Progress in Medical Virology

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Preface

Chemical carcinogenesis was observed as early as 1761, in descriptions of symptoms of cancer in snuff users, and by 1775 in the better-known association between scrotal skin cancer and coal soot to which chimney sweeps were regularly exposed. More recently, a number of types of radiation have been recognized as increasing the risk of cancer, and viruses have been shown to cause cancers in animals and to be strongly suspect in certain human cancers. In their article, CASTO and DIPAULO review studies concerning the interactions of chemicals, viruses and radiation that have been conducted, chiefly in model systems *in vitro*, and discuss the significance of these data in concepts of carcinogenesis and the mechanisms by which interactions of tumorigenic agents may take place.

Another article in this volume focuses upon viral oncogenesis. MCALLISTER reviews the evidence which suggests that members of four groups of viruses – adenoviruses, herpesviruses, type-B and type-C oncornaviruses – might be involved in human cancer. He also discusses the two current hypotheses of oncornaviral carcinogenesis, the viral oncogene hypothesis and the protovirus hypothesis:

"The [oncogene] hypothesis states that most or all vertebrates contain the genetic information for producing a type-C RNA virus in their somatic as well as in their germ cells. This information has been part of the genetic make-up of vertebrates since early in evolution and can persist for many generations in cell culture without overt production of virus. The virogenes (genes for production of type-C viruses) and the oncogenes (that portion of the virogene responsible for transforming a normal cell into a tumor cell) are maintained in an unexpressed form by repressors in normal cells. Various agents including physical and chemical carcinogens may transform cells by "switching on" the endogenous oncogenic information... In the protovirus hypothesis, the genetic information required for cell transformation is hypothesized not to exist in the germ cells. (In the oncogene hypothesis the entire information of a transforming type-C virus is transmitted in the germ cells.) In the protovirus hypothesis, a normal process of RNA to DNA to RNA information transfer, operative in development, is deranged to give rise to the formation of the genes for neoplastic transformation. The oncogene and protovirus hypotheses therefore differ in the type of changes that lead to neoplasia. In the oncogene hypothesis the change is derepression of existing information; in the protovirus hypothesis the change is a series of RNA to DNA to RNA information transfers that lead to modification of the original information. This modification is usually for physiological processes; however, the influence of carcinogenic agents can lead to misevaluation and the production of information for neoplastic transformation.'

It has been shown that, in the replication of poxviruses in cell cultures, most of the virus remains inside the infected host cell and that no more than 10 % of the total yield is released into the medium. Most studies of poxviruses have been performed with intracellular virus released artificially from infected cells; the small amounts of extracellular virus have been discarded, on the tacit assumption that, since both forms are infective, they are identical. BOULTER and APPLEYARD have contributed important recent demonstrations that the intracellular and extracellular forms of poxvirus differ in several respects. They describe what is currently known of the properties of extracellular poxvirus, whose differences from intracellular virus – most importantly in the nature of their surface antigens – the authors assess to be as great as those between distinct serotypes of other viruses. They also discuss the implications of this phenomenon with particular emphasis on its significance for immunity to poxvirus infections and in development and assay of vaccines.

With the increasing knowledge of fundamental biophysical and biochemical properties of the agents ecologically classed as arboviruses, it has become possible to classify many of them in groups which include chiefly members that are not arthropod-borne, e.g., arenaviruses, rhabdoviruses, etc. When the togavirus group was established to include RNA viruses with a lipoprotein envelope and with other structural properties like those of arbovirus serologic groups A and B, it could be foreseen that agents with similar structure might also be identified among hitherto unclassified viruses without known arthropod transmission. HORZINEK has compiled the available information on these 'non-arbo togaviruses', which include the viruses of rubella, equine arteritis, bovine virus diarrhea, and hog cholera, and lactic dehydrogenase virus of mice. For comparison, relevant recent data are also presented on the arthropod-borne togaviruses alpha- and flaviviruses, which constitute serologic groups A and B, respectively). The author points out that many of the non-arbo togaviruses are likely to escape detection in routine virologic studies, since many of those recognized have been shown to be noncytopathogenic, or to be cytopathogenic only under special culture conditions. Yet the ability of the togaviruses to multiply in invertebrate, vertebrate, and even plant cells indicates great versatility of the members of this group; their properties merit further study from both theoretical and medical considerations.

In a volume of this series published ten years ago, LEVINE reviewed, in terms of the effect of X-irradiation of the host cell on animal virus infection, the then-current reports dealing with radiation as separating the ability of a cell to divide from its ability to grow, radiation as a tool for following intracellular development of virus, and other studies in this area that had been made possible by advances in tissue culture permitting the effects on individual cells to be measured. Since that time, there has been a great expansion of knowledge of the biochemical events occurring during replication of animal viruses, and radiation has been used extensively to study various problems regarding the responses of cells to virus infection. In the current review, LEVINE incorporates the new studies not only with X-irradiation but also with other kinds of radiation, and reexamines the earlier studies in the light of the new information that has been amassed. The significance of X-ray survival curves, the effects of X-irradiation on animal cells, and mechanisms in animal cells that repair X-ray or UV damage are summarized. The effects of host-cell irradiation on the cell's response to virus infections, on its yield of virus, and on the induction of latent oncogenic viruses are discussed. Information on intracellular development of viruses, obtained by use of radiation methodologies, is also surveyed. Explanations of the observations are proposed in terms of differing virus replication mechanisms and the mechanisms of X-ray and UV action.

The science of serological epidemiology has reached a high degree of sophistication in a relatively short time, thanks to John R. Paul, Richard M. Taylor, and other pioneers who developed this field under vastly more difficult conditions than those of present-day laboratory workers. But the application of this science in periodic serologic surveys to monitor the immune status of population groups is a relatively new approach which has been too little exploited. With the widespread availability of effective vaccines against poliomyelitis, measles, rubella, and other viral diseases, there are still problems remaining in the control of these preventable viral infections. In her review, HORSTMANN describes the means that are at hand for serological surveillance of vaccinated populations to ensure that immunization is reaching all sectors of supposedly well-immunized populations, to determine whether 'herd immunity' is being established and maintained at levels sufficient to block introduction and spread of disease agents, and to investigate whether vaccine-induced antibodies persist over the years at protective levels. Such monitoring can provide advance warning of deficiencies in immunity and can identify target populations whose protection requires special efforts to reach those who are failing to receive adequate immunization or to revaccinate those whose levels of immunity may be waning.

Viral diagnostic laboratories now occupy an important place in public health. BRADSTREET, PEREIRA, and POLLOCK update the article published a decade ago in this series, describing the development, organization, and current activities of the Public Health Laboratory Service, a national Service covering England and Wales and supervised from its central headquarters in London. From the Central Public Health Laboratory at Colindale, which is a group of Reference and Special Laboratories, the scheme spreads out to ten Regional Laboratories located at University centers, and to more than 50 Area Laboratories situated throughout the regions served. Important features of the Service include the stimulation and coordination of individual and group research, the training of medical and science graduates as a regular on-going activity of the laboratories, and the maintenance of close association with the Hospital Service and with Government Departments. Weekly reports of diseases diagnosed in each laboratory are analyzed at headquarters and the analyses are distributed each week to the participating laboratories and to other health agencies, thus providing an early warning system concerning the prevalence and distribution of various infecting agents in the country. Directors of laboratories meet regularly, providing a basis for cooperative efforts in handling emergency needs and for establishment of Working Parties to undertake special investigations. In the virologic area, in addition to the regional and area laboratories working together with the Virus Reference Laboratory at Colindale, virologic investigations in more than 50 laboratories attached to teaching hospitals and universities throughout Great Britain are assisted by reagents supplied from the Central Standards Laboratory for Serological Reagents; these laboratories also participate in virologic surveys and investigations set up by the Epidemiological Reference Laboratory.

Diseases associated with cutaneous eruptions have been reported throughout human history. Correct definition on clinical bases alone is not always possible even today. WENNER has brought together in his review clinical, epidemiological, and biological aspects of virus infections which are associated with eruptive fevers. Discussions center largely around interaction of the virus with the human host; properties of the virus in culture are dealt with as these serve as modified models of the probable events that occur at the cellular level in the human patient. The author gives special attention to virus diseases which have not been recently reviewed, and to new information that has been gained in the decade since the earlier review by WENNER and LOU in this series. Sections are included on eruptive syndromes associated with enteroviruses, herpes simplex virus, varicella/zoster virus, cytomegalovirus, infectious mononucleosis, poxviruses, arboviruses, rubella, measles, and a number of other virus diseases having some cutaneous manifestations. The bibliography has been enhanced in value by subgrouping it in accordance with the viruses discussed.

Virus classification has not arrived at a stage in which groupings can be made with absolute certainty, as if based on firm phylogenetic relationships, and changes in groups, names, and even in some of the criteria for classification may be expected. Nevertheless, some groups established initially as only tentative and expedient begin to look like 'real' taxonomic groupings that may reflect natural relationships. The time seems to have arrived for the International Committee on Nomenclature of Viruses to become the International Committee on Taxonomy of Viruses. In the final chapter of this volume, the Editor reports on progress in classification and nomenclature of animal viruses. Schematic diagrams show separation of RNA- and DNA-containing viruses into major groups on the basis of physical and chemical properties. Also included is a tabulation of virus groups in terms of the polymerases which they contain or induce in the infected cell.

Readers of this series are encouraged to propose topics that they recommend for review, and also to offer suggestions for authors who might be invited to prepare such reviews. Presentations on topics requiring more lengthy coverage than would be available in this series may be proposed for inclusion in single-volume form as a part of the companion series, Monographs in Virology.

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