LETTERS

Note to authors of letters: Please note that all letters submitted for publication should be typed with *double spacing*. Failure to comply with this may lead to delay in publication.

Type A influenza

Sir,

As Dr Hope-Simpson points out in his editorial (June *Journal,* pp.267-269), type A influenza is a true global phenomenon with distinct seasonal patterns of incidence, showing a coordinated rise and fall in epidemic viral activity. Type A epidemics commonly affect distant places, over a narrow belt of latitudes, simultaneously (as can be seen from studies of the 1957,[1] 1968/9[2,3] and 1918[4] pandemics caused by antigenic shifts in the type A influenza virus). As Hope-Simpson suggests, the question raised is not whether we make the present model of transmission from type A influenza based on person to person spread fit the observed epidemology (it has been shown there is little evidence to support this belief), but can we find a new theory which leads to a more realistic prediction than we have at present? One theory put forward in Hope-Simpson's editorial — the latent carrier hypothesis — clearly needs further investigation. The theory has distinct advantages over older ideas in that it is able to account for both the seasonality shown by epidemics, the contemporanoeus nature of household infections and also the correlation of epidemic peaks in widely separated places. It can also account for the antigenic shift seen in the influenza virus during pandemic years.

Another attraction of this theory is that it predicts observable effects by which it can be tested (like any good scientific theory). We should observe an increased incidence of influenza in the households in which one or more individuals contracted clinical influenza in previous winters. Unfortunately, the present limited amount of available evidence does not support this prediction.[5,6] One study has shown that households previously infected with type A influenza had a 70% reduction in influenza attack rates in subsequent winters.[6]

It is also difficult to see how identical strains of the virus can arise and cause epidemics over widely separated areas simply by random mutation to escape specific host immunity. By this mechanism the odds that random mutation of a particular subtype would give rise to identical offspring must be infinitesimal. Clearly more detailed studies are required to test the validity of this idea. One final objection to the idea that the influenza virus is lying latent in the tissues of the carrier host is raised by Kilbourne who states 'There is little evidence to suggest that the influenza virus has the potential for persistence and latency indeed, even the most temporate viral strains...are found to be cytonecrotizing if infected cells are carefully examined by microscopy...Therefore it is logical to look beyond man himself for the origin of pandemic viruses.'[7]

An alternative viewpoint is to abandon all attempts to confine influenza under the mantle of infectious diseases and return to the commonly held belief of 200 years ago, that type A influenza is a true airbourne pathogen spread on a global scale by atmospheric phenomena.[8] Again this idea can account for the observed epidemiology, the seasonality, the nature of household infections, the correlation of epidemic peaks in widely separated places and the latitude dependence of influenza. However, it does not offer any explanation as to the origin of the causative viral strains, for the antigenic drift seen in the interpandemic years, for the antigenic shift causing pandemics and why viral subtypes of type A influenza reemerge after many years of absence.

Despite the limitations described, both these theories agree better with the observed behaviour of type A influenza than does the present theory of person to person spread and they warrant further evaluation.

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Familial hypercholesterolaemia

Sir,

In their letter (July *Journal,* pp.348-349) Drs McCormick and Skrabanek summarize difficulties in showing any benefits of treatment for hypercholesterolaemia. This was, however, mostly irrelevant with regard to the special problems of familial hypercholesterolaemia, previously addressed by Lorimer, Mann and others including myself (June *Journal,* p.299). Familial hypercholesterolaemia is rare, and general population studies overwhelmingly recruit patients with less specific problems, where the duration and consistency of the lipaemia then found is not known. From studies of genetic disorders, including those with delayed expression, the duration of abnormalities in plasma correlates with the rate of clinical expression. Thus in most trials the background of lipaemia in patients recruited is uncertain, and clear results from intervention trials are improbable. A further confounding factor is the habit

of the control population to adopt the advice on diet and life-style given to the test group, as happened in Finland (Pyorala K. Lipoproteins and coronary heart disease in diabetic and non-diabetic subjects in eastern and western Finland. Presented at Symposium on Lipoproteins and Coronary Heart Disease, Espoo, Finland, January 1985).

Familial hypercholesterolaemia is different. The lipoprotein changes in plasma — elevation of low-density lipoproteins plus some reduction of high-density lipoproteins components — are expressed from the first few days of life with little change until diagnosis and treatment,[1,2] and thus the integrated, that is, time-based exposure to component abnormality, can be approximately determined.[3] Clinical expression is also severe, although variation and particularly interfamilial variation is wide. It is not clear that growing interest in and recognition of this disorder in recent years has led to clinical benefits, but experienced units do not write off patients with familial hypercholesterolaemia for the following reasons:

1. Most patients are still identified because of a clinical event, including death. The benefits of earlier recognition and treatment remain to be assessed, for which greater awareness and extensive family screening are required.

2. Rigorous treatment of some patients plainly induces regression of tissue deposits, with freedom from clinical cardiovascular disease to an age beyond that at which such expression has arisen in other untreated members of the same family. This has also been shown for homozygote sibling pairs, in studies from the Hammersmith Hospital and St George's Hospital.[4,5]

3. In assessment of response to treatment, denial of treatment to a control group is unethical. Comparisons between good and bad responders are also unhelpful as the basic defects involved may differ. Experienced units also see patients and families where major treatment and apparently good compliance produces trivial change in lipoprotein profiles or clinical course. Parental studies in homozygotes, and more recent gene probe studies in heterozygotes show that familial hypercholesterolaemia is significantly heterogeneous,[6] and responses to treatment may also vary. Subgroup analysis is proceeding rapidly, and may allow improved definition of prognosis, and of amenability to treatment by different approaches: some patterns may indeed be untreatable.

4. Calculations based on integrated exposure to plasma abnormalities, as determined from age and lipoprotein profiles at first presentation,[3] show that progression of features like corneal arcus and clinical ischaemic heart disease, are more closely related to age than to extent of abnormality in plasma, indicating that progression is becoming time-dependent rather than dose-dependent. These observations also suggest that inadequate advice and treatment, with only moderate control of lipoprotein abnormalities, are unlikely to offer benefits; many patients receive such advice before referral to informed units.

5. New drugs now on trial which inhibit the rate-limiting enzymatic step of endogenous cholesterol synthesis, appear in combination to offer the prospect of complete normalization of lipoprotein profiles in many patients, although any other effects remain to be revealed.

6. Patients identified should also be allowed the benefits of control of other major risk factors such as hypertension and smoking.

Present approaches to familial hypercholesterolaemia are not widely effective, but the assessment of reasoned changes to those approaches, through which any benefits can be assessed, cannot be ethically dismissed. For a start we need to know what can be done if patients are identified early, treated rigorously, and offered the diagnostic and therapeutic advances now in hand. The original point of this correspondence remains that general practitioners are important in early recognition; from this all else follows.

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Deaths — why inform just the hospital?

Sir,

I agree with Dr Balfour that it is indeed an unhappy experience to be faced by a relative whose loved one has died, when we have had no knowledge of the fact (August *Journal*, p.401). This does not only happen when the hospital forgets to notify the surgery, but also when the family or close relative forgets to inform us. As a practice administrator in a four-partner group practice with 11 700 patients, I have always had a special interest in medical records and their upkeep. We still use the Lloyd George envelopes, and, though these are often regarded as too small for the amount of detail to be recorded, I still believe it is possible to use them efficiently.

Many of the patients who require the district nurse may also need the services of other agents, for example, social services or after care services, or may require a wheelchair. Our practice has devised a system to ensure that these other agencies are informed about a patient's death. If a request is made to any service the procedure is as follows:

1. An entry in red is made in the patient's records. For example, 'D/Nurse — general care, Tel: 12345. Wheelchair ordered from Leeds (ALAC), local office 25656. '

2. The front left-hand corner of the record envelope is coded. (This is usually in the space for the last change of address. For example, 'D/N 12345. SS 23456. ALAC 25656. ')

Recording the telephone number makes it quicker for the next person using the notes to contact the same service, considering that there are several social service teams covering our practice area, and in some cases two teams covering the longer roads.

When the practice is notified of the death of a patient, the record envelope and the age–sex cards are removed from