uterine bleeding.¹ It would be interesting to see if the results of our investigation could be related to these cases.—We are, etc.,

N. K. BHIDE
S. T. GOGTE

Department of Pharmacology,
All-India Institute of Medical Sciences,
New Delhi, India

1. Shirokar, V. N., in *Review of Research Work in India on Intra-uterine Contraceptive Devices*, ed. K. R. Laumas, pp. 109, 110. New Delhi, Indian Council of Medical Research, 1969.
2. Oskoui, M., *Archives Internationales de Pharmacodynamie et de Therapie*, 1968, 175, 223.
3. Jacobsson, B., and Nilsson, I. M., *Scandinavian Journal of Haematology*, 1969, 6, 386.

Canavan's Disease and Spongiform Encephalopathy

SIR,—Your leading article (19 August, p. 433) reviewing conditions associated with spongy brain describes in some detail the autosomal recessive Canavan's disease but refers only to intoxication—namely, experimental hexachlorophane poisoning in animals. In this regard the recent epidemic in France of probable talc powder intoxication is relevant in that the 90 or so reported cases manifested signs consistent with what is thought to be hexachlorophane toxicity.

Since April of this year some babies who had been treated for diaper rash allegedly with contaminated powder sustained progressively anorexia, extensor spasms, signs of decerebration, coma, and death. Results of extensive investigations were unremarkable but at necropsy massive oedema of myelin, predominantly in the deeper parts of the cortex and brain stem, with widespread cystic changes were found—that is, signs and pathology almost identical with those of Canavan's disease.

It is possible therefore that the inborn error in Canavan's disease is a defect somewhere along the metabolic pathway of a common extrinsic factor, which after a degree of exposure to that factor results in over-production of an intermediate that is toxic in excess to myelin. Notwithstanding, your fleeting reference to a toxic aetiology in animal experiments and its relegation to the bottom of the list should be reviewed. Indeed toxicity should be more often suspected as a cause of morbidity than it is.—I am, etc.,

H. PRATT

Australian Embassy,
Paris

Inappropriate Secretion of ADH

SIR,—Your leading article (26 August, p. 489) discussing the pathophysiology of the syndrome of inappropriate secretion of antidiuretic hormone states that the treatment of patients with the syndrome is by fluid deprivation and treatment of the underlying aetiology. This suggestion is probably based on the finding that (hypertonic) saline infusion does not alleviate the hyponatraemia because of prompt renal elimination of the sodium ion.¹ However, if coma is the direct consequence of hyponatraemia and water retention the physician faced with a comatose patient may wish to consider a form of therapy other than passive fluid restriction. Might not the use of peritoneal dialysis provide a rational alternative? Using normal saline as the dialysing fluid it should be possible to accelerate water elimination and

restore sodium balance, thereby hastening recovery.—We are, etc.,

J. SACK
M. A. SPERLING

Harbor General Hospital,
Torrance, California, U.S.A.

1. Bartter, F. C., and Schwartz, W. B., *American Journal of Medicine*, 1967, 42, 790.

Australia Antigen and Pulmonary Tuberculosis

SIR,—A high incidence of Australia antigen (Au/Ag) has been reported among lepromatous patients,¹ those with Down's syndrome,² and among drug addicts³ as well as in patients with other chronic diseases. We have tested patients in a sanatorium for pulmonary tuberculosis for Au/Ag by cross-over electrophoresis and have compared the findings with those in patients newly-admitted to the sanatorium, patients in a general hospital, and healthy blood donors. The results are shown in the Table.

Patients	Number Tested	Au/Ag Positive
Pulmonary tuberculosis (old patients)	427	45 (10.5%)
Pulmonary tuberculosis (new patients)	143	4 (2.7%)
General hospital	1,000	2 (0.2%)
Blood donors	1,200	2 (0.14%)

The higher proportion of Au/Ag carriers among patients with long-standing pulmonary tuberculosis compared with the new patients is statistically significant ($P < 0.025$). The difference between new tuberculosis patients and general hospital patients and blood donors is also significant ($P < 0.001$). This high incidence of Au/Ag among pulmonary tuberculosis patients could be due to a higher risk of contamination during prolonged stay in hospital or to an unknown immunological disorder, or both.—We are, etc.,

J. M. MARTINEZ-V
J. GUARDIA
J. VILASECA
E. BUENDIA
J. CIVIL
R. BACARDI

Autonomous University,
Barcelona, Spain

1. Blumberg, B. S., and Melartin, L., *Archives of Internal Medicine*, 1970, 125, 287.
2. Nordenfelt, E., Kaij, K., and Ursing, B., *Vox Sanguinis*, 1970, 19, 371.
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Gentamicin in Urinary Infections

SIR,—I note that the promotional literature of both the makers of gentamicin still recommends a dose of 40 mg eight-hourly for the treatment of urinary infections. Such doses would achieve levels in the urine satisfactory for treating simple cystitis, but the type of resident organisms one has in mind when using this agent—for example, *Pseudomonas* and *Klebsiella-Enterobacter* species—is not usually associated with uncomplicated infections. It would be wise, as indeed I am sure it is in all urinary infections, to use a dose giving adequate tissue levels.

As I have previously stated,¹² patients with pseudomonas in the urinary tract often carry it at other sites, including the bronchi and skin surfaces. In these locations a 40-mg

dose will produce negligible concentrations of gentamicin, serving only to select for resistance. For these reasons, and because I think there is far more danger of under-treatment with this drug than of toxicity, I wonder whether the time has not come to abandon the eight-hourly, 40-mg dose for urinary tract infection. The adoption of an eight-hourly, 80-mg dose of gentamicin for such infections in patients of average body weight and normal renal function would seem appropriate.

It is, of course, highly desirable that the dose should in fact be more accurately weight-related. In life-threatening infection 5 mg/kg body weight in divided doses is the minimum dosage level and even higher doses may be justified. Even in renal failure the first dose and probably the entire first day's treatment need not be reduced, though after this serum estimations will be required to control treatment.—I am, etc.,

J. H. DARRELL

Royal Postgraduate Medical School,
London W. 12

1. Darrell, J. H., and Waterworth, Pamela M., *British Medical Journal*, 1967, 2, 535.
2. Darrell, J. H., and Waterworth, Pamela M., *British Medical Journal*, 1969, 3, 141.

Call the Doctor

SIR,—Dr. J. S. W. Little (30 September, p. 831) clearly misunderstands the objectives of the yellow form issued to visitors to the United Kingdom.

The first is to alert the doctor who may be called to the fact that the visitor may be incubating some exotic infection, such as malaria, cholera, or smallpox. Secondly, imported smallpox cases are frequently admitted to general hospitals pending diagnosis. It is hoped that the yellow card, by suggesting that a visit be asked for, will reduce the number of primary contacts and lead to immediate admission to an isolation or smallpox unit, whichever is appropriate.—I am, etc.,

W. G. DAVIDSON

Regina, Saskatchewan,
Canada

Serum and Urine F.R.-Antigen in Renal Disease

SIR,—Since we¹ first realized the possible importance of the study of fibrin products in renal disease much work has been done that enables me to clarify some of the points raised by Dr. J. D. Briggs and others (14 October, p. 82).

Firstly, though it is true that fibrin products are raised in any type of shock, and might not be excreted if oliguria ensues, yet of course acute renal failure itself arises in the course of shock. Intravascular coagulation in acute renal failure indicates a very poor prognosis.² Its real importance is, therefore, in the analysis of how far the acute renal failure syndrome itself can be seen as the result of microthrombosis within the kidney. That fibrin can be found in the renal glomeruli and in the peritubular capillaries has been confirmed.³ Radiofibrinogen studies in humans⁴ and animals have been used to show that increased fibrinogen catabolism and fibrin deposition in the kidneys continues in the early days of anuria, in particular in cases of acute renal failure due to

septicaemias, trauma, and obstetric accidents. These are situations in which intravascular coagulation has been expected for several reasons, and not only because sympathetic nerve stimulation is accompanied by activation of coagulation. Perhaps the most cogent reason for believing that intravascular coagulation plays its own role in the genesis of some types of acute renal failure has been the finding that in some situations inhibition of fibrinolysis actually precipitates renal cortical necrosis as opposed to mere renal shutdown.

However, as Dr. Briggs and others imply, elevation of fibrin products in uraemia may also arise as a result of that very process. Thus increased fibrinogen catabolism has been demonstrated in nephrectomized animals.⁵ It may also be true that because of inhibition of fibrin-stabilizing factor (FSF) fibrin may be lysed to F.R.-antigen products without implying the formation of thrombi. However, for this to be true blood urea levels must be very high. In these latter situations extravascular deposition of fibrin and subsequent lysis also occurs.⁴

Secondly, study of platelet mechanisms in glomerulonephritis⁶ has led to the understanding that F.R.-antigen is not only a by-product but is also central to the pathogenesis of, in particular, proliferative glomerulonephritis. For example, I have found that it is precipitating antibody to B.S.A. antigen that is particularly associated with intravascular coagulation. However, I have voiced my doubts about the meaning of F.R.-antigen in the urine without consideration of selectivity and the fact that in proliferative disease whole red cells appear in the urine. We also have attempted to relate F.R.-antigen to selectivity of IgG and to total urine protein loss, and, like Dr. Clarkson³ but unlike Dr. Briggs and colleagues in their Fig. 5, we have found no relation.

What we have found is that there is a good relation between urinary F.D.P. and the urinary excretion of fibrinogen measured by a chemical method (to be published). This not only suggests that the expensive immunochemical method is unnecessary but again raises the question of the relation of urinary F.D.P. to fibrinogen selectivity.—I am, etc.,

E. N. WARDLE

Royal Victoria Infirmary,
Newcastle upon Tyne

- ¹ Wardle, E. N., and Taylor, G., *Journal of Clinical Pathology*, 1968, 21, 140.
- ² Kleinknecht, D., et al., *Journal de Urologie et de Néphrologie*, 1972, 78, 330.
- ³ Clarkson, A. R., MacDonald, M. K., Fuster, V., Cash, J. D., and Robson, J. S., *Quarterly Journal of Medicine*, 1970, 39, 585.
- ⁴ Wardle, E. N., *Quarterly Journal of Medicine*, in Press.
- ⁵ Wardle, E. N., *Angiologica*, 1971, 8, 94.
- ⁶ Wardle, E. N., *Journal of Royal College of Physicians*, 1972, 7, 5.

Effect of Ultrasound

SIR,—Dr. U. Abdulla and others (30 September, p. 797) show that ultrasound in diagnostic doses had no ill-effect on the chromosomes of lymphocyte cultures. However, I would like to comment further on the subject.

It is often stated that the sound intensity of pulsed ultrasound in diagnostic procedures amounts to a few mW/cm²—namely, 500 to 1,000 times weaker than that used in therapy.

This is quoted to show ultrasound in diagnostic doses must be harmless. Nevertheless, the fact should not be forgotten that the intensity of a pulsed dose is the average of the intensities of each of the wave-trains,¹ some of which individually may be quite high.² The mechanical effects of pressure and acceleration that must result are disquieting to think of.

For example, particles exposed for periods of 2 μ sec 600 times a second to ultrasound of 1.5 MHz frequency, an average intensity of 0.8 mW/cm², and a peak intensity of 14W/cm² would be subject to a vibratory movement of a frequency of 1,500,000 cycles/sec disturbing them from their position of balance sideways up to a maximum of 0.004 μ . Two points located at a distance of one half wave length from each other, or 500 μ , are submitted to a difference in instantaneous pressure of 13.38 atmospheres. The calculations do not allow for the fact that all physical media absorb some of the energy that passes through them. If this were taken into account the equations of propagation would be more complicated and the solutions would take the form of Bessel functions.

Nevertheless, the example we have given can be related roughly to the situation of the fetus in utero subjected to diagnostic ultrasound. If the cellular framework joined by the desmosomes manages to resist the changes in local pressure one may wonder what happens with weaker structures such as the mitochondria. One may also wonder what effect the molecular massage resulting from variations in atmospheric pressures would have on fetal cells whose metabolism is already disturbed because of a threatened abortion.—We are, etc.,

P. FLAMME

Hôpital Saint-Georges,
Mons

C. LARDINOIS

Ecole Polytechnique de Mons,
Mons, Belgium

- ¹ Kossoff, G., *Ultrasonics*, 1969, 7, 249.
- ² Abdulla, U., et al., *Lancet*, 1971, 2, 829.

Phoenix from Physical Medicine

SIR,—We all welcome the ashes of the old bird but has the right new phoenix emerged? Certainly, the term "physical medicine" (methods of treatment) has been out of date for many years as a title for a department concerned as much with diagnosis as with treatment.¹ The later attempt to combine the term with rheumatology (a branch of medicine) was a marriage of very unequal bedfellows. But the Royal College of Physicians's recent change to "rheumatology and rehabilitation" (a statement of intent) appears no more logical.

It has long been the laudable custom to send to what will no longer be called physical medicine departments patients with every sort of medical disorder of the locomotor system. The new title is cumbersome, as all double names are, but what is far worse it excludes a good half of the proper work of the department. Cervical, thoracic, and lumbar disc lesions, strained tendons, sprained ligaments, displacement of intra-articular loose bodies—all these disorders can by no stretch of nomenclature be regarded as falling within the sphere of rheumatology. Yet they provide the commonest cause of avoidable absence from work.

The term that includes both the rheumatic and the mechanical disorders of the moving parts and rehabilitation is "orthopaedic medicine." This title carries the further advantage of facilitating the creation of an orthopaedic department staffed by an interested consultant for each type of lesion—surgical and medical. This arrangement worked very well at St. Thomas's Hospital during my time there.

Every so often each of us suffers from the non-surgical, non-rheumatic disorders of the locomotor system. More unnecessary disablement and industrial invalidism stem from them than from any other cause. In my view, the time has come for adequate provision to be made for this huge mass of patients within the N.H.S. Our neglect keeps many willing people away from work and forces them to frequent all sorts of laymen. This lamentable hiatus should be filled by the provision of orthopaedic physicians—preferably one to each orthopaedic surgical team throughout the country. Then at last the non-rheumatic no less than the rheumatic conditions would receive prompt and effective attention.—I am, etc.,

JAMES CYRIAX

London W.1

- ¹ Cyriax, J., *Textbook of Orthopaedic Medicine*, Vol. 1, 4th edn., p. 714. London, Bailliere Tindall, London, 1962.

Electrotherapy

SIR,—A recent leading article (17 June, p. 670) on the use of electricity in the treatment of a widespread distressing disability—namely, incontinence of urine—opens an important question. Where stand today the electrotherapeutic treatments of 50 years ago? I find it extremely difficult to believe they were all of little or no genuine value. But the fact remains that now most of these treatments have disappeared from physical medicine departments. And it is also unfortunately true that a high percentage of practitioners consider them near akin to quackery.

In the second world war, when bombing of Germany became heavy and effective, one air station on the North Road was often free of fog and bad visibility and was much used for landing crippled aircraft with their crew shocked, wounded, or suffering from exposure. The medical officer soon realized that one of the standard first treatments of putting the crew under radiant heat lamps or infrared tunnels not only was not moving pulses and blood pressures in the desired direction but the opposite. So he had the "gas attack" treatment set up with increased warming and humidifying gear so that patients were continuously in a stream of ambient air capable of being warmed and moistened. The effect was immediate and beneficial. But no proving research was set in motion as a result of his work. The only practical result was a small supply of tunnels from which a stream of warmed air could be directed up on an open-ended cage, thus largely avoiding the patients being exposed to any direct electromagnetic radiation, as in the case of radiant heat or infrared. Their success or disappointment for the casualties of the Normandy landing is unknown.

Again, during the strenuous training of air-crews, when they were practising parachute landings, "sprained ankles" were the most common of all injuries. The Director General, R.A.F., set up a small trial. An alternate, comparably injured group was drawn from the main bunch, and the only difference in their whole course was that this group received 20 minutes of direct current