figures) that radioactivity increase was absent on a subsequent study, due either to the heparin therapy or to the disappearance of the effect of wound healing. A similar increase of surface radioactivity was observed in the operative field after surgical operations other than transplantation.

It may be concluded from the foregoing that surface measurements following injection of labelled fibrinogen may become a useful diagnostic tool for the detection of

late renal transplant rejection, but unfortunately will probably not be of value in non-functioning transplants during the first few weeks after transplantation.—I am, etc.,

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REFERENCE

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Beta-blockers in Hypertension

SIR,—Dr. A. W. D. Leishman and others (7 November, p. 342) state in the introduction to their paper on practolol and oxprenolol in hypertension that both drugs are relatively cardio-selective. By this they mean that the two drugs show "much less activity than propranolol in blocking other beta-receptors." No reference is given to support this statement.

Though beta-receptors are widely distributed throughout the body,¹ the clinically important beta-receptors are found in the heart and bronchial smooth muscle, blockade of the former reducing cardiac activity and of the latter preventing beta-stimulated bronchial relaxation. When a beta-blocking drug is said to be cardio-selective, this implies that the dose of drug which blocks the cardiac beta-receptors has little or no effect in blocking bronchial and peripheral vascular beta-receptors.² The effects of oxprenolol, propranolol, and practolol on cardiac, bronchial, and peripheral vascular beta-receptors in animals have been reported. The dose of propranolol that

blocks the cardiac response to a standard dose of isoprenaline (0.2 µg/kg i.v.) also blocks the peripheral vascular beta-receptors.^{3,4} In contrast, practolol in doses which completely block cardiac beta-receptors has no effect on the peripheral vascular receptors.⁴ We have compared also the effects of oxprenolol on cardiac and vascular receptors. The results, comparing the three drugs are given (A), which show that oxprenolol resembles propranolol in being non-selective.

This lack of selectivity of oxprenolol on cardiac versus peripheral vascular beta-receptors is confirmed by the studies reported from the laboratories of the manufacturers of oxprenolol.⁵ They compared oxprenolol and propranolol and showed that it had identical effects on both cardiac and peripheral vascular beta-receptors at the same dose in the cat. Turning to the bronchial beta-receptors, the same authors⁶ showed that oxprenolol was extremely active in blocking the bronchial beta-receptors, in that 1-3 µg/kg i.v. of oxprenolol antagonized

by 50% the actions of isoprenaline on bronchospasm induced by pilocarpine in the cat. This potent activity on bronchial beta-receptors is confirmed by Marmo *et al.*⁷ We have compared the three compounds for their effects on bronchial smooth muscle in vivo in the guinea-pig.⁵ The results of such studies (B above) show that the dose of propranolol and oxprenolol causing 50% of guinea-pig death is between 0.1 and 0.18 mg/kg., while that of practolol is 15 mg/kg. In other words, 150 times as much practolol must be given to achieve the same effects on bronchial beta-receptors as propranolol or oxprenolol.

The conclusion that may be drawn from these studies, and those from Switzerland and Italy, is that there is no evidence from pharmacological studies in animals to suggest that oxprenolol differs from propranolol in being cardio-selective, though there is ample evidence⁵ to show that practolol is.

Dr. Leishman and colleagues mention the quinidine-like properties of propranolol but omit to mention that oxprenolol has similar properties.⁷ They also omit to state that while Barrett *et al.* showed that practolol is 40% as active as propranolol in antagonizing the action of isoprenaline on the heart,⁸ it is equally active in blocking endogenously released noradrenaline in the cat.⁹ It is appreciated that brevity is the essence in writing a report, but it should not be such that it may be misleading.—I am, etc.,

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Serum Trypsin Inhibitor and Paraquat

SIR,—Recently, we had the opportunity of estimating serum antitrypsin levels in three patients suffering from paraquat poisoning. In all three we found depressed levels. One patient, who subsequently died, had a serum antitrypsin level of 0.77 µmoles trypsin inhibited/min./l. Our normal value is 2.16 by the method of Dietz.¹ Two patients who subsequently recovered had levels of 0.99 and 1.10. The latter patient's level increased to 1.64 at a time when his lung function was returning to normal.

We were prompted to examine the serum trypsin inhibitor level following a report of abnormally low levels in certain patients with respiratory distress syndrome.² Paraquat poisoning has been suggested as an experimental model for the respiratory distress syndrome. Emphysema is another lung condition where there is a depressed

TABLE.—Comparison of the effects of propranolol, oxprenolol, and practolol on heart, peripheral blood vessel and bronchial smooth muscle.

Drug	A		B
	*ED ₅₀ (µg./kg./min)	% blockade of depressor response	50% mortality in G.P. bronchospasm test (mg./kg.)
Propranolol	62.0 ± 5.0	†64%	0.1
Oxprenolol	30.25 ± 5.0	61%	0.18
Practolol	162 ± 4.0	0%	15.0

*ED₅₀ is the dose of drug giving a 50% blockade of isoprenaline induced rise in heart rate in the cat.
†A figure higher than 50% indicates a greater activity on peripheral vessels than on the heart.

antitrypsin level.³ These three conditions have well described lung involvement and the common occurrence of antitrypsin deficiency may have important implications. This problem is now under investigation in this laboratory.—We are, etc.,

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Male Sterilization

SIR.—Dr. Pauline Jackson and others (31 October, p. 295) require two semen analyses to show azoospermia at an interval of one month. In order to avoid the patient having to use contraceptives longer than necessary, it is perfectly reasonable to ask for two specimens at an interval of 7-14 days—that is, long enough to allow the seminal vesicles to fill up again.

After vasectomy, I ask that at least two months shall have elapsed since the operation, and that he shall have ejaculated at least 15 times. After that, he should not ejaculate for at least three days, in order to produce the biggest possible specimen straight into a 50-ml. container which has a wide mouth, and is provided by the laboratory. If that is clear, a second specimen is requested 7-14 days later. If one of those is not clear, he is sent another container for use not before 10 days have elapsed and after he has had at least another five ejaculations. When two consecutive specimens have been found free of sperm, contraceptive precautions can be abandoned.

The object of asking for two specimens is to make assurance doubly sure, and to satisfy a court of law in the event of litigation.¹ It is not to check whether recanalization has taken place. Hanley² has shown that this takes considerably longer.

As a matter of terminology, aspermia, which means complete absence of sperm, seems a more accurate term than azoospermia, which means absence of living sperm and implies that non-motile sperm can be present.—I am, etc.,

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Phentolamine in Heart Block

SIR.—I am prompted by the recent remarks in your columns (31 October, p. 307, and 28 November, p. 558) about the drug treatment of heart block to comment that, in my experience, a short course of a glucocorticoid (such as prednisolone, starting at 40 mg. per day) will nearly always change A/V block (complete or incomplete) and/or bundle

branch block (left or right, complete or incomplete) back to sinus rhythm when the conduction fault follows a recent myocardial infarction.

Presumably the action of the drug is to reduce oedema, as it will do in uncomplicated cerebral oedema following concussion.—I am, etc.,

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Colistin Sulphomethate Sodium and Renal Function

SIR.—We refer to the paper by Mr. D. J. E. Price and Dr. D. I. Graham (28 November, p. 525) where the summary appeared to misrepresent the actual findings. We wish to point out that although the authors considered renal failure to have contributed to the final cause of death in some cases, which it should be noted were severely ill patients with refractory infections when treatment was started, in only one case was renal failure the actual cause of death in this difficult group of cases receiving exceptionally high dosages of colistin.

Furthermore, no mention was made in the summary of the reversible nature of the biochemical changes which occurred following colistin, as indicated by the findings in all patients who survived, including those considered to have developed acute tubular necrosis and as suggested by the available biochemical data in those patients who died. In our opinion the summary does therefore not accurately portray the content of this paper.—We are, etc.,

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** We have shown the above letter to Mr. D. J. E. Price and Dr. D. I. Graham who reply: "We would like to thank Dr. E. Sproston and Mr. M. P. McConnell for drawing to our attention that our summary was incomplete. As they have rightly pointed out, the high dosages of colistin used produced completely reversible nephrotoxicity in the surviving patients even though the biochemical data suggested that it had produced acute renal failure in some and acute tubular necrosis in others. In those patients who died there was an indication that the nephrotoxicity was also reversible, and again we would like to stress that renal failure may have contributed to the fatal outcome in some of our patients but in the majority they died from the primary neurological disease."—ED., *B.M.J.*

Accident and Emergency Services

SIR.—I have followed the recent correspondence on the accident and emergency services with interest, and from the viewpoint of a career appointment in this branch of hospital medicine would like to make a few observations.

I am afraid that I cannot confirm that three quarters of the patients attending the casualty department of this hospital could

be regarded as general practitioner cases. Letters from Mr. F. C. Durbin and Dr. R. W. Stephenson (28 November, p. 557) prompted me to make a quick check by selecting a week at random and analysing all the attendances. Total attendances were 443, of which 226 were new cases. Of these latter 12 could have been dealt with by a general practitioner by examination and prescription only and an additional 42 could possibly have been dealt with if every general practitioner had 24-hour facilities for minor suturing, dressing small burns, strapping minor sprains, incising paronychia, etc. Even this latter maximum figure only represents 7 to 8 patients a day. Of patients referred to other faculties for admission or outpatients follow-up 36 were orthopaedic and 28 for other departments.

To subdivide the work into "orthopaedic" or "general practitioner," as suggested by Dr. Stephenson, is an oversimplification, as it does not easily accommodate such cases as the ruptured spleen or spontaneous pneumothorax. Many emergency ambulance cases will involve other specialties and will require assessing and possibly immediate medical treatment or even resuscitation. Someone will be required to receive and assess such cases, including those of multiple trauma, at the same time rendering the condition non-urgent before referring to the relevant specialty. This person will also be able to deal with the less severe trauma and illnesses that can have a high morbidity if not treated vigorously.

To effectively liaise with senior members of other departments, with general practitioners, ambulance, and other outside services it is surely a considerable advantage to have a permanent member of staff in the department, and with junior medical and ancillary staff this person can then run the department and represent its interests first hand. That this requires experience and training is recognized by Mr. Durbin's suggested "special crash courses of training." So if the person will end up as a "specialist" why not a "consultant"?—I am, etc.,

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Survival Rates with Dialysis

SIR.—I read with interest the article by Dr. J. F. Moorhead and colleagues on survival rates of dialysis and transplantation (10 October, p. 83). While sympathising with the difficulties that the authors must have had in compiling data going back seven years when none of them was actively involved in the early years of this work, I nevertheless feel that it is necessary to add three apparently unreported early deaths in the hospital series.

In September 1963 a male patient aged 20 died after five months of treatment from inhalation of blood following epistaxis associated with heparin. In December 1963 a male patient¹ aged 35 died after 10 months from a massive right heart embolus associated with the use of indwelling femoral catheters, and in March 1966 a male patient died aged 45 after three weeks' treatment from a cardiac tamponade. I could not find any mention of these deaths in their mortality analysis. Furthermore,