serotonin in the striatum. In the light of these findings and our present clinical finding it seems reasonable to conclude that mid-brain 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's¹ 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. Burry² 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 observations³ 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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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. Amelar¹ states: "In a survey of American urologists a success rate of 45% has been reported for 420 vasovasostomies . . . but there is a world of difference between sperm appearing in the ejaculate and the occurrence of pregnancy." Blandy² 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