MR. VAUGHAN: I agree about more democracy—it's very important. If I were a doctor I'd be very angry about the lack of it in the G.M.C. at present. I think the G.M.C.'s functions should be narrowed rather than be extended; there's far too much interference with what doctors are doing. I'd restrict the functions to maintaining the *Register* and to supervising medical education.

DR. ALLEN: I'm totally against retaining the G.M.C.: it's a handicap both to the community and to the profession. But, given that it's going to stay, the fundamental principle is severely

to restrict its functions. Education must be taken away from it—it's wrong that the same people who are running education also decide on the policies which underly it.

References

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A New Look at Infectious Diseases

Infectious Mononucleosis

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Infectious mononucleosis is an illness of uncertain cause which is characterized by the clinical features of fever and lymphadenopathy, haematological changes of mononuclear leucocytosis and atypical mononucleosis, and by the presence in the serum of agglutinins to sheep red cells which can be removed by absorption by ox red cells but not by guinea-pig kidney.

Aetiology

It is usually assumed that infectious mononucleosis is the result of infection with a specific virus, but a causal agent has never been demonstrated with certainty. Recent observations have indicated an apparent association with the Epstein-Barr virus (E.B. virus), but more research is needed to define the exact role, if any, of this organism in the causation of infectious mononucleosis.

Epidemiology

INCIDENCE

Since infectious mononucleosis is not a notifiable disease and since the diagnosis is often made without all the diagnostic criteria being fulfilled, it is not possible to give a reliable figure for incidence. Nevertheless, findings from a variety of studies suggest an incidence of infectious mononucleosis in the general population of the United Kingdom of between 2 and 6 per 10,000 each year. The incidence of cases confirmed by laboratory findings has increased in recent years but this probably reflects only a more frequent use of laboratory facilities.

The condition has been reported at all ages but it occurs mainly in older children, adolescents, and young adults. There is no evidence of a striking predominance in either sex.

INFECTIVITY

The use of the adjective "infectious" in the name implies ready transmissibility but infectious mononucleosis as it occurs today is a sporadic illness and only rarely is a history obtained of contact with a known case. This implies either (a) a non-infective cause, (b) low infectivity, or (c) a high incidence of asymptomatic carriers.

Outbreaks of "infectious mononucleosis" have been described but, so far as I am aware, in none of these have strict modern diagnostic criteria been fulfilled.

TRANSMISSION

If the condition is indeed an infection the mode of transmission is, like the cause, uncertain. Volunteers have occasionally become ill after inhalation of material from the mouths and throats of patients, after inoculation of material from lymph nodes of patients, or after transfusion with blood from patients. Nevertheless, only rarely have the illnesses in the volunteers fulfilled the criteria for diagnosis of infectious mononucleosis, so that coincidental development of the disease cannot be ruled out.

Spread by kissing, especially where intimate enough to lead to transfer of droplets of saliva, has been suggested as the most likely mode of transmission largely to explain the peculiar age distribution. This suggestion has been taken up with enthusiasm by patients, doctors, the writers of medical articles in the lay press, and interested public alike and has been largely instrumental in the condition becoming extremely fashionable. For those who find the concept of transmission by kissing unacceptable, spread by sharing of drinking utensils is often offered as a suitable alternative.

INCUBATION PERIOD

As case-to-case infection is rarely detected, the exact moment of infection and so the incubation period cannot be accurately known, though figures are frequently quoted within the range 7–49 days. Clearly any figure is surmise.

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Pathology

As its name implies, infectious mononucleosis is a condition characterized by the proliferation of mononuclear cells—which are most readily found in the blood but which may occur as infiltrates in any organ of the body. The spleen and lymph nodes are the most commonly involved organs resulting in their enlargement in most cases. The mononucleosis is due to an increase in normal lymphocytes and monocytes but also to the appearance of atypical mononuclear cells varying greatly in size, shape, and staining properties. These atypical cells do not differ from those found in several other conditions such as rubella, infections hepatitis, malaria, brucellosis, and some drug hypersensitivity reactions but they are more numerous in infectious mononucleosis than in these conditions.

The mononuclear proliferation is accompanied by definite immunological changes but the most characteristic change is the development of agglutinins to sheep red cells (Paul-Bunnell test). Such heterophile agglutinins may also be found occasionally in normal people and in such conditions as serum sickness, infections hepatitis, aplastic anaemia, leukaemia, and reticulosis—but those found in infectious mononucleosis are different from the others in that absorption with ox red cells removes the agglutinins while guinea-pig kidney suspension does not remove the agglutinins (Paul-Bunnell-Davidsohn test). These pathological changes form the basis for the laboratory diagnosis of infectious mononucleosis.

Clinical Features

Although infectious mononucleosis is frequently described as having protean manifestations, most patients present to the practitioner with one or more of three complaints—sore throat, swollen glands in the neck, and fever. These features may be of sudden onset in a patient previously well but often there has been previous vague ill health for several days or even weeks with symptoms including malaise, excessive fatigue, headache, anorexia, nausea, excessive sweating, and abdominal discomfort which may be generalized or localized to areas overlying the liver or spleen or both.

SORE THROAT

Sore throat may occasionally be present without obvious signs in the throat but usually throat changes of pharyngitis are present. In most instances it is impossible to distinguish on clinical grounds the pharyngitis of infectious mononucleosis from that of other viral infections or streptococcal involvement, for inflammation of pharynx and palate and non-exudative or exudative (follicular or confluent) tonsillitis may occur in any of these conditions. When throat involvement in infectious mononucleosis is severe and when sore throat has been present for several days the changes may be those of thick creamy exudate over most of the tonsillar surfaces, thickly furred tongue, obvious halitosis, nasal congestion resulting in a nasal tone to the voice, and an isolated cluster of petechiae at the junction of hard and soft palates—and there will be associated tonsillar lymphadenopathy, posterior cervical lymphadenopathy, and, usually, enlargement of the lymph nodes deep to the upper parts of the sternomastoids. Such changes are highly suggestive of infectious mononucleosis, especially if the patient has already been treated with an antibacterial drug for several days without improvement and is within the 15-25 year age group.

LYMPHADENOPATHY

Posterior cervical lymph node enlargement may not appear for several days but is thereafter almost invariable even if other lymph nodes are not palpably enlarged. If the throat is affected (as it usually is) other cervical nodes will be palpable, as des-

cribed above. A minority of cases have more widespread lymphadenopathy and if such nodes as submental, preauricular, postauricular, epitrochlear, or the nodes along the nerves to the serratus anterior are prominent, then infectious mononucleosis is highly likely in the absence of local causes.

The spleen becomes palpable in about half of the patients with infectious mononucleosis but rarely extends to more than two finger-breadths below the costal margin.

FEVER

Like posterior cervical lymphadenopathy, fever is almost invariable, though it may be low grade and rarely exceeds 103°F (39.4°C). Its duration varies from a few days to several weeks.

RASHES

A wide variety of rashes—erythematous, urticarial, and purpuric have been described in infectious mononucleosis in up to about 15% of patients in large series. In patients untreated by ampicillin the commonest rash is a sparse, discrete, non-irritative, small macular erythema, transient but sometimes recurrent and variable in distribution though frequently involving the trunk and the extensor aspects of the forearms.

Patients with infectious mononucleosis who are inadvertently treated with ampicillin almost invariably develop an extensive and florid, irritative, maculopapular erythema, which tends to become confluent and often has a purpuric element. This rash—which is often associated with an exacerbation of fever—usually appears about a week after commencing ampicillin, even if the drug has been discontinued in the meanwhile. The cause of this phenomenon is quite unknown but, in view of the frequency with which ampicillin is used in the treatment of sore throats and febrile illnesses, it is becoming one of the commonest types of rash to be seen in infectious mononucleosis.

JAUNDICE

Most patients with infectious mononucleosis have anicteric hepatitis as indicated by liver function tests but a proportion have obvious jaundice in addition to other features mentioned above. Some present with an illness clinically indistinguishable from infective hepatitis.

Complications

Complications are rare. The commonest is that of gross tonsillar enlargement and pharyngeal oedema, which may seriously impair the airway and even require tracheostomy. Haematological complications include thrombocytopenic purpura, haemolytic anaemia, and marrow depression resulting in agranulocytosis and even aplastic anaemia. Neurological complications include lymphocytic meningitis, encephalitis, transverse myelitis, polyneuritis, and mononeuritis. Splenic rupture—either spontaneous or after injury—may occur. Many other complications have been reported including myocarditis, pneumonitis, pancreatitis, parotitis, orchitis, and nephritis.

Prognosis

The duration of acute symptoms is variable but usually between one and three weeks. Some patients have a prolonged period of debility, during which they complain of tiredness, general malaise, and inability to concentrate. It is not clear what part the widely known reputation of the condition for producing this

debility is responsible for these features but a patient told he will probably feel unwell for several weeks is likely to do just that.

Complete recovery can be virtually guaranteed even when serious complications have occurred. Deaths are exceptional. Relapses and recurrences in which all diagnostic criteria are fulfilled appear to be extremely uncommon.

Diagnosis

In addition to an appropriate clinical picture it is necessary to demonstrate appreciable atypical mononucleosis (more than half of the white cells in the peripheral blood should be mononuclear—that is, lymphocytes and monocytes—and many of these should be “atypical”) and a positive Paul-Bunnell-Davidsohn test (a titre of at least 1 in 40 is usually considered necessary for a “positive” test) before a definitive diagnosis can be made.

Differential Diagnosis

CLINICAL FEATURES

Consideration of all the possible causes of the clinical features found in infectious mononucleosis is not possible in this article. From a practical point of view the most important disorders to consider are those which have specific therapy and which are severe enough to require such therapy. Most acute sore throats are due to viral infections or streptococcal infections, but other causes include Vincent's angina, diphtheria, candidiasis, and blood dyscrasias. When there is severe exudative pharyngitis with development of a “pseudomembrane” it is particularly important to consider diphtheria and blood dyscrasias such as agranulocytosis and acute leukaemia. Bacteriological examination of a throat swab and examination of a blood film will distinguish these various conditions. Most febrile illnesses without localizing signs have a viral aetiology but other infections, connective tissue disorders, hypersensitivity reactions, reticulosis, leukaemia, and neoplasia may all present in this way. If after observation and symptomatic treatment of a febrile patient for a few days the condition has not either settled or revealed itself in its true colours, a definitive diagnosis will usually be suggested by a limited number of investigations including full blood count, blood film and E.S.R., blood culture, urine examination (for blood and bile, microscopy, and culture), and chest x-ray film. It is also useful at this stage to have serum separated and stored in a pathology laboratory as the first of paired sera should the detection of various antibodies become necessary. Other investigations and even admission to hospital may become necessary but it is remarkable how commonly the diagnosis can be made as the result of the above relatively few investigations.

Apart from infectious mononucleosis and other viral infections glandular swellings in the neck may be due to local sepsis of the face, scalp, teeth, or throat—or to mumps, tuberculous lymphadenitis, reticulosis, and leukaemia. Clinical acumen will enable local sepsis or mumps to be diagnosed but examination of blood film, chest x-ray film, or even lymph-node biopsy may be necessary in some cases.

Differential diagnosis of patients with rashes will include mainly other viral infections, drug eruptions, and dermatological conditions but if pharyngitis is prominent streptococcal infection may be considered.

The only other common cause of jaundice in the age group in which infectious mononucleosis usually occurs is viral hepatitis.

HAEMATOLOGICAL CHANGES

Similar changes may occur in other viral infections, especially infective hepatitis and cytomegalovirus infections. Toxo-

plasmosis, malaria, mycoplasma infection, brucellosis, enteric fever, and tuberculosis are other infective causes of atypical mononucleosis. Non-infective causes include drug hypersensitivity reactions—especially to PAS and phenylbutazone—and reticulosis.

Paul-Bunnell-Davidsohn Test

This test, using sheep red cells, is highly specific for infectious mononucleosis and only a few adequately documented false-positive test results have been reported. It should, however, be realized, before attributing any illness with a positive Paul-Bunnell-Davidsohn test to infectious mononucleosis, that after an episode of infectious mononucleosis the test may remain positive for six months or even longer and also that anamnestic rises have been reported.

Treatment

One of the first principles of therapeutics, often forgotten, is to “do no harm.” When a condition is benign and self-limiting, as infectious mononucleosis usually is, this principle is especially important. Unfortunately, many practitioners have fallen into the habit of prescribing antibacterial drugs for patients with acute sore throats or with febrile illnesses without attempting to define the cause. The assumption is made that these conditions are usually infective and may be bacterial and that, even if viral, no harm will be done by the administration of antibacterial drugs. Full discussion of the merits or otherwise of such an assumption is not appropriate here, but some comment is justified by the occurrence of severe ampicillin rashes—often associated with considerable systemic upset—in patients with infectious mononucleosis treated with this antibiotic on presenting with sore throat or fever and before the diagnosis is appreciated.

Ampicillin is frequently given because of its broad spectrum activity when the practitioner is uncertain of the causative organism in presumed infections. In the case of sore throats most, if not all, common bacterial pathogens are more sensitive to penicillin than to any other antibacterial drug and most bacterial throat infections will respond to phenoxymethyl penicillin orally provided adequate dosage is prescribed and *provided the penicillin is given at least half an hour before meals to prevent interference with absorption by food*. Almost all bacterial sore throats will respond to benzyl penicillin by injection. Neither benzyl penicillin nor phenoxymethyl penicillin produce rashes in infectious mononucleosis. If penicillin cannot be given because of hypersensitivity, erythromycin estolate and clindamycin are preferable alternatives. Of course, there is no evidence that infectious mononucleosis is a bacterial infection and none that it is beneficially influenced by antibacterial drugs. Such drugs are not indicated in infectious mononucleosis.

Symptomatic treatment with bed rest and simple analgesics such as soluble aspirin or paracetamol is usually sufficient. Gargling with one of a variety of antiseptics is traditional. There should be no set period of bed rest and the patient should be allowed up when he feels able. The tendency to a prolonged period of debility should not be stressed lest it become a self-fulfilling prophecy.

Corticosteroids have been used, allegedly successfully, to shorten the period of illness but the merits of their use is debatable. In my opinion, corticosteroids should be reserved for patients who have important complications such as impending airway obstruction in severe pharyngitis, severe thrombocytopenic purpura, acute haemolytic anaemia, and, possibly, severe polyneuritis.