interpretation of the assay figure may ensue.—I am, etc.,

P. D. GRIFFITHS.

Bishop's Stortford, Herts.

REFERENCES

[1] Aebi, u., Richterich, R., Colombo, J. P., and Rossi, E., *Enzymol. biol. clin.*, 1961–2, **1**, 61.
[2] Lehmann, H., and Griffiths, P. D., *Lancet*, 1963, **2**, 498.
[3] Griffiths, P. D., 1964, M.D. Thesis. University of London.
[4] Hughes, B. P., in *Research in Muscular Dystrophy*, Proceedings second symposium, p. 167, 1963. Pitman, London.
[5] Pearce, J. M. S., Pennington, R. J., and Walton, J. N., *J. Neurol. Neurosurg. Psychiat.*, 1964, **27**, 1.
[6] Griffiths, P. D., in the press.

Aortic Medionecrosis and the Marfan Trait

SIR,—In Dr. M. G. Lewis's article (5 June, p. 1478) on the association between aortic medionecrosis and aortic incompetence in the elderly he also mentions that some of these cases show evidence of arachnodactyly, suggesting the presence of an underlying congenital connective-tissue defect. The classical Marfan syndrome of arachnodactyly, aortic dilatation, and congenital eye defects is fairly easily recognized in young adults, but patients have now been described in whom the cardiovascular changes have presented in the sixth decade.[1,2] In these cases the Marfan trait must be less severely expressed, as the abnormal aorta is able to withstand the haemodynamic thrust of the circulation for a longer period before starting to dilate.

For several years I have been searching for patients with the characteristics of the skeletal disorder of dolichostenomelia (long slender limbs),[3] originally described by Marfan.[4] Viewed from this aspect, vascular and eye defects are uncommon, although the arachnodactyly may be as severe as that seen in patients with these complications. However, one of my patients was found to have aortic regurgitation and radiological evidence of dilatation of the first part of the aorta at the age of 61 years.

Sinclair *et al.*[5] devised the metacarpal index from bone measurements of radiographs of the hands. I regard measurements above the 3 × Standard Deviation (S.D.) of the normal range of this index as being indicative of arachnodactyly.[6] It is beyond this amount of bone slenderness (occurring in about 1 in 400 persons) that I began to find patients with an aorta which has dilated. Unfortunately the metacarpal index does not always detect the minor degrees of arachnodactyly, which one might expect in the older patients presenting with a vascular abiotrophy. Consequently I devised a method of estimating the relative slenderness of all the metacarpals and proximal phalanges.[3] I now present this information on skeletal hand charts, in which the abnormal measurements are clearly indicated as multiples of the normal standard deviation. This has produced the interesting finding that the Marfan trait is expressed extremely irregularly even in one region such as the hands and may even be confined to one hand. In McKusick's case[2] the cardiovascular defect was also expressed irregularly, so that the aortic valve and descending thoracic aorta had dilated and yet the ascending aorta had withstood a greater haemodynamic thrust. Idiopathic Erdheim's cystic medionecrosis without the Marfan trait is a diagnosis of exclusion, and skeletal hand charts may help to determine the presence of a connective-tissue defect before it is too late.

Now that it is possible to splint the aorta with a sleeve of synthetic material or replace a segment with a synthetic graft—a life-saving procedure in one of my patients—the diagnosis of this condition has become increasingly important.—I am, etc.,

J. G. PARISH.

Passmore Edwards Medical Rehabilitation Centre, Clacton-on-Sea, Essex.

REFERENCES

[1] Sloper, J. C., and Storey, G., *J. clin. Path.*, 1953, **6**, 299.
[2] McKusick, V. A., *Heritable Disorders of Connective Tissue*, 1960, 2nd ed., p. 70. Mosby, St. Louis.
[3] Parish, J. G., *Proc. roy. Soc. Med.*, 1960, **53**, 515.
[4] Marfan, A. B., *Bull. Soc. méd. Hôp. Paris*, 1896, **13**, 220.
[5] Sinclair, R. J. G., Kitchin, A. H., and Turner, R. W. D., *Quart. J. Med.*, 1960, **29**, 19.
[6] Parish, J. G., *Brit. J. Radiol.*, 1965, in press.

Experience in an Anti-smoking Clinic

SIR,—Dr. Keith P. Ball and his team (26 June, p. 1651) are to be congratulated on their splendid work at their anti-smoking clinic. The group therapy idea which forms the basis of several such clinics in this country has certainly much to be recommended from the very sound reasons stated in the report. While I don't think that any method employed in the treatment of smokers who really want to give up smoking can claim better results than those shown by Dr. Ball and his colleagues, I succeeded quite as well with the personal clinical approach. In January 1963 I inaugurated with the support of the Ministry of Health a "Smokers' Advisory Clinic" as a new service of the corporation's health and social services department in one of Newcastle's public health clinics. During the first year this new enterprise had been run as an experimental clinic with the special approval of the Ministry. After an interval of several months we reopened the clinic nine months ago. Since then 78 people—mostly referred by their doctors, unless they came from reasons of their own—attended the clinic. Though the corporation charges a fee of 35s. per patient in order to cover the expenses (overheads and drugs)—a payment also designed to deter those time-wasters who are not really serious about this business—15 customers (*c.* 20%) dropped out after the first or second session. Of the remaining 63 patients—among them many bronchitics—four are not yet "consolidated." Of the 59 under assessment 16 (27%) did not respond or gave up treatment prematurely; 43 (72%) gave up smoking, usually the same day as strongly suggested. The almost immediate results with a few exceptions who needed a week or so was, I believe, only possible by supplying the strong moral support and psychological influence (i.e., by demolishing the myth of the benefit of smoking and by dealing carefully with the patient's individual problems) with effective drug treatment. I used either lobeline (no less than 12–16 mg. per day) in order to prevent the craving, or Atarax (hydroxyzine) in individually required doses (10 mg. two to four times per day) for the suppression of "deprivation symptoms." The patient has to be warned against a possible somniferous effect of hydroxyzine during the first two days.

Following up is notoriously difficult, as many people don't return the short follow-up questionary. So far we could trace nine relapses; three of these want to repeat the course of treatment. Of those who replied, 10 are still abstinent for periods from three to eight months.—I am, etc.,

E. G. W. HOFFSTAEDT.

Newcastle upon Tyne.

Buphthalmos and Photophobia

SIR,—In the section on buphthalmos in Mr. K. Wybar's interesting article on eye diseases in children in the *B.M.J.* of 22 May (p. 1361) he gives increasing myopia in early childhood, haziness of the cornea, redness of the eye, and photophobia as presenting signs, in that order. I entirely agree with him that these conditions occur, but would give a different order of, as it were, priority, and add lacrimation.

Increasing myopia would be unlikely to become manifest until the child is at least 2 or 3 years old, whereas lacrimation and photophobia present themselves in the first months or year of life, and this is the time when it is most important for the case to be observed and treated. Furthermore, it is remarkable how often these two symptoms are not given the consideration they deserve. The lacrimation is ascribed to blocked tear ducts and the photophobia is thought to be something out of which the child will grow; so that it is sometimes months or even longer before it is realized that there is something seriously wrong.

Congenital glaucoma is treatable, and satisfactorily so if it is "caught" in the first year of life, after which the prognosis becomes progressively worse. The reason for this letter, therefore, is to draw the attention of all who have to do with young children to the possibly sinister significance of photophobia and lacrimation, especially the former.—I am, etc.,

London W.1. ARTHUR LISTER.

Death after Combined Dexamphetamine and Phenelzine

SIR,—Episodes of hypertension may occur during treatment with monoamine-oxidase inhibitors, and are sometimes related to the simultaneous administration of other drugs—e.g., amphetamine—or to eating cheese. The following is an account of a case in which dexamphetamine was taken during a course of treatment with phenelzine, resulting in a rise of blood-pressure, cerebral haemorrhage, and death.

A 30-year-old woman with depression was being treated with phenelzine (Nardil) 15 mg. three times daily, and trifluoperazine (Stelazine) 2 mg. at night. One afternoon, after she had been taking these drugs for some five weeks, she acquired some dexamphetamine tablets (Dexten) from a friend, and took two (each equivalent to 10 mg. dexamphetamine sulphate). Within a quarter of an hour she was complaining of a headache, so severe that she called her doctor and told him "her head was bursting." Her blood-pressure when taken an hour after the ingestion of the dexamphetamine was 150/100 mm. Hg, but at this time there were no physical

signs of any abnormality in the central nervous system. The blood-pressure was known to have been within normal limits previously. The patient was put to bed and sedated, but it was later found that she could not be roused; when seen again by her doctor two hours after the first examination she was comatose, with a blood-pressure of 170/100 mm. Hg; the patient was sent to hospital, but died very shortly after admission.

Post-mortem examination showed a haemorrhage in the left cerebral hemisphere disrupting the internal capsule and adjacent areas of the left corpus striatum. No other abnormality was found—in particular, no intracranial aneurysms—and no evidence of long-standing hypertension.

—We are, etc.,

J. T. ALBAN LLOYD.
D. R. H. WALKER.

Department of Pathology,
Royal Alexandra Hospital,
Rhyl, Flintshire.

Anaesthesia and Monoaminase-oxidase Inhibitors

SIR,—I read with interest the letters of Dr. H. C. Churchill-Davidson (20 February, p. 520) and of Dr. M. D. A. Vickers (24 April, p. 1126). I should like to comment that indeed many physicians believe that if any major side-effect occurs in response to a newer drug it is due to the "sensitivity," and somehow an allergic reaction is implied.

As a psychiatrist I have investigated most tranquillizers and energizers, and while we have, fortunately, relatively few severe and fatal reactions to these drugs, such reactions do occur, sometimes due to avoidable circumstances. One of the side-effects from these psychotropic drugs which has been neglected much too often is secondary hypotension. Fatal reactions to shock occurring from hypotension may be avoided at times if the "predisposition" of the patient is known. It has become the belief of many researchers in this field that side-effects from these drugs occur more frequently in the presence of a diffuse impairment of the autonomic nervous system. The observation of the blood-pressure pattern may be helpful. In a recent survey of the blood-pressure patterns in a 600-bed mental-patient hospital we found that only 57.44% had normal blood-pressure patterns; 8.48% were classified as hypertensive; hypotension was present in 18.86%; and labile-borderline patterns were found in 15.22%. This means that hypotension is more frequent than is in general believed (at least three times as frequent as in a general population).

It is quite possible that hypotension is present to a marked degree in patients who take psychotropic drugs for some time. When these patients are in need of anaesthesia and surgery and are given analgesic drugs or additional phenothiazines as a sedative and/or anti-emetic, shock may be aggravated and may result in death; nausea in itself is considered a shock-producing agent.[1] It would probably be best to avoid giving monoamine-oxidase inhibitors during anaesthesia and immediately following surgery, because of their severe hypotensive action, especially in the elderly. This problem may easily be overlooked because of a latent cardiovascular lability frequently present and the unpredictable response of the autonomic nervous system to the monoamine-oxidase inhibitors. The physician and surgeon are quite often unaware of the status of the autonomic nervous system of his patient, which is not easily established.

While the blood-pressure is a good measure of the autonomic nervous system, a frequent mistake of many researchers, as well as the practising physician and surgeon, has been to use only one or two blood-pressure measures taken at random. By taking systematic blood-pressure measures at regular intervals—for instance, four times a day for one week, blood-pressure patterns may be established which permit the physician to ascertain the presence of any abnormality such as hypertension, orthostatic hypotension, or a labile-borderline condition, any one of which may be a warning in the use of psychotropic drugs.[2]

There are many factors in drug administration about which little is known. Doubtless an important one is the occurrence of metabolic by-products, which may act as toxins. In the recent discussions of tranylcypromine (Parnate), an effective monoamine-oxidase inhibitor, Himwich[3] concluded that imipramine (Tofranil) therapy promotes the accumulation of some substance in the brain which is normally destroyed along a pathway blocked by tranylcypromine. While it is impossible to generalize, any toxic reaction to drug substitutes (e.g., pethidine for morphine) may occur on a similar hypothesis—that is, the accumulation of toxic metabolites which may be fatal.—I am, etc.,

KURT WITTON.

Veterans Administration Hospital,
Fort Meade,
S. Dakota, U.S.A.

REFERENCES

1 Selzer, A., and Rytand, D. A., *J. Amer. med. Ass.*, 1958, **168**, 762.
2 Witton, K., and Goldman, A. R., *J. nerv. ment. Dis.*, 1965, **140**, 58.
3 Himwich, W. A., *Rec. Adv. biol. Psychiat.*, 1961, **4**, 257.

Imipramine in Parkinsonism

SIR,—I would like to comment on the trial of imipramine against a placebo in the treatment of Parkinsonism, reported by Dr. R. R. Strang (3 July, p. 32).

Twenty-seven out of 35 of his placebo group were removed from the trial because of clinical deterioration or failure to respond. None of his imipramine group was removed for this reason. We are not told whether, in the case of any of the patients receiving imipramine, the code was broken because of failure to respond and the patient kept on the trial because he was found to be receiving imipramine. If this did not occur, the difference in failure rate between the two groups is very large, χ^2 being over 39 with one degree of freedom, surely the highest degree of improbability in any of the many reported trials of imipramine.

If, on the other hand, patients receiving imipramine were selectively retained in the trial, and thus given a further chance to improve, a bias has been introduced in favour of imipramine. We cannot therefore conclude that "a most satisfactory degree of improvement in 16 patients (53%) confirms the value of imipramine in Parkinsonism."

Incidentally, Dr. Strang need not be surprised to find imipramine of value in Parkinsonism in spite of its chemical similarity to the phenothiazines. Of the anti-Parkinsonism drugs listed in the 1958 edition of Martindale's *Extra Pharmacopoeia* two are phenothiazine derivatives (ethopropazine hydrochloride and diethazine hydrochloride). Two others are reported to alleviate mental depression in patients with Parkinsonism (benzhexol hydrochloride and cycrimine hydrochloride).—I am, etc.,

London S.E.19. J. S. PRICE.

Undescended Testicle

SIR,—Your leading article "Undescended Testicle" (15 May, p. 1259) called to mind a diagnostic test differentiating pseudocryptorchidism from cryptorchidism, described by Dr. Paul L. Bunce,[1] the original description being attributed by him to Mr. Louis Orr. I have found the test most useful in examining large numbers of boys at school examination. It prevents many needless over-referrals to urologists, a source of annoyance to urologist and parents.

In essence, the test consists of having the boy sit on a straight-backed chair and draw up his legs so that the soles of his feet rest on the chair seat. By hugging his knees to his chest pressure is directed to the inguinal canal in such a way that a freely movable testis will appear in the upper scrotum, where it can be examined without difficulty.—I am, etc.,

Utica, New York, U.S.A. JOHN H. POWELL.

REFERENCE

1 Bunce, P. L., *Pediatrics*, 1961, **27**, 165.

SIR,—The increased risk of malignancy in the ectopic or abdominal testis is, as Dr. R. T. H. Shepherd (26 June, p. 1670) says, a powerful argument in favour of treatment of the maldescended testis. I suggest, however, that in advising orchidectomy Dr. Shepherd may have overlooked one important point. Whilst many studies, including my own,[1] have noted a marked tendency in the undescended testis to undergo malignant change this has only been found in testes remaining in the undescended position through puberty, whether or not they are subsequently brought down by surgery; it appears to be exceedingly rare for the testis undergoing orchidopexy *before* puberty to develop malignant change. This is an important reason for deciding well in advance whether the testis can descend to the scrotum with puberty (i.e., the retractile variety) and undertaking orchidopexy without delay if spontaneous descent does not seem possible. This offers protection against malignancy, and at this age sacrificing an otherwise well-formed testis would not seem justifiable. I do agree with Dr. Shepherd, however, that when puberty has overtaken a testis unable to descend there is a strong case for orchidectomy rather than accepting the enhanced risk (probably about one in fifty) that will otherwise remain in spite of orchidopexy. It is worth emphasizing that this dilemma need not arise, since a testis of this sort can be recognized without difficulty at an early age, and of course nowadays few escape our system of school health examinations.

It seems important that our knowledge upon this should be more detailed, and may