

complex from the vascular compartment of normal and nephrectomized rabbits, suggesting an effect on vascular permeability.⁴ Moreover, administration of renal extract to rats pretreated with D.O.C.A. (desoxycorticosterone acetate) leads to an eclampsia-like syndrome characterized by generalized oedema and convulsions, together with vascular necrotic lesions which resemble those seen in the malignant phase of hypertension.⁵ A similar syndrome results from injection of renal cortical extract into nephrectomized or renal hypertensive rats and it has been shown that these effects are due to an increase in vascular permeability to plasma proteins.⁶⁻⁸

Since pure preparations of renin are not available, it is not possible to say whether the ability of renal extract to increase vascular permeability is due to renin itself or to a separate vascular permeability factor. This problem is now being studied. Nevertheless, it seems relevant to draw attention to the effect of renal extract on vascular permeability in considering the possible role of renin in the pathogenesis of pregnancy toxæmia.—We are, etc.,

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Surgery for Peptic Ulcer

SIR,—Lythgoe's paper¹ mentioned in Mr. I. M. Orr's letter (8 August, p. 382) did much to undermine confidence in the electrical stimulation test. It led others to condemn it from hearsay alone. His paper has been quoted in writing elsewhere to condemn the test.² I cannot regard Lythgoe's criticism as valid for the following reasons:

(1) He used D-tubocurarine as the relaxant in his 25 cases. We were strongly advised not to use this drug because of its possible anticholinergic action, although its place in the electrical stimulation test has not yet been fully assessed. We have always advised the use of gallamine triethiodide.

(2) In three of his cases he found no pressure response to stimulation. Clark and Murray,³ writing of the stimulation test, recorded that four of their 100 patients received incorrect premedication and as a result gave a poor response. In three other patients there was a poor response although the correct premedication had been given. No mention has been made in either of these papers of the possible use of fluothane, which seriously diminishes or abolishes the pressure response. No paper can discuss the stimulation test and its responses without giving careful consideration to this common problem. If no anticholinergic drugs have been given and the test is properly performed, there are no cases which give a poor response. In our early work not a few patients had, un-

known to us, been taking one or other of the many preparations put up especially for peptic ulcer patients and containing either phenobarbitone and belladonna or a tranquillizer and an anticholinergic drug. Some of the tranquillizers themselves have an anticholinergic action. A few patients have brought such drugs into hospital and have taken them on the morning of operation and spoil the test.

(3) Lythgoe claimed that there were three of his 22 cases in which the stimulation test showed complete nerve section while the insulin test demonstrated incomplete section. Clark and Murray,³ writing of their 100 patients, stated: "... the insulin test meal results show that in one case the Burge test was fallacious in indicating complete vagotomy when the insulin test was later found to be positive. The pressure readings in the case were low and this may be the explanation of the missed nerve trunk." Perhaps their low reading was caused by an anticholinergic drug, or even by the electrode. The electrode now is made of rhodium-plated silver; until it was plated in this way low responses were sometimes due to a silver electrode made dull, presumably from oxidation during boiling.

(4) Lythgoe stated that trunks might remain outside the electrode because surgeons might fail to find the posterior trunk. No trunk can remain outside the electrode if the coeliac division of the posterior nerve is felt. We cannot provide for a surgeon who is unable to carry out this major step in the operation.

(5) He regards the absence of atropine as a serious drawback to the test because of chest complications. Clark and Riddoch⁴ have found that the absence of atropine in this operation does not increase the incidence of chest complications.

Lythgoe concluded that the routine use of the test does not appear to be justified, yet when it is used and a pyloroplasty properly made the recurrence rate is 0%. How can a test not be of value when by its use 30% of patients would have nerve trunks divided which would otherwise be left intact?

I believe that Mr. Orr can be reassured that gross hypersecretion matters only in the Zollinger-Ellison syndrome. There is never need to estimate gastric acids before operation.—I am, etc.,

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Methyldopa and Parkinsonism

SIR,—The article by Dr. M. J. T. Peaston (18 July, p. 168) describing Parkinsonism in a patient receiving methyldopa has just come to my notice. I recently encountered a further variant of this condition in a 54-year-old negro woman with essential hypertension. She had been treated with methyldopa satisfactorily for about three months, though a dose of 3 g. daily was required to bring her standing blood-pressure down from 200/130 to 125/80 mm. Hg. One day she called me, requesting an urgent appointment, and when

I saw her she was in a state of considerable agitation. There was a striking coarse regular tremor affecting mainly the right upper limb, though the left arm was slightly involved also. Mild cogwheel rigidity of the right arm was present, but there was no generalized increase in muscle tone. Apart from the mental state referred to, there were no other abnormalities to be found on examination except for a standing blood-pressure of 220/130 mm. Hg. She told me that the tremor had developed slowly over a period of 48 hours, and was accompanied by an inability to sleep and a sensation of fearful anxiety. The methyldopa was withdrawn for 24 hours and then restarted at a dose of 2 g. a day. She was also given butobarbitone 30 mg. q.i.d., and when I saw her three days later all her symptoms and the tremor had disappeared and she appeared her usual cheerful self again. The dose of methyldopa was subsequently increased again to 3 g. a day with no recurrence of the tremor.

Agitation, depression, and nightmares have previously been seen after administration of methyldopa, and together with the extrapyramidal syndromes already reported are probably due to altered amine levels in the brain. There have been several controversial reports in the literature concerning the effect of methyldopa in Parkinson's disease. Barbeau *et al.*¹ considered that both tremor and rigidity were made worse, but Marsh *et al.*² were cautiously optimistic, and felt that tremor was reduced when methyldopa was administered at doses of up to 2 g. a day. It is of interest that in the patient described above, as in the cases reported by Groden³ and Peaston, extrapyramidal signs did not appear until after several weeks of treatment with methyldopa. There is no doubt that methyldopa can occasionally cause Parkinsonism, and this would seem to be completely reversible by drug withdrawal or reduction in dosage.—I am, etc.,

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Cramps in Pregnancy

SIR,—I would like to reinforce the views of Dr. Jean R. C. Burton-Brown on the treatment of leg cramps in pregnancy (1 August, p. 312). I have used quinine sulphate in the way she suggests for many years without any complications, and with complete relief of symptoms. Its oxytocic action, a fairly weak one, is only manifest after labour has started.¹

Occasionally I have found that a patient who seems particularly prone to leg cramp has been consuming large quantities of milk in the belief that "it was a good thing to do." Reduction of their intake to a normal level has often caused the cramps to disappear. This is no doubt due to the increased calcium-absorption blocking effect of the raised phosphorus intake.

I searched Mr. Elliot E. Phillip's article (21 March, p. 749) on "Minor Disorders of Pregnancy" for mention of another minor