LABORATORY VIROLOGY - DIAGNOSTIC OR TESTING SERVICE?

BASED ON A LECTURE TO "PROGRESS IN CLINICAL VIROLOGY", PRAGUE, 11-14 SEPTEMBER 1995

C. R. Madeley
Department of Virology, Royal Victoria Infirmary & University of Newcastle, Newcastle upon Tyne, NE1 4LP, UK

INTRODUCTION

Viruses can cause severe and life-threatening illnesses. Examples include rabies, AIDS, hepatitis and, more recently, the epidemic of Ebola fever virus in Zaire in May 1995. However, many virus infections are less dramatic and, though they cause considerable morbidity and have economic importance through days lost from work, are often regarded as trivial. No specific treatment is available for most of them and sufferers are advised that they will get better; their discomfort is "just another of life's problems". Doctors frequently tell patients that their respiratory affection is "just a virus" and have made this a useful (and, to be fair, often a correct) "dustbin" diagnosis, meaning that "it's uncomfortable but not serious, and I can offer no remedy other than symptomatic treatment and time will bring healing."

To virologists this attitude is infuriating, not least because it will be true less and less often, with increasing numbers of patients receiving immunosuppression and older citizens living closer to the edge of life where an insult which would have been minor earlier in life becomes much more severe and may even be fatal. Children, too, are vulnerable and need protection by vaccines.

This paper is not a summary of virus diseases; it is rather an exploration of the rationale of virus diagnosis without which we would know little about the activities of individual viruses. Few of them cause such characteristic and unmistakable illnesses that they can be identified with certainty by their clinical presentation.

Until now, virus diagnosis has been something of a craft activity, performed by a relatively small number of enthusiastic doctors, scientists and technicians. Their laboratories, if not providing universal coverage throughout the world or even for individual countries, have provided enough epidemiological data to identify the viruses prevalent in their area. They have also provided many diagnoses which have been useful in managing and treating patients.

The methods used in diagnosis have frequently been unique to individual laboratories, evolved to fulfil local needs. They have often reflected the interests and drive of the senior virologist and diagnostic virology laboratories are consequently far from uniform in the service they offer and the methods they use. This slightly untidy state of affairs is now being assailed by changes in available techniques and by new ways of thinking about virus diagnosis.

FORCES FOR CHANGE

There have been four main forces which are changing the nature of diagnostic virology (Table 1). Two have been advances in technology and two have come from changes in how we think of medical science.

1. Monoclonal Antibodies

Until Kohler and Milstein (1) showed how to make monoclonal antibodies, production of good polyclonal antisera was an expensive activity with no guarantees of success. The response of individual animals to administered antigens was unpredictable. Other unwanted antibodies produced in response to contaminating antigens in the immunizing preparation had to be removed, usually by absorption. Good antisera were difficult to make and only a small number of laboratories succeeded. The costs of materials and labour meant that few reliable antisera were available commercially for such exacting purposes as immunofluorescence or enzyme immunoassays in which non-specific reactions could totally invalidate results. Other than some neutralizing sera, diagnostic laboratories made their own sera laboriously or did without them. Because the immunogen could be prepared adequately pure, commercially produced antiglobulin sera conjugated to fluorochromes or enzymes for use in sandwich assays were available but even here wise users assumed the worst and confirmed that they were free of unwanted antibodies (and absorbing them out, if necessary before using them). This frustrating situation was transformed when monoclonal antibodies became available.

Monoclonal antibodies were and are difficult to make. The process is long, painstaking and labour-intensive and, even if it becomes easier with practice, is not certain to be successful. Even those which react unequivocally with viral components may not be suitable for all intended tests but, once a suitable clone is obtained, virtually unlimited production is available. It is this which has made all the difference because the answer to the virologist's prayer is also an answer to commercial companies. Hitherto unable to produ-