INFECTIOUS MONONUCLEOSIS IN GENERAL PRACTICE

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THIS is a description of cases of infectious mononucleosis occurring in general practice over a period of 14 years. The majority occurred in the relatively closed community of a training school for young adult men; other cases occurred in the course of normal practice in a widespread country area, and are only briefly described in order to illustrate the difficulties in diangosis which can arise.

It is certain that many more cases occurred in the practice during this period but because of the nature of the disease, and in particular the variability of its symptoms and signs they either would have been diagnosed as infectious mononucleosis or would have been diagnosed and treated as tonsillitis, upper respiratory tract infections, or infectious hepatitis.

The fact that the majority in this small survey occurred in the one training school tends, I think, to support the contention that infectious mononucleosis is more common than is generally supposed, because in the training school, all cases of unexplained pyrexia are considered to be due to infectious mononucleosis until proved otherwise. In other words, the possibility of infectious mononucleosis has to be borne in mind in a wide variety of presenting symptoms and signs otherwise it may be mistaken for appendicitis, infectious hepatitis or acute follicular tonsillitis, to mention just a few.

It was first described by Pfeiffer in 1887. He reported many cases of an acute benign illness with characteristic enlarged lymph glands occurring in children and he called it glandular fever. In 1921 Tidy described three clinical types—glandular, anginose and febrile. He noted the characteristic increase in the mononucleor cells in the blood and he called the disease infectious mononucleosis. In 1932

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Paul and Bunnell described a diagnostic test for infectious mononucleosis based on the accidental discovery that the blood serum contains heterophil antibodies in the form of an agglutinin for sheeps red cells. They considered that this test was specific for infectious mononucleosis. Since that time many series of cases have been described (Field Study 7/54 12/56 by Hobson, Radcliffe Infirmary Berkshire and Oxford County; 478 cases over 30 months: Dunnett (1963) 80 cases over three years and others) and although much more is now known concerning the various manifestations and pathological changes the casual virus is still unknown; it may be that more than one virus is involved.

As a result of these publications it is now realized, but perhaps not sufficiently widely appreciated, that infectious mononucleosis can involve practically every tissue and organ in the body. It has been shown to cause liver damage, myocarditis and neurological involvement (Dunnett, 1963) already referred to. In a recent article Smith (1964) described nine cases of a " syndrome resembling infectious mononucleosis after open heart surgery ". Two of these had a positive Paul Bunnell and it was considered that it was " most reasonable to regard the syndrome as a viral disease closely related to infectious mononucleosis and that it is transmitted by blood transfusion ". This article prompted further correspondence especially relating to the neurological complications of infectious mononucleosis. It is apparent that infectious mononucleosis is a condition of no little significance.

A total of 28 cases from the training school since 1950 to date (one of which must be discounted since it was eventually diagnosed as brucellosis) and four which occurred in practice since 1962, are briefly described to illsutrate difficulties in diagnosis (table I).

Clinical features

The one characteristic feature of all cases is the glandular involvement, although even this varied in degree and site from one patient to another. In the great majority the glands of the neck were enlarged; in particular the glands of the left posterior triangle—the enlargements being discrete and not necessarily tender. There may also be palpable glands in the axillae and groins. The spleen was palpable in about half the cases although this was not necessarily an indication of the severity of the disease.

Seventy-five per cent of cases had sore throats although the degree of tonsillar and faucial reaction seemed to bear no relation to the degree of cervical glandular enlargement.

I have seen one case (not included in this series) where the tonsillar enlargement was so great and the fetor so marked that the condition

TABLE I

ANNUAL INCIDENCE OF INFECTIVE MONONUCLEOSIS

	Months	*No.*	*Diagnosis*	*Paul Bunnell*	*Treatment*
1950	April	2	? ?	—	Symptomatic
1951	Jan. July	2	I.M. ?	+	,,
1952	Dec.	1	I.M.	+	,,
1953	March	1	I.M.	+	
1957	May–July	1	Abort fever		
1959	1. 4. 5. 6. 7.	5	3. IM; 2.?	3 + 2?	Antibiotic
1961	1. 5. 6. (5) 7. 9.	9	3 IM 3 ?	3 + 6?	(4. S) (5 Antibiotic)
1962	Dec.	1	I.M.	+	Antiobiotic
1963	1. 3. 5.	3	3. IM	3 +	(1 S) 2 Antibiotic
1964	2. 3. 5.	3	3. IM	3 +	(1 S) 2 Antibiotic
		28	16	16 + 12 (doubtful)	

might have been mistaken for diphtheria and at one stage breathing was so much embarrassed that tracheostomy was considered.

Although Caird and Holt (1958) described a " characteristic enanthem of glandular fever is an eruption on the palate consisting of multiple pin-point petechiae" and stated that petechiae may occur from the second to as late as the twenty-sixth day and their duration is related to the duration of the illness, no characteristic palatal lesions were seen.

From 1955–57 they described 200 cases which occurred in military hospitals, 51 of whom had palatal lesions which varied in nature from red macules, linear macules, white macules and vesicular lesions.

Although no palatal lesions were seen in the cases under review, it was noticed that those patients who were regular smokers could not bear the taste of a cigarette—but the significance of this is open to doubt.

Skin rashes have been described in several series of cases. The rash is usually morbilliform and may be confused with measles or german measles, or it may be scarlatiniform. In the present series only two patients were observed to develop a rash. In one this was morbilliform and persisted for two days. The other case developed a well-marked generalized erythematous rash after admission to hospital. This particular case demonstrated some of the difficulties in diagnosis. He first appeared to have a simple coryzal infection which after five days necessitated admission to sick bay because of

headache, rigors and some cough. There was then a recurrent pyrexia with an evening rise to 101°–103° F. and rigors and sweating. The tip of the spleen was just palpable and there were some moist râles audible at the left midzone. He was treated with antibiotics without effect and a blood count was normal apart from a slight leucopenia. He was then admitted to hospital and another blood count, eight days after the first, showed typical glandular fever (16 days after the onset of the illness); x-ray of his chest showed linear atelectasis in the right midzone and patchy loss of translucency in the left lower zone. His temperature remained 101° F. for a further five days and then fell promptly. The rash developed two days after admission; it was slightly irritating, and faded after two days.

Another sign which has been described and which was not observed in this series is Hoagland's sign, which consists of periorbital oedema affecting particularly the upper eyelids.

Haematological findings

It has not been possible to collect the records of all the blood pictures because the case notes of former patients are not available.

However, of the 28 cases, one can be excluded because of a final diagnosis of abortus fever. The only object in including this case in the series is to illustrate the fact that this condition may have to be included in the differential diagnosis.

Of the remaining 27 cases 16 had a positive Paul Bunnell and 11 were negative.

Haematological reports of nine cases have been tabulated and the following is a summary of the outstanding features (table II).

Eight had a positive Paul Bunnell and one was negative. The total white cell count varied from 5,000 to 15,500. The polymorph count in two was as low as 5 per cent and in those with a positive Paul Bunnell the highest polymorph count was 37 per cent. The lymphocyte count in those cases with a positive Paul Bunnell was invariably high—varying from 21 per cent to 60 per cent and atypical lymphocytes were present in all these cases in numbers varying from 62 per cent to three per cent. The E.S.R. was not unduly high in any of these cases—the highest reading being 17.

The amount of heterophil antibody present, as indicated by the titre of the Paul Bunnell did not appear to be related to the severity of the disease. In the case which has been already described the titre was only 1:28 (absorbed) and in another case, in which the illness was not so severe, nor did it last so long, the titre was 1:896 (absorbed)

It would be reasonable to expect a positive Paul Bunnell in those cases where the blood count shows a relatively high lymphocyte count together with atypical lymphocytes but the reasons for the wide variations in the titre level in different cases is a matter for speculation. It has not been possible to establish when the Paul Bunnell first becomes positive after the onset of the illness. The only estimate is that in one case it was negative eight days after the

apparent onset and positive 16 days after the apparent onset. On the other hand, it has been shown that the Paul Bunnell can sometimes remain positive for as long as three months after the onset of the illness, and when the patient has long recovered clinically.

There was one feature which appeared to be common to all and that was the recurrent pyrexia—all cases showed a regular rise of temperature in the early evening to 101°–103° F., often associated with a rigor and sweating and a fall practically to normal or below in the morning.

TABLE II

BLOOD COUNTS AND SEROLOGY

	HG%	*T.W.C.*	*Polys*	*L.*	*M.*	*A.L.*	*A.M.*	*E.S.R.*	*P.B.*	
1	107	5,100	37	40	7	5	11		1:56	
2	105	9.500	25	50	4	15	5		1:112	
3	101	5,900	66	22	8			2	—	(+ 3 mths later)
4a	91	9,600	5	21	5	62	7		1:224	14/1/63
4b	82	6,900	20	58	7	11	2		1:56	24/1/63
5	83	7,100	22	57	5	5	8	17	1:896	
6	96	12,600	72	22	5			55	—	
7a	105	15,100	25	60	5	3	6	5	1:128	19/3/64
7b	112	9,500	53	33	12	1			—	6/6/64
8	91	15,500	5	25	4	40	26	7	1:28	20/2/64
9a	82	9,200	29	50	8	7	5	7	1:56	28/5/64
9b	79	7,500	35	56	7				1:448	3/6/64
9c	83	11,600	56	40	1	1		21	1:56	29/6/64

HG% = Haemoglobin percentage
T.W.C. = Total white cell count.
Polys = Polymorph count (%)
L. = Lymphocyte count (%)
M. = Monocytes count (%)
A.L. = Atypical lymphocyte count (%)
A.M. = Atypical monocytes (%)
E.S.R. = Erythrocyte sedimentation rate
P.B. = Paul Bunnell

Complications of infectious mononucleosis affecting practically every organ and tissue in the body have been described by various authors, but in these patients no real complications were observed. Jaundice to a varying degree occurred in three cases but in view of the fact that liver involvement is reported in a high percentage of cases some degree of hepatitis must be regarded as part of the illness rather than a complication. No evidence of cardiac complications, such as have been described elsewhere, supported by ECG changes, were observed, nor of neurological involvement.

The duration of the illness varied within wide limits. Some patients returned to duty after 10–12 days whilst others required 17–24 days in the sick bay followed by periods of ' convalescence ' of up to 2–3 months before they had completely recovered from the debilitating effects of their illness.

The desire to return to work also varies within wide limits but this characteristic is not confined to glandular fever, especially in this day and age. Even so I think it is true to say, that in many cases the debilitating effects of this illness are greater than is generally appreciated. Perhaps these effects would be more appreciated if the doctor contracted the disease himself.

Treatment

The main factor influencing the decision as to whether to give an antibiotic or not, was the degree and severity of throat infection; but apart from this the administration of antibiotics appeared to have no specific effect on the course or severity of the illness.

The antibiotics used were tetracycline, penicillin or chloramphenicol. Steroid therapy was not employed, nor was it considered necessary, although in several series it has been used with apparent benefit, especially in cases of the anginose type or those with complications such as encephalitis, polyneuritis or severe hepatitis.

All the cases so far considered occurred in the relatively closed community of a school. The remaining four occurred sporadically in widely separated localities, having no apparent contact with one another, and, as far as could be ascertained, with one very doubtful exception, no other cases appeared as a result of having been in contact with them. The doubtful exception was a butcher, who would of necessity have made many contacts, and who developed infectious mononucleosis in November 1963. In June 1964 his niece, apparently not a particularly close contact developed infectious mononucleosis; confirmed by positive Paul Bunnell. His brother and his sister-in-law developed sore throats in January and February but in both the blood count was normal and Paul Bunnell negative.

This butcher, and another patient seen in December 1962 presented very similar features. The onset in both consisted of several days

(3–7) general malaise, anorexia, nausea and vomiting. There was only a mild degree of pyrexia and no obvious glandular enlargement. Obvious jaundice developed after a further 2–3 days and in addition to tenderness in the right hypochondrium the spleen became palpable and tender. Blood counts in both were typical of infectious mononucleosis—low polymorph count, 18 per cent and 15 per cent; high lymphocyte count, 58 per cent and 30 per cent; atypical lymphocytes 30 and 5 per cent and positive Paul Bunnell. In one liver function tests were done and these demonstrated that liver damage was present to a moderate degree and a subsequent test indicated recovery of normal liver function. Both were treated symptomatically and it was six weeks before they were fit to return to work.

The third patient was a young school teacher who for 4–5 years had been a fairly regular customer at the surgery because of recurrent attacks of sore throat, laryngitis and head colds. In March 1962 she appeared to have another such attack but on this occasion the symptoms were more severe than usual, and in addition to quite marked faucial inflammation many small glands were palpable in the neck and blood count showed a typical picture with positive Paul Bunnell. In this case ' convalescence ' was prolonged and it was 12 weeks before she returned to work, but whether this was due entirely to the effects of the disease I would not like to say—it may well be that her natural ' delicate state of health ' contributed to the prolonged convalescence.

The last case is that of a little girl aged seven who developed a swelling in the left side of her neck. Her mother said that she had not been well for several weeks having had a persistent slight cough with feverishness in the evenings. The swelling was in the left tonsillar area, firm and not unduly tender, and the tonsils were not obviously infected. There were no other discrete glandular swellings. There was a family history of tuberculosis and I thought that this might have a tuberculous cervical adenitis. However, the Mantoux test was negative and blood count showed typical infectious mononucleosis in the Paul Bunnell (absorbed) to a titre of 1:896. Recovery was uneventful and no secondary cases occurred in the family or other contacts.

Discussion

These cases seem to confirm what is already known about this disease, but as has already been suggested it may not be sufficiently widely appreciated that it can present itself in so many different guises and unless this fact is borne in mind the correct diagnosis will be missed. In view of the fact that fatalities are extremely rare, it might be suggested that this is of academic interest only, but, quite apart from the fact that it is a valuable exercise to establish a

correct diagnosis whenever possible, it is not wise to operate upon someone for appendicitis when the symptoms and signs are due to mesenteric glands in a patient with infectious mononucleosis.

In spite of its name, infectious mononucleosis is not highly infectious. As far as the school is concerned the 27 cases were spread out over a period of 14 years, although in 1959 and 1961 there were five and nine cases respectively, and in the month of June 1961 there were five cases.

The school draws its students from all parts of the British Isles and there are many foreign students from Africa, India and Ceylon, but no cases occurred in students from overseas. As far as could be ascertained it is unlikely (though not impossible) that the school acted as a sort of reservoir for cases, which would otherwise have been classified as sporadic, having been drawn from various parts of the British Isles; because in all cases they had been at the school at least several months before developing the disease.

No source of infection was discovered at the school itself, although at one time the matron and the chef were considered to be suspect, until they were exonerated—the matron by virtue of the fact that cases occurred after she had left, and the chef after blood examinations proved negative.

Another fact which tends to confirm its low infectivity is that no secondary cases were discovered following the cases of the butcher and the school teacher. Clinically, it is difficult, if not impossible, to differentiate between the cases which would have a positive Paul Bunnell and those which would be negative. However, complete blood counts suggest a definite picture in those cases with a positive Paul Bunnell and this raises the question as to whether a single virus is involved in these cases in contrast to the clinically positive seronegative cases which may be caused by a related virus or viruses.

The incidence of the disease in this area does not appear to be increasing, but this statement might need revision if all the cases occurring were correctly diagnosed.

In view of the increasing importance of virus diseases in general, I think that a correct assessment of the incidence of the disease is essential. This cannot be achieved without the constant realization of the many forms in which the disease can present itself, and unless clinical findings are supported by haematological and serological examinations.

Summary

Thirty-one cases of infectious mononucleosis occurring in a rural practice over a period of 14 years are described.

It is suggested that the disease is more common than is generally

realized, and that its effects are more severe than is generally supposed.

Haematological examination suggests that a characteristic blood picture is of great diagnostic significance, and the occurrence of clinically positive seronegative cases suggests that more than one related virus may be involved.

The apparent absence of contact cases suggests that there is either a high degree of general immunity, or that the disease is one of low infectivity.

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REFERENCES

Caird, F. I., and Holt, P. R. (1958). *Brit. med. J.* **1**, 85.
Dunnett, W. N. (1963). *Brit. med. J.* **1**, 1187.
Hobson, F. G., Lawson, Barbara and Wigfield, Mary (1958). *Brit. med. J.*, **1**, 845.
Paul, J. R., and Bunnell, W. W. (1932). *Amer. J. med. Sci.*, **183**, 90.
Smith, D. R. (1964). *Brit. med. J.* **1**, 945.
Tidy, H. L., and Horley, E. B. (1921). *Brit. med. J.*, **1**, 100, 452.

General Practice Tomorrow. JOHN FRY. *Brit. med. J.* 1964. **2**, 1064.

In this address, given to the Annual Meeting of the B.M.A. in Manchester, Dr Fry points out that many people have queried whether there is, indeed, a ' tomorrow ' for general practice at all, or whether it is an anachronism in the modern world of specialization and new techniques. This problem is a world-wide one and not a particular by-product of the British National Health Service. A World Health Organization committee reporting to, the question is of the opinion that general practitioners will continue on fulfil an essential function for the foreseeable future but " This is not to say that all is well in general practice today, or that it should be left to continue as it now is ".

To plan for the future it is necessary to know more about general practice as it is today. Dr Fry analyses available information on work load, the spectrum of disease as seen by the general practitioner, practice premises and ' morale '. He concludes that a ' Beeching-type ' analysis of general practice should be urgently undertaken with, if indicated, the closure of uneconomic ' lines ', and expansion of those ' lines ' more profitable medically and sociologically. A possible model for the future may be found in the Swedish type of general practice where one general practitioner, working with three to six nursing-social workers, can cope with six to ten thousand patients. Much can also be learned from the training methods for general practice employed by the R.A.M.C., and also from the incentives supplied by the career structure of this corps where it is possible to rise from ' Captain ' to ' Brigadier ' in general practice.