non-immune rosette formation are the facts that a relatively large proportion of lymphocytes of unimmunized animals participate in the reaction, and that thymocytes are more active than non-thymic lymphocytes.

The proportion of human lymphocytes which adhere to sheep red cells is often relatively large in non-immunized human subjects, and human fetal thymocytes are more active than peripheral lymphocytes.⁹ The adherence of non-immunized human lymphocytes to sheep red cells is therefore likely to occur through non-immune rather than immune mechanisms. The adherence probably occurs through fortuitous cross-reactivity of sheep red cells with human lymphocyte surface receptors concerned with an autologous non-immune adherence.—I am, etc.,

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- 1 Zaalberg, O. B., *Nature*, 1964, **202**, 1231.
- 2 Siegel, I., and Christy, N. P., *Federation Proceedings*, 1972, **31**, Abstract No. 2932.
- 3 Siegel, I., *Cellular Immunology*, in press.
- 4 Siegel, I., *Journal of Immunology*, 1970, **105**, 879.
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- 6 Siegel, I., and Sherman, W. B., *Journal of Allergy and Clinical Immunology*, 1972, **50**, 65.
- 7 Siegel, I., *Journal of Cell Biology*, 1970, **47**, 191a.
- 8 Jondal, M., Holm, G., and Wigzell, H., *Journal of Experimental Medicine*, 1972, **136**, 207.
- 9 Wybran, J., and Fudenberg, H. H., in *Transactions of the Association of American Physicians*, 1971, **84**, 239.

Major Accident Teams

SIR,—To my surprise the one member of the consultant staff not included in Mr. P. E. A. Savage's major accident action card (1 July, p. 42) is the ophthalmologist. Some 15 years ago an explosion in a coal mine resulted in about 20 patients being admitted to the Victoria Hospital, Burnley, where, thanks to the presence of the orthopaedic surgeon, a major accident procedure had been instituted. Every one of these patients had eye injuries.—I am, etc.,

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Activated Charcoal in Tricyclic Drug Overdoses

SIR,—The letter by Dr. J. L. Crammer and Dr. B. M. Davies (26 August, p. 527) calls for comment. It is stated, without reference, that tricyclic drugs undergo enterohepatic circulation and that "large amounts are secreted into the bile and delivered into the duodenum." The importance of being certain that "large amounts" of the active drug are excreted in the bile lies in the fact that if such secretion did occur then there would be a temptation to undertake biliary drainage as an emergency measure in the management of acute tricyclic poisoning.

At one time biliary drainage was considered an acceptable measure in severe acute glutethimide (Doriden) overdose¹ on the assumption, since discounted, that substantial enterohepatic circulation of the active drug occurred. Other heroic measures in tricyclic poisoning included gastrostomy undertaken by French toxicologists with no operative mortality but a death rate of 50% in 16 patients.² The procedure has understandably been discontinued.

Drs. Crammer and Davies also make an

inaccurate statement about the effect of activated charcoal on aspirin ingestion. They state "activated charcoal was shown to prevent the absorption of aspirin from the human gut." As your leading article in the same issue (p. 487) points out, activated charcoal does no more than reduce absorption of salicylate, the degree of reduction depending on a number of factors. It has never been claimed that prevention of absorption will be achieved.—I am, etc.,

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Royal Infirmary,
Edinburgh

- 1 Maher, J. F., Schreiner, G. E., and Westervelt, F. B., *American Journal of Medicine*, 1962, **33**, 70.
- 2 Gaultier, M., Fournier, E., Gervais, F., Dalayun, J., and Frejaville, J. P., in *Deuxième Congrès Européen des Centres de Lutte Contre les Poisons*, 1966, p. 17. Paris, Masson et Cie, 1967.

SIR,—The communication of Dr. J. L. Crammer and Dr. B. M. Davies (26 August, p. 527), which was brought to our attention only in October, has prompted us to submit some preliminary results obtained by us.

Early this year we considered activated charcoal as a means of intercepting the enterohepatic circulation of imipramine and its active metabolite desipramine. We compared levels of imipramine plus desipramine in hearts, lungs, and livers of control rats and of rats pretreated with activated charcoal after parenteral infusion of imipramine (approximately 3 mg/kg intravenously and 10 mg/kg intraperitoneally). The parenteral route was chosen to prevent adsorption of imipramine to charcoal before intestinal absorption had occurred. Imipramine plus desipramine was determined by the method of Wallace and Biggs¹ using an improved extraction procedure according to Maes.²

We often found a lowering of the organ concentrations in the pretreated group, suggesting immobilization of part of the imipramine dose. The concentration ratios pretreated/control are shown in the Table. Owing to a large biological variation not all experiments yielded significant results. Equilibrium dialysis with charcoal showed a near quantitative binding at pH 7.4 in the concentration range 0.50 µg/ml under our conditions, 1 mg activated charcoal adsorbing 1.25 mg imipramine at 50 µg/ml. We are now changing the design of our animal experiments to obtain more clear-cut results.

	Intravenous Infusion			Intraperitoneal Infusion		
	A	B	C	D	E	F
Heart ..	0.54*	0.90	0.70	0.47*	1.00	0.92
Liver ..	0.60*	0.94	0.85	0.76	1.10	1.10
Lungs	0.72*	0.70*	0.75	0.74	0.84	0.66*

*Significant at the 0.05 level.

Even if binding is not quantitative and irreversible the resulting levelling off of the imipramine load on the target organs may improve the prospects of patients with imipramine poisoning. On the basis of these preliminary results the National Poison Control Centre in the Netherlands now stresses the use of activated charcoal even in cases where absorption of the tricyclic anti-

depressant dose may well be complete before therapy is started.—We are, etc.,

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- 1 Wallace, J. E., and Biggs, J. D., *Journal of Forensic Sciences*, 1969, **14**, 528.
- 2 Maes, R., 1972, personal communication.

Hormones in the Treatment of Psychoses

SIR,—I believe the neurophysiological matrix of tension and depression is a central functional organizational scheme related to stress and increased drives, while the neurophysiological matrix of schizophrenia is a central functional organizational scheme related to reduced stress and drives. It seems that the hippocampus and the pineal gland are related to the second functional scheme, and the biochemistry of the pineal is related to that of schizophrenia. I believe, further, there are some hormones which affect these functional schemes of adaptive behaviour. In recent years in my outpatient practice I have found that Choriogonin (chorionic gonadotrophin) is effective in the treatment of affective disorders and tension with depression. I used this hormone in doses of 1,500 I.U. to 3,000 I.U. daily, using four or more injections for a course.

Oxytocin had a favourable effect in the treatment of acute schizophrenia and, in a less degree, in the treatment of chronic schizophrenia. I used 10 I.U. to 15 I.U. of oxytocin intravenously (with 10 ml to 15 ml of glucose) or 20 I.U. to 25 I.U. of oxytocin intramuscularly (one daily injection); the course is six to ten injections. I observed some rapid therapeutic effects and, then, some hospitalizations were prevented. It seems that prolactin has also some antipsychotic effect (25 I.U. daily).—I am, etc.,

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Spironolactone and Ammonium and Potassium Chloride

SIR,—In a programme of intensive drug monitoring we have found a possible interaction between spironolactone, ammonium chloride, and potassium chloride.

The patient, a 58-year-old woman with paralysis due to a compression fracture of the D 8 and 9 vertebrae and extradural compression of the cord, required an indwelling catheter and urinary antiseptics. Treatment with digoxin and frusemide for mild congestive heart failure was continued after admission, and potassium supplements were given as potassium chloride (about 50 mEq/day). The plasma potassium fell slowly to reach 2.9 mEq/l. 14 days after admission. Frusemide was discontinued and spironolactone, 25 mg four times a day, substituted. The potassium chloride was continued, and a week later ammonium chloride 4 g/day together with methenamine mandelate was started.

At the beginning of spironolactone treatment plasma sodium was 140 mEq/l., plasma potassium 4.1 mEq/l., plasma CO₂ content 28 mEq/l., and blood urea 28 mg/100 ml. Twenty days after beginning ammonium chloride the patient's condition deteriorated and she appeared acidotic. All drugs were stopped. On this day the plasma sodium was 120 mEq/l., plasma potassium 5.7 mEq/l., plasma CO₂ content 13 mEq/l., blood urea 24 mg/100 ml, plasma