value and therefore any improvement in homoeostatic control would have been obvious during pregnancy. Thus our argument that the shape of the curve may be a more important indicator of homoeostatic control than any actual level reached appears to be supported by these cases.

It is probable that factors controlling fasting blood glucose concentrations are separate from those affecting homoeostatic control of a glucose load. Thus a curve indicating poor homoeostatic control can occur from a low as well as a high fasting concentration. The converse can also be true, but usually patients with a very high fasting concentration have curves of abnormal shape. It has long been appreciated that the fasting glucose concentration is lowered during pregnancy and this change appears to be independent of the progressive changes in blood glucose concentration which occur after an ingested glucose load.[2]

All that seems to have changed in the cases reported by Drs. Sheldon and Coleman is the fasting level; while this is a phenomenon worthy of further research, it would seem unwise to regard this change alone as indicative of "remission" during pregnancy, particularly if by this is meant a reduction of risk to the fetus.—We are, etc.,

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1 Billewicz, W. Z., Anderson, J., and Lind, T., *British Medical Journal*, 1973, **1**, 573.
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Enteric-coated Potassium Chloride—A Continuing Hazard

SIR,—Small-bowel ulceration due to enteric-coated potassium chloride tablets was first described 10 years ago.[1 2] Since that time there have been many reports confirming the original observations[3] and similar lesions have been demonstrated in animal experiments. Other, apparently safer, forms of potassium chloride have been developed. In particular, small-bowel ulceration has not yet been described with wax-cored slow-release tablets or effervescent tablets containing potassium chloride.

The continuing risk of small-bowel ulceration was recently shown in a patient who had taken an overdose of Hydrosaluric-K tablets (hydrochlorothiazide 25 mg with potassium chloride 572 mg in an enteric-coated core). His total intake of potassium chloride was 15-20 g. Twenty-four hours after admission he developed signs of peritonitis. At laparotomy he had multiple punctate ulcers and an area of haemorrhagic necrosis in the mid-ileum which necessitated a fairly extensive small-bowel resection.

The dangers of enteric-coated potassium are widely known and simple enteric-coated potassium chloride tablets must rarely be prescribed. However, enteric-coated potassium is still present in some widely used diuretic/potassium mixtures, and the readily available prescribing information makes no reference to this fact in the case of the preparation implicated in this instance.[4 5]

We should like to draw attention to this continuing hazard and question the justification for the continuing manufacture and sale of compound tablets of this type.—We are, etc.,

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Shigella sonnei Septicaemia in a Child with Acute Monocytic Leukaemia

SIR,—Dr. Eileen E. M. Moore's account (5 January, p. 22) of *Shigella sonnei* septicaemia in a neonate prompts me to report the development of fatal septicaemia and meningitis in a child who was exposed to *Sh. sonnei* during initial treatment for acute monocytic leukaemia.

A 3½-year-old girl presented at another hospital with a month's history of pallor and transient febrile episodes. Blood examination suggested, and bone marrow aspiration confirmed, a diagnosis of acute monocytic leukaemia. She was transfused and given prednisone by mouth. On transfer to a children's ward at Hammersmith Hospital six days later she was much improved, with a voracious appetite and no gastrointestinal symptoms. Cultures of ears, nose, throat, and urine showed no pathogens. She was nursed in a single room but not strictly confined to it. The day after admission she began treatment with a combination of eight antileukaemic drugs,[1] and after the first five-day pulse of this therapy the peripheral blast cell count had fallen from 18,000/μl to nil; the neutrophil count was 400/μl.

The day after the patient's admission *Sh. sonnei* was isolated from the stools of another child in the ward. Although this child was immediately discharged, our patient developed fever and severe diarrhoea on her fifth hospital day and *Sh. sonnei* was isolated from three successive stools and two rectal swabs. Cultures of urine and cerebrospinal fluid at the onset of fever were sterile. Initial treatment with phthalylsulphathiazole by mouth was changed after 24 hours to oral chloramphenicol because of persisting fever up to 39.5°C. On the ninth hospital day, despite 48 hours of chloramphenicol treatment, she was drowsy, febrile, and very ill, and *Sh. sonnei* was found in two separate blood cultures. Intravenous gentamicin and cephalothin were substituted for chloramphenicol and a transfusion was given of 1×10^{11} granulocytes from a compatible donor with chronic granulocytic leukaemia. The temperature fell to 38.5°C and she improved slightly, but that evening aspirated a quantity of vomitus and suffered cardiac arrest.

Necropsy disclosed multiple petechial haemorrhages, enteritis with subserosal bleeding, and consolidation of the lower lobes of both lungs. The cerebrospinal fluid was cloudy and patches of exudate were present on the surface of the brain. Histological sections showed a paucity of polymorphonuclear cells consistent with the neutropenia present before death.

Dysentery due to *Sh. sonnei* is usually a brief illness which subsides without antibiotics: the organism appears to be confined to the lumen and mucosa of the bowel. Dr. Moore's patient and other reported patients with *Sh. sonnei* septicaemia[2 3] were neonates or young children, though one adult case has been reported.[4] Septicaemia complicated by meningitis has been reported once only, in a 3-day-old-infant.[5] Our patient was older than in most previously described cases but had significant neutropenia attributable to her acute monocytic leukaemia and also to its treatment. The fatal outcome of this usually benign infection in a patient with reduced body defences emphasizes that infectious disease in leukaemia patients often fails to follow usual clinical patterns. Rare and serious complications are so common that it seems unwise to follow "accepted" methods of management derived from experience in treating less vulnerable individuals.—I am, etc.,

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1 Spiers, A. S. D., *British Journal of Haematology*, 1972, **23**, 262.
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Effect of Levodopa on Tremor in Benedikt's Syndrome

SIR,—Recent advances in our knowledge of the regional biochemistry of the brain, particularly that of the biogenic amines, have made possible a new understanding of the pathogenesis of Parkinsonism, and levodopa has been used successfully in the treatment of this disease.[1 2] From experience with Parkinsonism it was expected that levodopa therapy might be effective for the patient with Bendedikt's syndrome and improve some, if not all, of the manifestation of the disease. We wish to report a case of Benedikt's syndrome treated successfully with levodopa.

A 44-year-old man was admitted in February 1973 with the chief complaint of involuntary movement of the left arm which had appeared six years after a stroke in July 1963. This attack had produced oculomotor palsy on the right side and hemiparesis and hemianaesthesia on the left side. A few months after the stroke there had been a partial recovery, but he suffered relapses in May 1967 and July 1969, after which the involuntary movement developed. Cinematographic and electromyographic studies showed that the involuntary movement was a rhythmic, coarse tremor with an average frequency of 2·6-3·1 cycles per second. Though this tremor was present at rest, it became more intense with movement of the involved limb. It disappeared during sleep and increased with emotional stress, cold, and fatigue. The patient was given levodopa in doses of 200 mg three times a day and the dose was gradually increased to 1,000 mg three times a day. Marked improvement of tremor was noted within a few weeks and the efficacy of the drug was ascertained by means of a cross-over study. The other neurological signs were not altered.

It has been suggested by clinical observations and animal experiments that the mechanism of tremor in Benedikt's syndrome is associated with the cerebellofugal pathway and the rubrospinal tract. On the other hand Poirier[3] pointed out that experimental lesions in the ventral tegmentum of the midbrain producing sustained postural tremor in the monkey were associated with a decreased concentration of dopamine and

serotonin in the striatum. In the light of these findings and our present clinical finding it seems reasonable to conclude that midbrain tremor is most probably due to combined interruption of the cerebellofugal pathway, the rubrospinal tract, and the ascending monoaminergic nervous pathways.—We are, etc.,

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Effect of Alpha-blocking Drugs in Asthma

SIR,—The article by Dr. W. C. Alston and others (19 January, p. 90) in precise terms suggests a reversible "blockade" of "beta-adrenoceptors" in a mixed leucocyte population in peripheral venous blood in patients with respiratory allergy during acute asthmatic exacerbations. Data obtained from our work on the anti-anaphylactic effect of catecholamines, particularly the inhibition of mediator release,[1] also suggested this possibility, though obviously in a context completely different from that of the effect of these mediators on "target organs" such as bronchial smooth muscle in asthma, which has been suggested by Szentivanyi.[2]

We have been investigating the possibility of a defect either at the beta-receptor level or at some step beyond the receptor, including the adenylate (adenyl) cyclase system. Though, in general, we have not found significant differences between normal subjects and allergic asthmatics, whether they were investigated during acute exacerbations or not, we have come across a few patients whose follow-up suggested a relationship between clinical aspects of the disease and the ability of blood leucocytes to respond to isoprenaline by increasing the formation of cyclic 3′, 5′-adenosine monophosphate. One outstanding example was a patient with immediate-type allergy to the house dust mite, *Dermatophagoides pteronyssinus*, who had been under the care of Dr. Monica McAllen since 1967, during which time he had repeatedly undergone various investigations,[3 4] including a leucocyte histamine release test. Since 1969 he has been on low-antigen-dosage hyposensitization therapy. His leucocyte response to allergen challenge, which was very strong, remained unchanged until June 1973, when this response completely disappeared. This was associated with disappearance of response to challenge with various anti-human-immunoglobulin sera, including anti-IgE, and it occurred despite an increase in total serum IgE and allergen-specific IgG antibody. The disappearance of leucocyte response was associated with a remarkable increase in the ability of these cells to form increased amounts of cyclic adenosine monophosphate (AMP) in response to isoprenaline. Thus the presence of 8×10^{-5}M isoprenaline cyclic AMP formation rose from 120% (compared with control values) to 270%. To us it seems difficult to explain all these findings on the basis of "blockade" of beta-adrenoceptors.—We are, etc.,

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Analgesics and the Kidney

SIR,—It is Dr. R. A. Axelsen and Dr. A. F. Burry's interpretation of the pathology of analgesic renal disease (29 December, p. 784) that does not accord with observable and recorded facts. For instance, Nordenfelt and Ringertz's series[1] consisted of 30 patients who consumed large amounts of analgesic preparations and subsequently died in renal failure. Twenty-three patients came to necropsy; in eight there was moderate or advanced renal contraction without renal papillary necrosis and in four more there was advanced renal contraction with necrosis of only one papilla. Burry[2] was concerned to show that renal papillary necrosis evolved progressively from minor to major lesions and that renal cortical damage followed the major lesions. Mean kidney weight was, however, less for intermediate than for total renal papillary necrosis. Total renal papillary necrosis was found three times as frequently in females as in males and its maximum incidence was in age group 40-50, only one patient being older than 70 years. Only one patient less than 50 years old showed the earlier lesions and their highest incidence was in patients older than 70 years, the sex incidence being equal. While all types of lesions are found in age group 50-70, these differences in incidence for age and sex weaken the hypothesis that the lesions are necessarily part of a single progressive pathological process. It has yet to be suggested that analgesics could cause rejuvenation or sexual transmutation.

The real difficulty confronting Drs. Axelsen and Burry arises from their preoccupation with the clinical aspects of analgesic nephropathy. This has led them to neglect the wider problem of the effects of certain organic molecules upon mammalian renal tissue and to accept experimental findings only when these are consonant with their interpretations of clinical phenomena. The observations[3] which they dismiss so summarily constitute the only body of evidence that compounds related to phenacetin may be nephrotoxic, and the experimental model is designed to enable detailed studies to be made of the interaction of these compounds and renal tissue.—We are, etc.,

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1 Nordenfelt, O., and Ringertz, N., *Acta Medica Scandinavica*, 1961, **170**, 385.
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One Thousand Vasectomies

SIR,—I am surprised that Dr. M. Altman is shocked (2 February, p. 198). To describe one's reaction to a professional opinion as one of shock implies a tone of high moral fervour which is unbecoming to a subject from which as much emotion as possible should be removed. It is clear that Dr. Altman and I have completely opposite points of view on the purpose of vasectomy. He is concerned with a mass number of operations in an attempt presumably to influence a national birth rate; this is the system as is practised in underdeveloped countries and is fitting to their needs. I am concerned with a small group of individually treated patients in whom my main responsibility is to prevent any possibility of pregnancy. I feel no guilt for destroying 7·5 cm of the vas because I have warned my patients adequately in advance and they all accept this.

Dr. Altman bases part of his criticism on the fact that the lesser operation may be reversible. I thought that I had made it clear in my letter that equivocation in this matter was unsatisfactory and could be misleading to the patient. Amelar[1] states: "In a survey of American urologists a success rate of 45% has been reported for 420 vaso-vasostomies . . . but there is a world of difference between sperm appearing in the ejaculate and the occurrence of pregnancy." Blandy[2] has gone on record as saying that "few surgeons will expect more than a 25% success rate from attempts to re-join a divided vas and if a husband asks for an operation which can be undone again, it is best to decline to operate under these conditions." Hanley,[3] who is a known proponent of a potentially reversible vasectomy operation, reported on his results of vasal anastomosis following vasectomy in 35 patients. In 27 of these cases sperm appeared in the ejaculate, but only eight pregnancies resulted—that is, the overall success rate is 35 cases was of the order of 23%. It would seem, therefore, that until a fool-proof technique of reversibility has been tried and proved, the concept of a potentially reversible vasectomy is chimerical. I believe that I have a duty to inform my patients that the operation is permanently irreversible and to do my best to ensure that the operation fulfils these requirements.—I am, etc.,

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Brain Damage after Lithium and Phenytoin

SIR,—In their communication on "Permanent Brain Damage after Lithium Intoxication" (15 December, p. 673) Drs. P. Juul-Jensen and M. Schou describe two cases of persistent ataxia after overdosage with lithium plus phenytoin in the first