receptor–hormone interaction and its biological significance.

PREDICTIVE VALUE OF ACID PHOSPHATASE. B. MORGAN. Department of Chemical Pathology, University of Leeds.

There is increasing interest in the use of clinical and biochemical data to assess the probability that a patient has, or will develop, a particular state. The complexity of these techniques arises in part because they are based on many variables measured in each individual. Yet the aims of these techniques are identical with the aims of making a single measurement in each individual. It is these aims which will be discussed here in relation to a single variable, namely the serum acid phosphatase activity, and a single clinical condition, namely carcinoma of the prostate.

The ideal situation would have been as follows: (1) Two groups were defined which were comparable in all ways except that one group had carcinoma of the prostate gland (CA) and the other did not (N); (2) There was a measurement (acid phosphatase) which was simpler than the techniques used to separate the initial groups and which had different values in the groups CA and N; (3) There was no overlap in the values of X in the groups CA and N; (4) There was no other condition which could be confused with carcinoma of the prostate.

The real life situation is of course far from this ideal. One fundamental difference is that there is no complete separation of the values of serum acid phosphatase (AP) in the two groups (N and CA). Various changes in technique have been suggested in order to diminish this overlap of AP between the groups. These changes are largely aimed at improving organ specificity by the choice of substrate and the addition of isoenzyme inhibitors (Bodansky, Clin. Chem. 1972, 15, 43; Schwartz, Clin. Chem., 1973, 19, 10).

While these attempts will no doubt continue, it seems reasonable to conclude that in this clinical situation, as in so many others, a single measurement will not completely discriminate between the groups and that overlap of the results will remain.

What is so commonly done in practice is to define a value (the upper limit of normal) to assume that values above this will not occur in healthy persons. The finding of a high value then indicates the presence of the disorder. This approach is an attempt to make the situation like the ideal one with complete discrimination.

However, this approach makes no use of the information in the absolute value of the measurement. Thus, the higher the value of AP, the greater the probability of carcinoma of the prostate. This probability is rarely formally defined for a single variable although it is now part of some complex statistical analyses involving several variables (Hartz, Clin. Chem., 1973, 19, 113). This probability function must also take into account the relative prevalence (probabilities) of the disorders or states which are being discriminated.

MULTIPARAMETRIC TESTS IN THE STUDY OF GASTROINTESTINAL NEOPLASMS. E. H. COOPER. Department of Cancer Research, University of Leeds.

Several forms of cancer can be conveniently staged into a local growth, extension into local nodes, direct spread beyond the organ of origin and distant metastases. This sequence will have reached various stages when the patient first presents and after a variable time interval following the excision of the primary tumour local recurrences or distant metastases may develop. A team of laboratory workers and clinicians in the Leeds Region and at the Chester Beatty Institute, London has been examining the way in which laboratory tests may aid the diagnosis in gastrointestinal cancers, in particular, colorectal cancer. This was chosen partly in view of our participation in the MRC trial on the evaluation of carcinoembryonic antigen (CEA) and partly as the evolution of colorectal cancer follows reasonably well-defined patterns. It soon became apparent that apart from being able to distinguish metastatic colorectal cancer involving the liver from various types of hepatitis and cirrhosis, CEA alone was unable to discriminate the various stages of evolution of colorectal cancer. As the liver is the main site of distant metastasis the contributions of serum enzyme, known to be elevated in hepatic metastases, to a discriminant function have been examined. Gammaglutamyl transpeptidase, leucine aminopeptidase and alkaline phosphatase
have been estimated in parallel with the CEA values in a wide spectrum of clinical stages in the evolution of colorectal cancer. A combination of \( \gamma \)GT and CEA gave an improvement in the discrimination of hepatic metastases but this combination still appears to lead to error in some patients with residual diseases apparently confined to the pelvis.

The rise in serum \( \gamma \)GT is a more sensitive indicator of early metastases than AP or LAP, but once the level of \( \gamma \)GT was above 100 i.u./ml (normal = 13.9 ± 7.7 i.u./ml) the rate of rise of AP and LAP parallel the increase of \( \gamma \)GT. The rates of increase of these enzymes in advanced hepatic metastases have a fairly uniform course. On the other hand, the levels of CEA are extremely variable and there is no simple correlation between the apparent extent of the metastases and the CEA level.

Following individual patients by repeated measurements after the excision of the primary tumour has shown that the combination of CEA and \( \gamma \)GT can indicate metastatic cancer several months before clinical examination. Furthermore, the treatment of advanced colorectal cancer with chemotherapy produces a fall in the \( \gamma \)GT and the CEA values. Unfortunately, this combination of CEA and \( \gamma \)GT is reliable as an indicator of hepatic metastases in only a few types of tumours. It failed to identify many forms of cancer that gave positive evidence of metastases on liver scintiscans. This preliminary experience has suggested that it may be possible to set up other combinations of tumour antigens and chemical indicators of organ site involvement to help in the surveillance of common forms of cancer. This may be particularly appropriate when suitable forms of chemotherapy are available to warrant early treatment.

**PART III: THE 6th WALTER HUBERT LECTURE**

**PREDICTIVE TESTS IN CANCER**

Tuesday 9 April 1974

THOMAS C. HALL

*From the Los Angeles County–University of Southern California Cancer Center, Los Angeles, California 90033*

There are a number of reasons for desiring a set of predictive tests in cancer therapy. Since the number of patients who respond to radiation, hormonal and cancer therapy represents only a fraction of those treated, it follows that many patients are treated unnecessarily. Many therapies that are used to treat non-resectable cancer have toxic side-effects, so that if we could identify patients who would surely fail, and omit useless therapy, radiation and chemotherapeutic toxicity could be diminished. If we could predict that a conventional therapy would fail, this would facilitate early introduction of a new and possibly effective treatment. Since it usually takes 3 or more weeks to observe whether treatment is effective, the replacement of clinical observation with a predictive test could very possibly save 3 or more weeks of treatment. Since the median survival of patients with, for example, acute myelogenous leukaemia, is only 3 weeks, half of such patients could be offered a new and possibly effective therapy before death. Recently, combination chemotherapy has become very popular and toxicities not previously induced are now tolerated because of possible increased benefits. Yet, empirical choice of agents may result in addition of toxicity without increase of