during the past 18 months, but that the symptoms of which she complained had been present for only about two months. She was ordered to discontinue use of the pill but to make no other alterations in her way of life. Now, after about seven weeks, she is symptom-free and will soon be returned to contraceptive medication to determine whether subluxation will reappear.

The relaxation of the pelvic joints that occurs during normal human pregnancy is alleged to be associated with appearance in the blood stream of a polypeptide hormone, relaxin, secreted by the corpus luteum. This relaxin, however, has no associated oestrogenic or progestational actions, which therefore leaves us without explanation for whatever ligament-relaxing action the pill may be found to have.—I am, etc.,

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Coronary Disease and Personality

SIR,—Your leading article on coronary disease and competitiveness (January 4, p. 1) interested me very much. It shows that the psychosomatic aspect of coronary disease is still considered worthy of a large scale investigation. There must be a physical link between the "coronary personality," distinguished by great ambition, compulsive striving, and a drive for recognition, and the coronary arteries, and this link through the mediation of catecholamines may be hypertension.

Established hypertension is often found in patients who develop coronary thrombosis and is accepted as a predisposing cause. Labile hypertension may not be considered, as the basal blood pressure may give a misleading impression of normality. Nervous strain, anxiety and tension, fear, and repressed aggression will often produce quite marked hypertension, which will subside once the offending strain is removed. Modern, civilized, competitive existence with its overcrowding, persistent noise, constant mental stimulation and aggravation, traffic conditions, television viewing of violence, and of exciting political and sporting events, will all contribute to this considerable variation of blood pressure, which in some patients will remain permanently raised. It has been suggested that this latter tendency is due to high resting cardiac output and a normal peripheral resistance progressing to the more usual situation of a raised peripheral resistance and a cardiac output in the normal range. The idea that exercise protects from myocardial infarction was suggested by the work done by Morris and others on London bus drivers and conductors.¹ However, the greater incidence of sudden deaths and myocardial infarction in bus drivers could have been mediated through a labile hypertension produced by driving constantly in heavy London traffic.

Fluctuating hypertensive filling of the atherosclerotic coronary vessels in a usually normotensive or hypertensive person may cause the trauma to the arterial wall which sets off changes leading to thrombus formation. This mechanical intimal injury may lead to intramural or intimal haemorrhage with rupture into the lumen, the break in the artery then being the site of the thrombus formation, and increased coagulability of the blood being an additional factor; or the artery may become occluded by an intramural haematoma. This may occur particularly if there is an inherited inferiority of the vascular structure. Mechanical intimal injury may also be considered as a primary change which predisposes to the deposition of lipids, the rate and extent of

which depending to some degree on the plasma lipid level. Hypertension therefore accelerates and intensifies the atherosclerotic process. It is of significance that personality may also affect cholesterol and lipid metabolism, as it has been shown that emotional stress and activation can cause a rise in serum lipids.^{2,6}

A number of measures have been adopted to counteract this increasing incidence of coronary thrombosis. Reduction in weight and smoking are obvious, but the other measures such as anticoagulant or fibrinolytic therapy and the reduction of blood lipids by dietary or drug therapy have so far given inconclusive though often beneficial results. Early reduction of a raised blood pressure, labile or sustained, should therefore lower the incidence of coronary thrombosis. Propranolol may be used, as it diminishes cardiac output and pulse rate. The other hypotensive agents available today have already proved effective in preventing the abnormal rise in blood pressure in people exposed to stressful situations. Sedation in adequate doses to achieve the same result would have to be too powerful.

It is possible that certain predisposed persons have to pay a price in the form of medication for keeping up with their environment, which causes coronary thrombosis to assume almost epidemic proportions in the western world.—I am, etc.,

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Unusual Case of Emphysema

SIR,—A Royal Naval diver, at the outset of a recent trials series, sustained accidental damage to his left circumorbital region, on the night before doing an air dive to 300 feet in a compression chamber. Before diving he was sent to me, and as the injury was only minimal I passed him fit to dive. Four days previously he had had mild coryza, which had since cleared up. The chamber was compressed to the equivalent of 300 feet of sea water and the diver had no trouble with the descent. After 15 minutes at 300 feet the ascent to the first stop at 100 feet was begun. At about 260 feet the diver reported a sharp pain in his left cheek which was then observed by all present to be gradually swelling as the pressure was reduced. I entered the chamber at 70 feet to assess his condition.

On examination he had marked swelling of his left cheek and eyelids, and palpable crepitations. There being nothing to gain by recompressing him, I aspirated what air I could as he continued the decompression breathing oxygen. Using a 10 ml. syringe with a 21 gauge, 1½ in. (3.75 cm.) needle, I aspirated from a point about ¼ in. beyond the lateral margin of the orbit, the needle entering obliquely under the skin to about ¾ in. In spite of the withdrawal of 5 ml. of air at 50 feet and a further 5 ml. at 20 feet,

the swelling increased until it covered the entire left side of his face from neck to temple. At the surface the pain had gone and his condition was as shown in the photographs. His discomfort was further relieved by the aspiration of another 8 ml. of air. It was apparent that he must have sustained a minute fracture into his maxillary sinus, the ostium of which was presumably sufficiently obstructed by the residual inflammation of his recent coryza for the air to be forced out through the fracture instead of draining through the ostium. Regrettably two series of x-rays failed to reveal the location of the fracture. Later the same day he reported a few specks of blood in his nasal secretions.

During the following five days the swelling gradually disappeared, leaving only the bruising of his original injury. He passed from my care shortly after, and was returned to diving about six weeks later with no recurrence.

A similar case of swelling of the right cheek and side of forehead, accompanied by pain over the maxillary sinus, is reported in a civilian diver in July 1968, following a dive to 100 feet. Again there was no demonstrable maxillary sinus fracture on x-ray (Personal communication from J. M. Young, Surgeon Lieutenant Commander, Royal Naval Physiological Laboratory, Alverstoke.)—I am, etc.,

D. R. LEITCH.

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Delayed Neurological Effects of Electrical Accidents

SIR,—Your leading article (18 January, p. 135) prompts me to report a case of electrical injury of interest because of the neurological sequelae and the initial presentation in coma—a cause rarely listed in the differential diagnosis of the unconscious patient.

A 61-year-old man was admitted having been found unconscious in the engine-room of his houseboat. On examination he was stuporous, but responded to painful stimuli. The upper limb reflexes were absent, with marked spasticity in the right arm. There were no other abnormal neurological signs. There was a reddened area of skin over the left side of the lower back and a small superficial burn over the left elbow, but no other signs of external injury. Temperature 98.4° F. (32° C.), B.P. 130/80, pulse 80 per minute, sinus rhythm, heart sounds normal, no

murmurs. Examination of the chest and abdomen was normal. Lumbar puncture revealed clear C.S.F. under normal pressure with less than two leucocytes cu. mm., protein 50 mg./100 ml., sterile on culture, C.S.F. and serum W.R. negative.

His conscious level improved over the next 12 hours, but he remained disorientated and confused for a further 24 hours. During this time he complained of severe muscle spasm in the back and lower limbs. Forty-eight hours after the initial episode he was noted to have marked weakness in both arms, mainly involving the long extensors of the wrists and fingers. There was sensory blunting to touch and pinprick over the lateral aspects of the right forearm and hand. The upper limb reflexes remained absent. There were no abnormal signs in the lower limbs or cranial nerves. Electromyography confirmed the weakness was of neural rather than muscular origin. A normal conduction velocity in the right ulnar nerve supported the clinical diagnosis of a spinal cord and not a peripheral nerve lesion.

The patient recalled later that his last memory before the episode was of going to turn off the 240-volt A.C. mains supply. The electrical system was examined subsequently and found faulty. During the next six weeks the muscle weakness gradually improved, though he still experienced difficulty in fine movements of the hands. The sensory loss resolved except for impairment to touch and pinprick in the right index finger.

I should like to thank Dr. S. R. F. Whittaker for his permission to report this case.

—I am, etc.,

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Draining Loop Colostomy

SIR,—In his letter (18 January, p. 187) Mr. W. M. Keynes refers to the obsolescence of Paul's tubing and this I agree. The time-honoured glass rod can also be eliminated by the simple device of making the skin incision to accommodate the loop not linear but in V-shape. The apex of the V is drawn under the loop and the edges of the flap are sutured back around the limbs of the colostomy. This skin bridge supports the loop and thus disposes of the discomfort of a glass rod; moreover, the recession of the loop into the abdominal wall, a complication which sometimes occurs after removal of a glass rod, cannot take place.—I am, etc.,

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BRYAN N. BROOKE.

Management of Acute Salicylate Poisoning

SIR,—Dr. R. C. Mac Keith's letter (18 January, p. 185) suggests that a blood pH done in the casualty department would probably be life-saving in salicylate poisoning. Two recent authorities^{1,2} state that the change in the pH may be minimal and may not reflect accurately the degree of acidosis present in severe salicylate poisoning.

The most important investigation in salicylate poisoning is a rapid estimation of the plasma salicylate level. There are two simple sideroom techniques available now^{3,4} which allow such an estimation to be obtained