Letters to their Drs

In Defence of APTT Control of Long-term Anticoagulant Therapy

In their interesting and provocative paper, Drs Sarah Pearce and Sekar (1973) claim to have shown that the prothrombin ratio is a better test for the control of oral anticoagulant treatment than the activated partial thromboplastin test (APTT) using Bell and Alton phospholipid as the platelet substitute and a bentonite suspension for surface activation. Unfortunately they have chosen to express their APTT results as ratios of normal control values, which are not given, and have arbitrarily chosen a therapeutic range of 1.5 to 1.8.

When 168 paired results on plasma samples collected during long-term anticoagulant therapy were compared using Bell and Alton phospholipid or soya bean phospholipid with bentonite activation, good correlation between the two platelet substitutes was found (r=0.87). The therapeutic range of 50 to 70 seconds, based on the incidence of haemorrhage when soya bean and bentonite was used (Eastham, 1968), was found to correspond to 44-57 seconds when Bell and Alton phospholipid was used.

The normal untreated range of APTT results using soya bean and bentonite is wide (33-45 seconds), and it is therefore not sensible to express the APTT as a ratio. A time of 70 seconds, found to be critical in indicating potential risk of haemorrhage (Eastham, 1968), could be expressed as ratio values ranging between 1.6 and 2.1, wider than the therapeutic ranges chosen by Drs Pearce and Sekar (1973), depending on the normal control values found. Similar criticism can be levelled at the results of Drs Pearce and Sekar, their method of APTT estimation also having a wide normal range (26-40 seconds). It would be interesting to see their results plotted in the form used by Hamblin (1971). Using their method of estimation of APTT in their laboratory, he showed that the APTT was more sensitive than the prothrombin ratio in the detection of bleeding tendency. In 15 bleeding episodes during a three-month period of oral anticoagulant therapy, all these affected patients had abnormally raised APTT results (expressed as actual clotting times), whereas only five of these same patients had abnormally raised prothrombin ratios above the accepted therapeutic range.

Drs Pearce and Sekar found 29 bleeding episodes during a six-month period covering 906 patient/weeks of treatment, a rate of one bleed per 31 weeks of treatment. During a similar five-year period covering 13 780 patient/weeks of treat-
ment, I found 103 bleeding episodes, a rate of one bleed per 133 weeks of treatment, using the APTT expressed in seconds, and a therapeutic range of 50 to 70 seconds, to control warfarin dosage (Eastham, 1972). I submit that the use of the APTT in the form of a ratio inevitably makes the test insensitive and unsatisfactory, and partly explains the results reported by Drs Pearce and Sekar (1973).

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References


Malignant Hepatoma

Malignant hepatoma is a common neoplasm in Africans in Rhodesia, where it may comprise 4-9 (Ross, 1962) to 10-8 (Gelfand, 1949)% of all malignancies. Ninety per cent of cases appear to originate in patients with cirrhosis (Gelfand, Castle, and Buchanan, 1972) so that there is an obvious clinical need for a diagnostic test to determine when malignancy has developed. We therefore decided to examine the suggestion of Bell and Williams (1964) that a positive result in the Jirgl's flocculation test in patients with cirrhosis should arouse suspicions that a malignant hepatoma had developed. (This test was originally devised by Jirgl (1957) for distinguishing obstructive form hepatocellular jaundice.)

A modification of the technique of Bell and Williams was used, the test being read after 4 hr against a dark background in daylight. The results were reported as negative (clear), + (turbidity), ++ (flocculation), or +++ (precipitation). Strongly positive sera from two cases of obstructive jaundice were used as controls.

Sera were examined from 71 patients from Mpilo Hospital, who required liver function tests, and from 20 patients suspected of having malignant hepatoma at Harari Hospital. The results of the investigation are given in the table.

Ten of the patients at Mpilo were found to have a malignant hepatoma; eight cases were proven by liver biopsy or necropsy while the diagnosis of the other two cases (group A) was made by the cancer diagnostic panel on the basis of the clinical tetrad of a nodular enlarged liver, right hypochondrial pain, a bruit over the liver, and a raised right crus of the diaphragm on chest radiographs. A positive test was found in only two of the 11 hepatoma patients (20%) and two of the 13 histologically proven cirrhotic patients (15%). Neither of these two cirrhotics appears to have developed a malignant hepatoma during the last two years.

At Harari Hospital the diagnosis of hepatic malignancy was confirmed histologically in eight patients and made in an additional five patients on the basis of a positive alpha fetoprotein assay (cross-over electrophoresis technique) and a suggestive liver scan (group B). Only three of these 13 patients (23%) had a positive Jirgl test, whereas at the same hospital it has been found that 69% of hepatoma patients have a positive alpha fetoprotein test (T. C. Ashworth, personal communication); there were no false positives. None of the cirrhotics had a positive flocculation test.

In conclusion, these limited studies have shown that in the Rhodesian African there is only a slight association between malignant hepatoma and a positive Jirgl test and that the alpha fetoprotein test is a more useful diagnostic test. No direct evidence has been obtained to support the hypothesis that the Jirgl test might be of value in predicting the development of malignant hepatoma in cirrhosis; a longitudinal study with a large number of cirrhotics would be necessary to obtain a definitive answer to this question.

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References


Table

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