Mitral valvular inefficiency, manifest as regurgitation in the presence of atrial fibrillation, supports this hypothesis. Clearly, as the atrial filling curve moves to the left with exercise as heart rate increases and diastole shortens, atrial contraction assumes less importance in valve closure. The conclusion must be that at slow and probably at resting heart rates atrial contraction is indispensable to normal (high) mitral valve efficiency. Provision of a contracting atrial chamber would seem to be an essential part of an artificial heart design that utilizes a leaflet valve at the atrioventricular junction and which operates at near normal heart rates.—I am, etc.,

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Achalasia of the Oesophagus

SIR,—Recently an in vitro pharmacological study was reported on the muscle obtained at oesophagomyotomy for achalasia.¹ The conclusions of these authors were that the inferior oesophageal sphincter was abnormal. This was based upon the examination of the muscle excised from 18 cases of achalasia and 14 cases of normal controls. In association with the pharmacological studies histological examinations were also performed, and their results substantiated the contention that the sphincter was abnormal.

This was contrary to the findings of another similar investigation.² There is no dispute about the correctness of the in vitro study itself, but it is incorrect to correlate in vitro studies with what occurs in living man. The studies in man, with the oesophagus intact and in continuity, are of far more value than in vitro studies, and these indicate that the sphincter is normal. Much has been written on all aspects of this most interesting and controversial lesion.

It is accepted that the primary lesion is degeneration of the myenteric plexus of the body of the oesophagus only. This in turn eventually produces a grossly incoordinated or atonic viscus in which peristalsis or incoordinated peristalsis does not stimulate the normal sphincter to relax. Hence the correct terminology should be achalasia of the oesophagus (more specifically of the inferior oesophageal sphincter), and not cardiospasm.³ These factors were fully confirmed by in vivo physiological and pharmacological studies. In the latter both mecholyl (parasympathetic-mimetic drug) and Buscopan (hyoscine butyl bromide) have been used.

The question of ganglion cells is also open to dispute. Misiewicz *et al.* found that in the normal sphincter area cell counts were normal. In their cases they indicate, however, that 14 of the 18 cases of achalasia had gross dilatation of the oesophagus. It is accepted that as the oesophagus dilates it takes up the narrow segment (inferior oesophageal sphincter). In these cases it is difficult during surgery to know how much of the body is being incised, as distinct from the sphincter itself. Thus the ganglion cell counts are often misleading and as an indication of the region of abnormality are often incorrect as well. On the other hand, other studies where the oesophagus is not grossly dilated have shown that the cell counts for

the sphincter area are of normal limits. The degree of cellular infiltration and fibrosis can be explained as a secondary manifestation rather than part of the primary disease.—I am, etc.,

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REFERENCES

- Misiewicz, J. J., Waller, S. L., Anthony, P. P., and Gummer, J. W. P., *Quarterly Journal of Medicine*, 1969, 38, 17.
- Trounce, J. R., Deuchar, D. C., Kauatze, R., and Thomas, G. A., *Quarterly Journal of Medicine*, 1957, 26, 433.
- Silber, W., *Lancet*, 1965, 2, 1287.

Fibrinolytic Enzyme System

SIR,—Dr. R. T. Wensley's comments (23 August, p. 472), highlighting the important discrepancies between the results of Dr. John Bonnar and his colleagues (19 July, p. 137) and our own,¹ are well taken and certainly merit further investigation. Over the last three years we have used four different batches of Hoechst Pharmaceuticals anti-serum. A control test serum used throughout this period has shown a satisfactory degree of reproducibility between the different batches of anti-fibrinogen serum, as shown below.

Antisera Batch No.	806AC	1202M	1248K	1154D
Test serum: Mean $\pm$ S.D. (μ g./ml.) (50 observations)	6.1 $\pm$ 1.4*	6.4 $\pm$ 1.5	6.8 $\pm$ 1.2	6.8 $\pm$ 1.9

* 7 observations only.

It is perhaps worth adding that in a second study (as yet unpublished), designed to compare the changes in serum fibrin degradation products (F.D.P.) in response to caesarean section and intra-abdominal gynaecological operations, in an age-matched group of 11 pregnant and 12 non-pregnant women, respectively, the mean serum F.D.P. the day before the operation in the pregnant women (not in labour) was 14.2 ± 6.1 μ g./ml. and in the non-pregnant was 5.8 ± 4.2 μ g./ml. These findings are very similar to the original study, and the difference between the two means on this second occasion was again highly significant ($t=4.334$; $P<0.001$). Of particular interest to the present debate is that different batches of antisera were used for the two studies. Such data in no way invalidate Dr. Wensley's cautionary remarks, as we may have, fortuitously, obtained antisera of similar specificity.

One further point which may be relevant is the problem of residual non-specific sheep red cell haemagglutinin in the test serum. Persistence of this substance(s), following an unsatisfactory absorption procedure, will result in a proportion of assays being scored as zero (or simply less than the calculated sensitivity). If we have interpreted Dr. Bonnar's Fig. 1 correctly then in approximately 28% of his patients in the period before the 30 week mark no serum F.D.P. was detectable, and this appears to rise to 46% during the period from 30 weeks to term (calculations based on a maximum

sensitivity of 1 μ g./ml.). The average titre of the non-specific sheep red cell haemagglutinin in normal serum in our laboratory is 1/6, but values of 1/32 are recorded frequently—findings which compare favourably with those of Salo.² Moreover, we have demonstrated that red cells from different sheep vary alarmingly in their efficacy to absorb this antibody and in their sensitivity to agglutinate in its presence, particularly when treated with tannic acid. Thus it is at least possible that some of the serum samples recorded as less than 1 μ g./ml. were unsatisfactorily absorbed, and this may have contributed to the final conclusions which are at variance with our own. Such a postulate, however, would be untenable if controls on each sample had been run in which test serum and cells alone had been mixed and no haemagglutination had developed.

Those responsible for the production of the commercial kit for estimating serum F.D.P. (Burroughs Wellcome) will, we are sure, welcome the remarks of Dr. Wensley. We have had the opportunity of testing this kit against our own reagents and have found a highly significant positive correlation over a wide range of serum F.D.P. values. The kit therefore provides a ready facility for busy routine laboratories to undertake this immunoassay and a useful standard for those who wish to prepare and calibrate their own reagents.—We are, etc.,

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REFERENCES

- Woodfield, D. G., Cole, S. K., Allan, A. G. E., and Cash, J. D., *British Medical Journal*, 1968, 4, 665.
- Salo, O. P., *Annales Medicinæ Experimentalis et Biologiæ Fenniae*, 44, Supplement No. 1, 1966.

SIR,—In the discussion on fibrinolytic enzyme system (16 August, p. 387) Dr. J. Bonnar and others suggest that certain syndromes occur in late pregnancy in which fibrin is deposited intravascularly and fibrinolytic activity to remove it is inhibited. They regard this phenomenon as responsible for acute tubular necrosis, Sheehan's syndrome, and the Schwartzman reaction.

The refutation of the last has been dealt with by me in an earlier letter (26 July, p. 241). Sheehan has contributed considerable evidence in this field.¹ Patients who die rapidly of shock in obstetrics almost inevitably would have developed pituitary necrosis had they survived. They show thrombi if death had occurred six or more hours after the onset of shock. If disseminated intravascular thrombosis were the cause of pituitary necrosis or renal necrosis, thrombosis would have preceded the parenchymal necrosis. Although in the human subject it is difficult accurately to determine the time of death of the parenchyma, from experiments in animals in which necrotic changes have supervened on ischaemia the parenchymal necrosis resulting is detectable within the first three hours after