Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Oral Contraception and Coagulability

SIR.—The letter of Dr. P. A. Owren (May 11, p. 1283) on coagulability and thrombosis prompts a reply since his views and mine differ fundamentally. He regards blood coagulation as the primary factor both in haemostasis and thrombosis, whereas I look upon the vessel itself as having an integral part in initiating either haemostasis or thrombosis. My views may appear somewhat surprising in that many findings on coagulability have been obtained by methods that have evolved from my simple one-stage prothrombin time.

It should be remembered that in the process of evolution the blood vessel originated long before clotting factors appeared in the blood. Reflex contraction after injury constituted a primitive haemostatic reaction, which is still operative in the higher organism. The role of the vessel in haemostasis is forcefully demonstrated in telangiectasia. In this disorder coagulation is entirely normal—and this probably includes testing with adenosine diphosphate—yet bleeding from a telangiectatic lesion is one of the most difficult to control. The haemostatic defect lies within the vessel itself in its failure to react to traumatic injury. Normal coagulability is therefore of no help when the vessel does not possess its primitive response to injury.

Just as there is good evidence that the initial haemostatic step resides in the vessel, so there are many observations supporting the concept that the thrombus has its beginning on the vessel wall. The venous thrombus, which may be long enough to float in the blood-stream, is attached to the vessel wall and from its structure one can deduce that it gradually increases in size. Attempts to increase coagulability drastically by injecting thrombin directly into the blood-stream do not cause thrombosis, provided a dilute solution of thrombin is injected at a constant rate.¹ The marked reductions of fibrinogen and factors V and VIII that do occur illustrate the effective means the organism has to prevent dangerous intravascular clotting, even when the most powerful clotting factor—namely, thrombin—is injected.

According to my theory, the autocatalytic nature of the blood-clotting mechanism is the key to thrombosis. The chain reaction is mediated through thrombin, and the removal of this agent by adsorption to fibrin appears to constitute the basic means whereby intravascular clotting is held in check. It appears unlikely that an excess of any factor, including platelets, predisposes to thrombosis. According to our studies the platelets in thrombocytopenia are functionally normal. Despite the great excess, they do not predispose to thrombosis but rather induce a bleeding tendency. With regard to factor VIII, it is interesting that cases of coronary thrombosis have been reported in haemophiliacs. Since the concentration of factor VIII in this disorder may be only a fraction of 1% of normal, it is a little difficult to see a close relationship of this factor to thrombosis. It might also be mentioned that in the few women we have studied who are taking "enavid," no increase in factor VIII was observed.

As I stated in my earlier letter (March 16, p. 744), no means are known for measuring physiological coagulability. One must be particularly guarded in employing

terms such as hypercoagulability and even more timorous in interpreting them in terms of a thrombotic tendency.—I am, etc.,

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REFERENCE

- ¹ Quick, A. J., Hussey, C. V., Harris, J., and Peters, K., *Amer. J. Physiol.*, 1959, **197**, 791.

Methods of Urine Culture

SIR.—Recent papers by Cattell and Lefford (January 12, p. 97) and Guttman and Stokes (May 25, p. 1384) have both compared "routine" methods of urine culture with quantitative pour-plate methods in the diagnosis of urinary infection. The authors are fortunate that the culture methods routinely used at their hospitals are already semi-quantitative and so compare favourably with the more laborious pour-plate cultures. We feel, however, that semi-quantitative cultures are not "routine" at most hospitals, and that a statistical basis for such cultures has not been established, whereas it has been fully established in interpreting the results of pour-plate cultures.¹

Since 1961 quantitative pour-plate cultures have been carried out in this department using a method of serial tenfold dilutions of fresh voided or refrigerated urine and plating 1 ml. of each dilution with cooled, melted agar. To date, over 7,000 such cultures have been carried out, and in recent studies on bacteriuria of pregnancy the limits of this technique (which have been described by Kass¹) have been confirmed. If the first culture shows more than 100,000 organisms/ml. this finding will be confirmed on 80% of occasions by a repeat culture. If, on the other hand, the first culture shows less than 10,000 organisms/ml. a repeat culture will show a bacterial count of more than 100,000/ml. in less than 1%. Fewer than 5% of cultures contain between 10,000 and 100,000 organisms/ml., and these must be repeated. It must be pointed out that these findings are invalidated if a patient is receiving antibacterial drugs. The finding of large numbers of organisms in the urine depends on their multiplication in the bladder. Most antibacterial drugs are excreted in high concentrations in the urine and organisms (unless very resistant) are unlikely to multiply under these conditions. On the other hand, contaminating organisms will be exposed to the drug for a much shorter time and might occasionally be expected to grow on a culture plate.

Guttman and Stokes rightly deplore that only 20–30% of cases of pyelonephritis demonstrated at necropsy have been diagnosed during life. This implies that most patients do not complain of the symptoms usually ascribed to the disease and that the diagnostic methods at present employed are inadequate. Nevertheless, they consider that the cultures which are positive in their series are only significant when they are accompanied by urinary symptoms. Moreover, they do not culture the urine unless more than three white cells are seen per high-power field. If these criteria are used it is difficult to see how the percentage of ante-mortem diagnoses can be improved. If they are accepted one might conclude that any form of urine culture is unnecessary except to obtain the sensitivity of the organism. It is agreed that bacteriuria has been found in many patients who have had pyelonephritis. It must be stressed, however, that it can also be found in patients who have never had urinary-tract symptoms