competence than any disciplinary machinery that may evolve. Mr. Klein echoes the misapprehension of many laymen in saying that "the urgent need is to devise some system which does protect the public by maintaining standards." But the profession's reluctance to make "any constructive contribution" towards this is well founded on the belief that no disciplinary system will have any effect on standards: they are not maintained in that way at all. That some disciplinary machinery is needed cannot be denied. But a real risk is that it would be harmful to the patient by forever staying his doctor's hand from decisive action. The fulfilment of this bureaucrat's dream could reduce the number of complaints in proportion as it impaired the doctor's effectiveness.

[1] Klein, R., *Complaints against Doctors*. London, Charles Knight, 1973 (pp. 193; £4 net).

Sources of Influenza

The last few years have seen a considerable expansion of research into animal influenza. The interest in this subject stems less from the economic impact of influenza viruses on the animals than from the possibility that animal infections may be the source of the new pandemic strains of influenza in man. Studies of the infection in animals may also yield knowledge of its epidemiology, immunology, and pathology in man. The World Health Organization has played a leading part in stimulating and co-ordinating studies on animal influenza in several countries and has recently published a collection of original papers on this subject.[1]

In 1930[2] R. E. Shope isolated the causative agent of epidemics of swine influenza in the U.S.A. Later the viruses causing fowl plague, duck influenza, and equine influenza were isolated. However, little significance was attached to these viruses until after 1955, when W. Schäfer[3] and others recognized that fowl plague virus belongs to the same antigenic type as the human influenza A virus first isolated by W. Smith and colleagues[4] in 1933. Subsequently the other isolates from animals were characterized as influenza A.

The antigenic relationships between influenza A viruses in man and animals is based on their possession of common antigens located internally in the virus particle, namely the ribonucleoprotein and internal matrix protein.[5] However, influenza viruses from man, swine, horses, and birds vary considerably in the antigenic character of the two antigens present on the surface of the virus particle, the haemagglutinin and the neuraminidase. It is these two antigens, which exist in a wide range of antigenic varieties, which provide the antigenic basis for the classification of influenza A viruses into distinct subtypes.

Considerable emphasis has been placed on the search for antigenic relationships between the surface antigens of human and animal influenza viruses which might indicate epidemiological relationships. In early studies, which were based mainly on the properties of the haemagglutinin antigens, little convincing evidence of such relationships was detected. The first clear cut evidence of close antigenic relationships was provided by H. G. Pereira and colleagues,[6] who showed that several avian influenza A isolates contained neuraminidase antigens, of subtype N2, which were antigenically identical to the neuraminidase of human Asian influenza virus (A/Singapore/1/57 (H3N2)), which first appeared in the Far East in 1957. Later studies have disclosed numerous other antigenic relationships between influenza A viruses from different hosts.[7] The striking finding from these studies is that antigenic relationships between the neuraminidase antigens in viruses isolated from different species are frequent. In particular, avian influenza viruses frequently contain neuraminidase antigens identical to those of virus strains from mammals. Antigenic relationships in the haemagglutinin antigens were infrequent.

It was only recently that antigenically identical influenza viruses have been recovered from human and non-human hosts. During the recent human influenza pandemic caused by the Hong Kong strain (A/Hong Kong/1/68 (H3N2)) W. D. Kundin and others[8 9] produced evidence that the Hong Kong virus frequently caused asymptomatic infections in swine. Yet no evidence was found for infection in swine before the Hong Kong virus appeared in man in 1968, suggesting that the route of infection was man to swine rather than the reverse. There is now evidence from several countries that the human Hong Kong virus can infect a wide range of animals, including dogs,[10] cats,[11] chickens,[12] calves,[13] and bears,[14] and it seems likely that in each case infection is from human sources. In its ability to infect a wide variety of different hosts the Hong Kong virus appears to differ from former human influenza viruses, for which evidence of infection in non-human hosts has been infrequent and controversial. These findings strongly suggest that the human Hong Kong virus has the potential of establishing animal reservoirs of infection.

The epidemiological behaviour of Hong Kong virus may have historical parallels. P. Laidlaw[15] reported in 1935 that antibody to the Shope strain of swine influenza could be detected in the sera of persons who had been infected during the great pandemic of 1918. This finding, which has stimulated considerable speculation among epidemiologists, has been interpreted as indicating that the human influenza virus of 1918 persisted in swine populations as the classical swine influenza virus.

Genetic recombination (reassortment of genes) readily takes place between different strains of influenza virus, and this has led to the hypothesis that new human pandemic strains of influenza A virus might arise in nature as a result of the reassortment of genes between human and non-human strains of influenza virus. Genetic and biochemical studies on influenza have shown that genetic reassortment may be accompanied by the segregation of the genes coding for the haemagglutinin and neuraminidase antigens and virulence.[16 17] R. G. Webster and colleagues[18] have also shown that such genetic recombination may take place *in vivo* in experimental animals doubly infected with two different influenza A viruses. It is tempting to postulate that recombination between a non-human and a human influenza virus in nature might result in progeny which combine the surface antigens of the non-human virus with the property of virulence for man. Thus it is possible that one progenitor of the Asian influenza virus was an avian virus bearing neuroaminidase antigen N2. It may be postulated that conditions favouring the spread of such a recombinant in man would be the existence of an ecological niche which appears when immunity to the currently prevalent influenza A virus is at a high level, so that this virus no longer spreads.

Whether or not non-human sources of influenza are important to the appearance of human influenza pandemics either by direct crossing of host barrier or by recombination has yet to be established. Nevertheless there is much to

justify the study of the ecology and antigenic spectrum of influenza A viruses in non-human hosts. It may be of significance that influenza B virus, which has not been clearly shown to exist in animal hosts, has only a minor degree of antigen variation, with a single antigenic subtype, and is associated with localized outbreaks rather than widespread epidemics as in the influenza A virus.

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Aggressive Treatment for Hodgkin's Disease

It is only some 10 to 15 years since Hodgkin's disease was held to be incurable. Several retrospective studies then disclosed that significant numbers of patients were surviving for many years. Many had indeed been cured[2] of Hodgkin's and other related lymphomas in the sense that those who survived about 10 years from the date of treatment had by that time acquired an expectation of life identical to that of normal people of the same age and sex. The best results followed vigorous radiotherapy to patients whose disease was restricted to one or at most two contiguous lymph node regions. Moreover, a new histological classification[3] stimulated renewed interest in the many variable factors which influence prognosis—age, sex, histological features, extent of disease, and adequacy of treatment. Two important consequences followed. The first was an increasingly aggressive approach to treatment, both by irradiation and by cytotoxic drugs; the second an equally aggressive approach to the investigation of the patient before starting treatment.

The investigation of a patient with Hodgkin's disease was formerly confined to a routine general examination including chest radiographs, and analyses of blood, bone marrow, and urine. Today many though not all major centres demand in addition to these measures renal pyelography, venacavography, bilateral pedal lymphangiography, liver and spleen isotope scans, followed by laparotomy to permit splenectomy, selective lymph node biopsies, several wedge and punch biopsies of the liver, and in females the transposition of the ovaries to the midline with the object of protecting these organs from subsequent irradiation. This extensive investigation has several objectives. It permits a detailed mapping of all diseased areas, so that the patient may be assigned to an agreed stage—I, II, III, or IV. The presence or absence of symptoms or signs of systemic disease (pyrexia, pruritus, anaemia, weight loss) is indicated by the addition of the letter B or A. Thus stage III A signifies generalized lymphadenopathy without systemic features.

This staging procedure allows comparisons to be made between groups of patients, either in one or in different centres, and is a prerequisite for any therapeutic trial. The detailed mapping of disease also determines how extensive the treatment has to be and whether radiotherapy or chemotherapy or some combination of both is appropriate in any one case. When the abdomen is found to be free of disease radiotherapy is usually confined to the neck and thorax, though some clinicians prefer to add "prophylactic" irradiation to the para-aortic lymph node chain. When the abdomen is involved "total node" radiotherapy or chemotherapy or both are advised. In short, the essence of treatment for the patient with Hodgkin's disease today is attack, and it can be very trying for the patient. Moreover, the detailed investigations now carried out seem to be justified by the new and increasing successes from equally aggressive treatment.

Despite new knowledge and changing attitudes it remains true that when Hodgkin's disease is confined to one region, such as the neck and mediastinum, especially in young females with the nodular sclerosing type of the disease, radical radiotherapy is the best treatment. It offers high levels of cure in terms of normal life-expectancy. The transient but real discomfort created by such vigorous *x*-ray treatment is fully justified by the favourable prognosis. When the disease has become more widespread, occurs in older patients, and when lymphocytes are becoming scanty in histological sections, the prognosis is now known to be distinctly worse. Total node radiotherapy is employed in some centres for patients with generalized lymphadenopathy. This entails irradiating en bloc the lymph node chains in the neck, mediastinum, and axillae, followed by the abdominal para-aortic, iliac, and inguinal nodes, and also the splenic axis when the spleen proves to be involved at laparotomy. However, there is a tendency either to follow this radiation therapy with combination chemotherapy or even to rely on the latter alone.

Though cytotoxic drugs have proved useful in Hodgkin's disease since the 1940s, it is only during the past decade that their true value has been found to lie in combining the effects of several drugs at once. This form of treatment may be continued for a year or more depending on the response of the disease and on the resilience of the patient and his bone-marrow in the face of repeated courses of such toxic agents.

This new aggression against Hodgkin's disease reflects a new optimism among clinicians directly concerned with the management of the patient. It is an optimism which increasingly pervades the whole field of oncology. Unhappily, outside oncological circles there remains a disturbing despondency and uncertainty about whether "anything can be done" for a patient with a lymphoma. This attitude is to be found in the medical profession as well as in the general public. The answer to it must surely lie in aggressive education.

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