using larger numbers of patients, and with comprehensive laboratory coverage.

My thanks are due to Dr. P. J. Sequeira and Dr. J. Tobin for the virus studies, Dr. E. Busill Jones for clinical help, and Dr. A. W. Galbraith, of Geigy (U.K.) Limited Pharmaceuticals Division, for supplying the drug and placebo.

—I am, etc.,

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Withington Hospital,
Manchester 20.

REFERENCE

1 Sabin, A. B., *J. Amer. med. Ass.*, 1967, **200**, 943.

Plasminogen-activator-producing Tumour

SIR,—The identification by Dr. J. F. Davidson and others (11 January, p. 88) of a plasminogen-activator-producing tumour is fascinating. However, on the evidence produced I am doubtful about two of the conclusions.

There is no evidence that the tumour was rapidly growing—that is, multiplying, extending, and invading during the time that it was producing plasminogen-activator. The proximal extension of the swelling revealed only serosanguineous material which most likely reflects an accumulation of tumour fluid. It is conceivable, and perhaps likely, if one preserves the view that tumours may require a fibrin network as a matrix for growth, that this secondary tumour with its demonstrated thromboplastic activity grew rapidly first and then produced plasminogen-activator.

It cannot be concluded that a rare tumour of lung showed pathological plasminogen-activator production. This property can only be ascribed to the peripheral secondary carcinoma, presumably arising from a lung primary. No assessment is described of the lung primary's activity, and it may be inferred that the primary did not in fact produce plasminogen-activator, for, although haemorrhagic, it did not bleed. Equally, the other secondary tumours, similarly haemorrhagic, did not bleed.

It would seem worth while to comment that lung tissue is known to contain substantial amounts of tissue plasminogen-activator.[1] Malignant cells arising from the lung may therefore have a potential for producing large quantities of plasminogen-activator. The rarity in this report may be the circumstances under which a secondary from a giant-cell carcinoma of lung showed such an activity.

—I am, etc.,

Beaconsfield, Bucks. A. J. JOUHAR.

REFERENCE

1 von Kaulla, K. N., *Chemistry of Thrombolysis : Human Fibrinolytic Enzymes*, 1963. Springfield, Illinois.

Treatment and Prevention of Poisoning

SIR,—I was interested to read your leading article (28 December, p. 787) concerning the treatment and prevention of poisoning.

Approximately 75% of adults who have ingested poison present in hospital within six hours.[1] The same percentage of children present within two hours. If we subtract the length of time an ambulance takes to bring the patient to hospital then the earliest time that treatment may be undertaken is even shorter. An important early stage in the treatment of poisoning is getting the poison out.[2] Karlsson and Norén[3] have successfully used dilute solutions of copper sulphate as an emetic in poisoned children. Ninety-eight per cent. of 100 children vomited within 14 minutes. Twenty-eight per cent. vomited twice. They found copper sulphate safe and more reliable than ipecacuanha.

In most British hospitals it is the custom for the nursing staff to perform lavage.[1] Inducing emesis in a conscious patient is probably a less hazardous procedure. About 20% of adults are admitted to hospital unconscious ; children are rarely unconscious on admission. If suitable packs of dilute copper sulphate solution were carried as part of the standard equipment in ambulances, these could be administered to co-operative conscious patients by ambulance personnel, as soon as the patient was collected. With this arrangement, by the time the patients arrived at hospital they would probably have vomited. It would be necessary to carry a suitable receptacle in the ambulance.

With the increasing number of cases of ingested poison I wonder will the day come when as well as the obstetric flying squad and coronary ambulance we may have the "overdose" ambulance ? Or will we eventually evolve a system where there is a fleet of multipurpose ambulances equipped to start the early treatment of patients suffering from any acute medical emergency endangering life ?—I am, etc.,

MICHAEL BURKE.

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REFERENCES

1 Burke, M., *Practitioner*, 1968, **201**, 786.
2 Matthew, H., Mackintosh, T. F., Tompsett, S. L., and Cameron, J. C., *Brit. med. J.*, 1966, **1**, 1333.
3 Karlsson, B., and Norén, L., *Acta paediat. scand.*, 1965, **54**, 331.

Cerebral Haemodynamics and Metabolism in Hypnosis

SIR,—We have read with interest the articles on the value of the use of hypnosis in medicine and on the neurophysiological interpretations of the hypnotic state (12 October, pp. 67 and 71).

We have carried out a study of cerebral haemodynamics and metabolism in five normal subjects in deep hypnotic trance with analgesia and amnesia at the arousal. The study included the determination of cerebral blood flow, cerebrovascular resistances, and cerebral metabolic rate of oxygen, according to the methods previously described.[1] In comparison with a group of normal but alert subjects it was found that the hypnotic state does not cause any modification of the examined parameters (see Table). However, we wish to stress the fact that during the hypnotic trance the values of the standard deviation for each of the above-mentioned parameters were clearly below the levels of the normal and alert subjects.

Cerebral Haemodynamics and Metabolism in Normal Subjects (Mean values ±S.D.)

	No. of Cases	Cerebral Blood Flow (ml./100 g. Tissue/min.)	Cerebrovascular Resistances (mm. Hg/ml./100 g./min.)	Cerebral Metabolic Rate of O_2 (ml./100 g. Tissue/min.)
Alert subjects	6	54·9 ±10·8	1·90 ±0·49	3·68 ±0·77
Hypnotized subjects	5	51·0 ±4·7	2·08 ±0·31	3·57 ±0·59

We think that the difference which resulted between the hypnotized and the alert subjects may be due to a state of anxiety and fear caused by the method of examination used ; as in fact this state was present only in the alert subjects, even if clinically not evident.

This work is part of a wider investigation, and a full report is in preparation.

—We are, etc.,

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F. GRANONE.

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e Metodologia Clinica (II),
Milan University, Italy.

REFERENCE

1 Della Porta, P., Maiolo, A. T., Negri, V. U., and Rossella, E., *Metabolism*, 1964, **13**, 131.

C.S.F. Rhinorrhoea

SIR,—Your leading article on C.S.F. rhinorrhoea (18 February, p. 137) contains the following: ". . . Galen thought that the C.S.F. was formed by the brain, stored in the ventricles, and normally excreted through the nose."

It is now generally accepted that the C.S.F. was never described in antiquity and in fact the first certain reference to it was made by Berengario da Carpi as late as 1521. The first clear description of it was given by another Italian anatomist, Massa, 15 years later.[1] Galen was in fact referring to the animal spirits or vapours of the soul, which were thought to be formed in the vascular network said to be present in man at the base of the brain—the *rete mirabile*—but found in fact only in ungulates. The resulting waste products were excreted through the pituitary fossa and the olfactory plate if fluid, and, if gaseous, through the cranial sutures. There is, however, no suggestion whatever that the former may have been C.S.F.

I am sure that you would wish to avoid inaccuracies in scientific data submitted to your journal, and I see no reason why historical information should not be equally precise.

—I am, etc.,

EDWIN CLARKE.

Sub-Department of the History
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University College,
London W.C.1.

REFERENCE

1 Clarke, E., and O'Malley, C. D., *The Human Brain and Spinal Cord*. University of California Press, Berkeley, California. 1968.

SIR,—The leading article on C.S.F. rhinorrhoea (18 January, p. 137) was very interesting because it reminded the readers of an unusual clinical problem. We have much to learn about the anatomy of the roof of the nose, as well as the abnormalities. A patient of mine suffering from spontaneous C.S.F. rhinorrhoea was found to have a congenital fistula between his subarachnoid space and the roof of one of his frontal sinuses. The concept of a focal atrophy of the cribriform plate is also interesting. It would explain why a patient develops meningitis after removal of

nasal polypi. The thin bony walls of the ethmoidal labyrinth are destroyed by chronic sinusitis. This allows infection through the cribriform plate.

I would, however, disagree with the opinion that meningitis rarely occurs in patients with spontaneous C.S.F. rhinorrhoea. I have diagnosed this condition in three of my patients. Two of them developed meningitis. The diagnosis is not difficult provided one bears it in mind. A watery nasal discharge is a very common symptom in an otolaryngological clinic. It is usually due to allergic rhinitis or chronic rhinitis due to nose drops. In C.S.F. rhinorrhoea a sample of the fluid will contain glucose. This never happens in allergic rhinitis. A rapid test is to insert a Clinitest stick into each nostril. It will confirm the presence of glucose and show the side of the C.S.F. leak.

Tomography does not help to confirm a bony defect in the cribriform plate. The area is difficult to see clearly by *x*-rays. Looking for radioactive isotopes in the nose after they have been put into the lumbar theca is an important development. It may help us to diagnose this condition more often.—I am, etc.,

J. SIEGLER.

Liverpool.

Miliary Tuberculosis in a Nonagenarian

SIR,—In old age tuberculosis usually occurs as a chronic pulmonary infection, often indolent enough for grandchildren to catch the disease unaware. Even in "open" cases, symptoms and fever can be absent because age slows metabolism and defences remain firm. Miliary tuberculosis is now uncommon. Fifteen deaths from the disease were notified in 1962–66, with 26 cases in the preceding five years (General Register Office, 1967). But it should stay high in the list of differential diagnoses for pyrexia of unknown origin. We record this case as a reminder that miliary tuberculosis may occur at any age.

A young-looking 93-year-old woman had night sweats and felt tired for a month. She had no cough, breathlessness, headache, anorexia, dysuria, or ankle swelling. She had fever, without rigors, nine days before admission, and routine blood agglutination tests were negative. Her past health was excellent but her brother died of Addison's disease. She looked well, her temperature was 38.4°C., the pulse was regular at 76, and blood pressure 190/70 mm. Hg. Her skin, retinae, and lungs were clinically normal and the spleen and lymph glands were not enlarged. A soft apical systolic murmur was heard in her heart, and a provisional diagnosis of bacterial endocarditis was made. The haemoglobin was 11.83 g./100 ml., W.B.C. 8,000 per cm., E.S.R. 32 mm. Three blood cultures were sterile, repeated blood agglutination and sedimentation tests were normal, and the urine showed no abnormality. Stool cultures were negative and the chest *x*-ray was normal. A barium meal and liver function tests were normal and L.E. tests negative. Another mid-stream urine showed 60 mg. of protein, many leucocytes, and a growth of paracolon bacteria. Neither a course of ampicillin nor nitrofurantoin altered the fever. A chest *x*-ray two weeks later was again normal, but an abdominal *x*-ray showed a calcified gland. The hectic fever slowly subsided, the patient became doubly incontinent and died. At post-mortem a pulmonary embolus accounted for her death, and tuberculous ulceration of the lower ileum, with generalized miliary tuberculosis, was found. Calcified mesenteric glands were present and the organism was bovine in type. The infection was considered to be a recrudescence of an old intestinal infection.

This woman was not "geriatric" until her fatal febrile illness. A tuberculous focus presumably broke into the circulation after being quiescent for perhaps 80 years. A similar case was seen 18 years ago where radiotherapy appeared to have caused the dissemination. The patient, aged 76, had destruction of one lumbar vertebra and no primary neoplasm was discovered. After radiotherapy, given for pain, she developed a hectic fever and later miliary lesions in the optic fundi.[1] In the first month of this disease chest *x*-ray changes are often absent, as in these two cases. One of us (R.W.A.) had diagnosed, at post mortem, three other cases, aged 60, 68, and 83, in the last four years. The Registrar General's figures are bound to be an underestimate of the true incidence.

The diagnosis is made from the sputum, stool, or urine; occasionally biopsy of the marrow, liver, or pleura is necessary. Acid-fast staining and cultures for tuberculosis are essential in the old as in the prime of life.

We thank Dr. G. A. MacGregor for permission to publish this case.

—We are, etc.,

R. MILTON.
R. P. YADAVA.
R. W. AINSWORTH.

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REFERENCE

1 Macgregor, G. A., 1968, Personal communication.

Gastrointestinal Haemorrhage and Aspirin

SIR,—Dr. H. B. Valman and his associates in their paper on gastrointestinal haemorrhage and aspirin (14 December, p. 661) make the provocative statement, "Though the mechanism of bleeding after aspirin ingestion is still obscure some facts are known," but unfortunately they fail to disclose what some of the facts are. Since I have been interested in the problem of haemorrhage in surgical procedures since 1937, when I proposed the use of vitamin K for the treatment of cholaemic bleeding,[1] and have given considerable thought and effort to the bleeding problem, I should like to make a few comments on aspirin.

This drug has a systemic vascular effect which can be measured by the prolongation of the Duke bleeding time, which I have utilized for developing the aspirin tolerance test.[2] The action of aspirin is attributable to its acetyl linkage, since sodium salicylate has no such effect. Aspirin appears to act by preventing the vascular contraction after mechanical injury of the micro-circulation. Many normal subjects have a slight but distinct increase of the bleeding time two hours following the ingestion of 0·65 g. of aspirin. It is likely that it is this group which shows the occult gastrointestinal bleeding from aspirin. In the Minot–von Willebrand syndrome the bleeding time is significantly prolonged by aspirin, and these subjects have the more severe gastrointestinal bleeding from the drug.

The two conditions that should always be considered in idiopathic gastrointestinal haemorrhage are the Minot–von Willebrand syndrome and telangiectasia. The first disease is readily detectable even in the mild form by the aspirin tolerance test. Telangiectasia, which is equally as common, is likely to be overlooked because no specific laboratory tests are available and the diagnosis must depend on a careful physical examination, skill in recognizing the skin lesions, and on the hereditary history. When the diagnosis of these two diseases is established, aspirin as a factor in bleeding becomes more understandable.—I am, etc.,

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REFERENCES

1 Quick, A. J., *Amer. J. Physiol.*, 1937, **118**, 260.
2 Quick, A. J., *Amer. J. clin. Path.*, 1967, **47**, 459.

Motorway Madness

SIR,—In reading the newspaper reports of the dreadful pile-ups on the M1 and M4 in fog recently, two neglected explanations occurred to me:

(1) *Relative sensory deprivation.*—Safe motoring depends on the driver perceiving and acting upon a stream of visual and auditory clues. In thick fog a motorist is almost in the situation of a solitary astronaut in a blacked-out space capsule. In such conditions he may make disastrous errors of judgement. He may even begin to hallucinate or have delusions if his sensory input falls below a certain critical level.

(2) *Toxic effects of petrochemical fumes trapped at low level in fog.*—The central nervous system is very sensitive to petrochemical intoxication. Under certain atmospheric conditions the petrochemical content of fog at ground level in traffic may be high enough to affect perception and judgement adversely.

Taken together, these two factors could account for normally rational, careful drivers blinding along at 70 m.p.h. into almost certain destruction. Two remedies might help: infra-red lamps and sensing devices on all cars, and respirators for motorists to wear in fog.—I am, etc.,

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Management of Acute Salicylate Poisoning

SIR,—I read with interest the articles on the treatment of acute salicylate poisoning by Drs. A. G. Morgan and A. Polak (4 January, p. 16) and by Dr. T. M. Savege and others (4 January, p. 35). In reviving the combined use of bicarbonate and acetazolamide in adult salicylate poisoning Drs. Morgan and Polak have achieved an effective form of treatment in terms of alkalinization of the urine and reduction of plasma salicylate, but their regimen is no more effective than more generally accepted regimens of forced alkaline diuresis. They express concern at the high infusion rates of the latter forms of treatment, but in my experience of 307 adults admitted to the Regional Poisoning Treatment Centre, Royal Infirmary, Edinburgh, with acute salicylate overdosage, clinical complica-