Epidemiol. Infect. (1992), **109**, 199–209
Printed in Great Britain

Splenomegaly in acute infections due to group A streptococci and viruses

P. M. HIGGINS
Wallings, Heathfield Lane, Chistlehurst, Kent BR7 6AH, UK

(*Accepted 8 April 1992*)

SUMMARY

Over a period of 9 years in general practice temporary enlargement of the spleen was found in 29 episodes of pharyngitis or tonsillitis, in 2 episodes of acute upper respiratory tract infection other than pharyngitis and in 6 episodes of acute cervical lymphadenitis. In five patients more than one episode of illness associated with splenomegaly was recorded.

In 26 of the 37 episodes a possible aetiology was identified. Evidence only of infection with group A streptococci was found in 14 episodes, adenoviruses or coxsackie B viruses were isolated alone in 4 episodes and in 4 episodes the only finding was the presence in the blood of more than occasional atypical mononuclear cells; in 4 episodes there was evidence of both streptococcal and viral infection. Episodes with evidence of streptococcal infection only tended to be of shorter duration and to be more evenly distributed over the year than were episodes without such evidence. Temporary splenomegaly was noted also in two children with varicella (one of whom also had streptococcal infection) and in an adult with probable rubella.

INTRODUCTION

Few doctors routinely examine the abdomens of patients presenting with symptoms or signs suggesting acute infection of the upper respiratory tract since it is rarely helpful to do so. Such infections, due to group A streptococci or the common viruses, are not listed as possible causes of splenomegaly in a recent textbook [1].

The most recent report of splenomegaly in patients with streptococcal infection (scarlet fever) appeared 80 years ago [2]. An enlarged spleen has been reported in illnesses due to adenovirus type 7 [3] and in soldiers with clinically diagnosed influenza [4]. It may also be found in apparently healthy people; in 63 (2·9%) of 2200 freshmen undergoing routine examination on entry to college the spleen could be felt; in most there was no evidence of disease and in one third of them the spleen remained palpable for at least 3 years [5].

During August 1959 I saw three children with sore throats, enlarged glands and palpable spleens. Two had febrile illnesses lasting 7 days; throat swabs did not yield group A streptococci and blood smears showed atypical mononuclear white cells in large numbers. They were not subjected to venepuncture. In the third, who

had exudative tonsillitis, the illness and fever lasted only 3 days; abnormal cells were not present in the blood, the heterophil antibody test (Paul Bunnell) was negative and a throat swab yielded a heavy growth of group A streptococci.

I became interested in the possibility that streptococcal infection might produce a clinical picture resembling infectious mononucleosis and thereafter routinely examined the abdomens of patients presenting with febrile illnesses suggesting infection of the upper respiratory tract or with cervical lymphadenitis.

RESULTS

Over a period of 9 years from 1959–67 in two practices in the Midlands I saw 49 episodes of illness associated with a palpable spleen. In three episodes infectious mononucleosis was demonstrated to be the cause. Six episodes occurred in four patients in whom the spleen was palpable at all recorded examinations over periods of 8 months to 4 years; these patients are considered to have had persistent splenomegaly of unknown cause.

The remaining 40 episodes may be classified as follows:

1. Temporary splenomegaly: 30 patients with only one known episode; in 25 there is a record of follow up until the spleen was no longer palpable.
2. Recurrent splenomegaly: five patients with more than one known episode in whom the spleen was not palpable between episodes.

Twenty-two of these episodes were in males and 18 in females. In two instances two members of the same family were affected at the same time: father and daughter in one, brother and sister in another.

Six individuals were not patients of mine. One was a temporary resident. Five were patients of other partners; one I happened to see while on duty, four I was asked to see because they were found to have palpable spleens, in one case on three occasions. These patients were followed up by their own doctors and the outcome though probably favourable is not recorded. Thirty episodes in patients on my list were seen in my first practice over 7 years from 1959–66. My list averaged 2996 patients over the period. The incidence therefore was 1·5 episodes per 1000 person years.

Four episodes were encountered in my second practice over 2 years during which my list grew from nought to 5400 patients.

During 20 years in a London practice with an average list of 1000 patients I saw only one case of splenomegaly not due to infectious mononucleosis and that was in a boy of 5 not on my list of patients. I do not have details of this case and he is omitted from the analyses that follow. In all three practices there was, as compared with the general population, about double the proportion of children and of families in which the father was employed in unskilled or semi-skilled work. For 19 months in 1963–4 I recorded details of all patients seen with acute infections of the upper respiratory tracts of up to 5 day's duration. During that time I saw 270 episodes of acute sore throat among my patients, in 119 associated with a positive culture for group A streptococci. Over the 19 months I saw ten patients on my list with acute sore throat and splenomegaly: 3·7 % of all episodes of sore throat. In six throat swabs yielded group A streptococci: 5 % of all patients with sore throats yielding group A streptococci.

Table 1. *Episodes of splenomegaly by age of the individual and by diagnosis*

Age (years)	Pharyngitis	Cervical lymphadenitis	Other respiratory tract infection	Other* conditions	Total
0–4	2	1	0	0	3
5–9	22	5	1	2	30
10–14	2	0	0	0	2
20–29	0	0	0	1	1
30–39	3	0	1	0	4
All ages	29	6	2	3	40

*Other conditions: varicella (2 episodes), ?rubella (1 episode).
One child omitted (see text).

In London I saw, in an average year, ten patients with sore throat yielding group A streptococci.

Presenting illness

In 29 of the 40 episodes the patient presented with sore throat or was found to have exudate in the throat (Table 1). These are classified as episodes of pharyngitis. One of these patients is recorded as developing measles 3 days later. Three-quarters of all episodes of pharyngitis occurred in children aged 5–9; the three episodes in those over 15 were all in the 30–39 age group.

In six episodes the main complaint was painful swollen glands in the neck without sore throat though in five the patient had had a sore throat within the preceding 2 weeks. These are classified as cases of lymphadenitis.

In two episodes the patient presented with symptoms suggesting infection of the upper respiratory tract other than pharyngitis: a feverish cold in one case and a 'flu-like illness in the other.

Two patients (one with recurrent splenomegaly) presented with varicella; in one the rash was infected with group A streptococci.

One adult who presented with swollen occipital and cervical glands probably had rubella.

Investigations

Swabs for culture of bacteria were taken at the first consultation from all but two patients. A satisfactory throat swab could not be obtained in another patient (M.Se.) from whom nasal swabs were taken.

Facilities for virus culture were available from 1962–8 and nose and throat swabs were taken for culture of viruses as well as bacteria in 7 of the 33 episodes that occurred during that period.

Blood was examined for atypical white cells in 27 episodes. In 15 episodes a Paul Bunnell (PB) test was done and in 22 episodes at least one estimation of the antistreptolysin (ASL) titre was carried out.

Episodes with evidence of streptococcal infection

In 19 episodes (in 18 patients) evidence suggesting streptococcal infection was found. Group A streptococci were isolated from throat swabs in the first week of the illness in 12 episodes. In seven other episodes not yielding group A streptococci

Table 2. *Episodes with evidence of streptococcal infection*

	Sex	Age	Glands* T	C	A	Throat swabs	ASL U/ml 1	2	Comments†
Pharyngitis									
R.A.	M	3	+	−	−	Gp A‡	—	—	—
A.S.	F	6	+	+	+	Gp A	< 50	240	PB neg; WBC neg
A.W.	M	6	−	+	+	Gp A	—	—	PB neg; WBC neg; hepatomegaly
P.M.	F	6	+	−	−	Gp A	—	—	Measles rash later
K.B.	F	7	−	+	−	Gp A	—	—	Swab pos 5th day
S.Lo.	F	8	+	+	−	Gp A	230	—	PB neg; Occ atypical WBC
D.L.	M	5	+	+	+	Gp A	< 50	—	WBC neg; FU by own doctor
B.D.§	F	10	+	−	−	Gp A	< 50	300	PB neg; WBC neg
B.D.§	F	11	+	+	−	Gp A	—	—	No FU
J.D.§	M	31	−	−	−	Gp A	350	—	WBC neg; FU by own doctor
R.B.	M	5	+	+	−	Neg	—	500	CFT adeno 1/80; hepatomegaly; WBC neg; brother of K.B.
M.H.	F	6	+	+	+	Neg	420	—	PB neg; WBC 19% atypical; hepatomegaly
R.P.	M	10	−	−	−	Neg	—	400	WBC neg
Lymphadenitis									
L.A.	F	5	+	+	+	Gp A	320	> 800	PB neg; occ atypical WBC; CFT adeno 1/80–1/160
S.M.	M	5	+	+	+	Adeno	800	1280	PB neg; WBC neg; splenomegaly 17 days; CFT adeno 1/8–1/32
A.P.	F	5	+	+	+	Neg	—	> 800	WBC 21800/cm; N 88%; FU by own doctor
G.A.	F	9	+	+	+	Neg	200	400	Remitting fever 4 weeks; WBC neg
Influenza									
G.Ha.	M	23	−	−	−	?	300	300	PB neg; splenomegaly 32 days; GpA+ 15th day; WBC neg
Varicella									
M.St.	F	5	−	+	+	GpA	> 800	205	WBC 13800/cm; N 71%

* T, tonsillar; C, other cervical; A, axillary glands. +, present; −, absent.

† PB, Paul Bunnell; neg, negative; WBC, white blood count; pos, positive; occ, occasional; FU, follow-up; adeno, adenovirus; N, neutrophils.

‡ Gp A, β-haemolytic streptococci, group A.

§, recurrent splenomegaly.

at least one ASL titre was over 300 U/ml; in one adenovirus was cultured from nose and throat swabs (Table 2). A titre of 200 U/ml or more is assumed to indicate streptococcal infection [6].

In 13 of these episodes the patient presented with pharyngitis though in one patient (P.M.) measles was diagnosed 3 days later. Four patients presented with

https://doi.org/10.1017/S0950268800050160 Published online by Cambridge University Press

cervical lymphadenitis, one with a 'flu-like illness and one with varicella infected with group A streptococci.

Atypical white cells were found in the blood in 3 of the 15 patients tested, in small numbers in two (L.A., S.Lo.) but comprising 19% of all white cells in another (M.H.).

In 7 of the 19 episodes blood was taken for estimation of ASL titres during the acute phase of the illness and in convalescence. In 2 of the 7 episodes, both with pharyngitis yielding group A streptococci, the first titre was less than 50 U/ml and the second 240 U/ml or more, indicating streptococcal infection contemporaneous with the illness for which they consulted. In 5 of the 7 episodes the initial titre was 200 U/ml or more. In one patient, G.Ha., who had a 'flu-like illness without sore throat the titre did not change; in four episodes titres did change by more than two dilution increments, rising in three episodes of lymphadenitis following a sore throat and falling in one episode of infected varicella. In three of these patients (L.A., S.M., M.St.) there was evidence of a viral infection also.

For three patients whose throat swabs yielded group A streptococci only the ASL titres in convalescence are known. Titres were 400 U/ml or more in all three and in two (A.P. and R.B.) complement fixation tests (CFT) were positive for adenovirus at 1:80.

In four patients (two referred by other doctors) ASL titres in the acute phase were over 200 U/ml but blood was not obtained in convalescence. In two (S.Lo., M.H.) atypical white cells were found in the blood.

Two of the 18 patients in this group had recurrent splenomegaly though one (J.D.) was seen only once by me (see later).

All other episodes

In 21 episodes (in 17 patients) evidence of streptococcal infection was not found (Table 3). Swabs were not taken in two of these and in a third (in M.Se.) a satisfactory throat swab was not obtained. Eight patients were submitted to venepuncture but in only three were specimens obtained in convalescence; all ASL titres were less than 100 U/ml.

Viruses were isolated from 4 patients with pharyngitis 3–8 years old in this group: adenoviruses from 2 and coxsackie B virus from 2.

In 5 episodes, 4 of pharyngitis, 1 of lymphadenitis, the only significant finding was the presence of atypical white cells in the blood. Two of these children (S.Ll. and A.M.) were not subjected to venepuncture and the heterophil antibody titre is therefore not known. The father, B.M., of one of them had temporary splenomegaly at the same time; white cells and PB were both normal in his case.

In ten episodes of pharyngitis, in one of lymphadenitis and in one with an upper respiratory tract infection laboratory evidence of a possible aetiology was not found.

Rubella was the probable diagnosis in one patient (O.E.), a woman of 37 who presented with cervical and occipital lymphadenopathy. All investigations were normal and her daughter developed a typical rubella rash the day that she presented.

Varicella was associated with splenomegaly in one child (M.Su.) in this group who was found to have a palpable spleen during three illnesses over a period of 5

Table 3. *Episodes with no evidence of streptococcal infection*

	Sex	Age	Glands* T	C	A	Throat swabs	ASL U/ml 1	2	Comments†
Pharyngitis									
D.H.	M	3	?	?	?	Adeno 3	—	—	Temporary resident
L.J.	M	5	+	+	−	Cox. B4	—	—	WBC neg
D.K.	M	6	−	−	−	Cox. B3	—	—	—
J.B.	M	8	+	+	+	Adeno	—	—	—
S.Ll.	F	6	−	+	+	Str. vir	—	—	59% mononuclears; mainly atypical
A.M.*	F	7	+	−	−	Neg	—	—	16% mononuclears; mainly atypical
G.H.	F	7	−	+	−	—	70	—	PB neg; 8% atypical cells
M.Su*	M	5	+	+	+	HS not ACG†	—	—	—
M.Su*	M	5	+	+	−	Neg	< 50	< 50	CFTs neg
A.M.*	F	7	+	−	−	Neg	—	—	—
R.E.	M	7	−	+	−	HS not ACG	< 50	< 50	PB neg; occ atypical cell
M.Se.	F	7	+	−	−	Neg	—	—	Virus culture neg
R.M.	M	8	−	−	−	Neg	—	—	Virus culture neg
K.Bl*	M	8	+	+	+	Neg	< 50	—	PB neg; WBC neg
K.Bl*	M	8	+	+	−	Neg	—	—	—
B.M.	M	33	−	+	−	HS not ACG	—	—	PB neg; WBC neg; father of A.M.
Lymphadenitis									
M.W.	M	4	−	+	−	Neg	< 50	—	PB neg; 4% of white cells atypical; FU by own doctor
G.C.	F	5	+	+	−		—	—	Scarlat. 10 days previously
U.R.T.I.									
R.I.	M	5	−	+	+	alpha HS	70	75	PB neg; WBC neg
Other									
M.Su*	M	5	−	+	−	Not done	< 50	—	WBC neg; CFTs neg
O.E.	F	37	−	+	+	HS not ACG	< 50	—	PB neg; WBC neg

* Recurrent splenomegaly.
† HS not ACG, β-haemolytic streptococci not of group A, C or G.
For legend, also see Table 2.

months: two episodes of febrile exudative pharyngitis lasting 7–8 days despite penicillin and, in between, varicella. The spleen was palpable for 4 days during the first illness, on 1 day during the attack of varicella but not at follow up 2 days later and for 6 days but not at follow up 12 days after the onset of the third illness.

Three of the 17 patients in this group had recurrent splenomegaly.

Clinical features

Fever lasted longer in episodes of pharyngitis in which evidence of streptococcal infection was not found (Table 4). Five such episodes have been omitted; in one patient seen towards the end of her illness the temperature was normal, in two

https://doi.org/10.1017/S0950268800050160 Published online by Cambridge University Press

Table 4. *All episodes of pharyngitis: duration of fever*

	No. of episodes	Duration of fever: < 5 days	Duration of fever: 5 days or longer
Evidence of streptococcal infection	10 (7)*	9 (6)	1 (1)†
No evidence of streptococcal infection	11 (6)	1 (1)	10 (5)
Total	21 (13)	10 (7)	11 (6)

Eight episodes (3 with, 5 without evidence of streptococcal infection) omitted: see text.

* Figures in parentheses, patients with a single known episode of splenomegaly followed until the spleen was no longer palpable.

† S.Lo.; occasional atypical white cells.

there is no record of the temperature and in two the patient was seen only once. Three patients with evidence of streptococcal infection have also been omitted: P.M. and M.H. because in both there was evidence of a viral infection also and B.D. (second episode) because she was seen only once.

In all but one of the ten episodes of pharyngitis with evidence of streptococcal infection included in the table fever lasted 2–4 days. The sole exception was S.Lo. whose blood contained occasional atypical white cells. In all but one of the 11 episodes without evidence of streptococcal infection fever lasted 5 days or longer. The sole exception was M.Se. from whom a satisfactory throat swab was not obtained. The difference between the two groups is significant at the 0·1% level using Fisher's exact test ($P < 0{\cdot}001$). The difference persists if only those patients with a single known episode who were followed to the disappearance of the spleen are considered ($P < 0{\cdot}05$).

Exudate was noted in 8 of the 13 episodes of pharyngitis with evidence of streptococcal infection and in 8 of the 16 episodes without such evidence.

In 6 episodes of pharyngitis (3 in each group) glands were not palpable in neck or axillae and in 6 others (3 in each group) only the tonsillar glands were palpable.

The liver was palpable in 3 patients with pharyngitis with evidence of streptococcal infection and in 4 patients without such evidence. In 2 (M.H., G.H.) more than occasional atypical white cells were found.

In eight episodes of pharyngitis in children group A streptococci were cultured from the first throat swab. One (B.D., second episode) was not followed up and in one (P.M.) the child developed measles. In another, S.Lo., occasional atypical cells were found in the blood; her illness lasted 7 days. Five children had short-lived acute sore throats: the child, A.W., seen in August 1959, R.A., A.S., D.L. and B.D. (first episode). For two of them the ASL titres in the acute phase and in convalescence are known; in both a streptococcal infection beginning at the onset of sore throat was confirmed:

A.S., female aged 6, presented with sore throat, scarlatinal rash, palpable glands in neck and axillae and a palpable spleen. White cells normal; PB negative. Throat swab yielded type 3 group A streptococci. The illness was mild, fever lasting only 3 days. The spleen was not palpable at the second visit 2 days later.

B.D., female aged 10, presented with exudative tonsillitis and palpable tonsillar glands and spleen. White cells 14500/cmm (neutrophils 81%); PB negative. Throat swab yielded type 4 streptococci. Fever lasted 3 days but slight soreness of the throat persisted and on the seventh

day a shallow yellow ulcer was visible on one tonsil; type 4 streptococci were again cultured and oral penicillin was prescribed. On the eight day of the illness she was well; the spleen was still palpable but not at follow-up 12 days later. She presented again with exudative tonsillitis 18 months later and the spleen was again palpable; throat swab yielded a heavy growth of type 5 group A streptococci but she did not attend for follow-up.

A.S. appeared to be a straightforward case of scarlatina. In B.D. the appearance of an ulcer in the throat raises the possibility that a viral infection followed on the streptococcal infection. However her sore throat eased within 24 h of starting penicillin.

In an adult referred because of recurrent splenomegaly the illness also appeared to be mild and straightforward. The history suggested that streptococcal infection had been present in the family for 8 months:

J.D., male aged 31, had been found by his own doctor to have temporary splenomegaly during two febrile illnesses lasting 2–4 days, 3 months and 8 months before he presented with fever, nasal catarrh, sore throat and splenomegaly. When I saw him 2 days later he was afebrile; exudate was present on the tonsils and the spleen was palpable. Throat swab yielded a heavy growth of group A streptococci and the ASL titre was 350 U/ml. One daughter, aged 2, had had a febrile illness at the time of his first illness and since then had had fever and sore throat every few months. The other daughter, aged 8, had nasal catarrh and a perforated eardrum a week after her father had first fallen ill and had had green nasal catarrh ever since. Nasal swabs from the mother and the elder daughter yielded group A streptococci. The whole family were treated with penicillin for 12 days. Two visits to collect convalescent specimens were made but Mr. D. was not at home. He was followed up by his own doctor.

In two of the four children with lymphadenitis in the first group (S.M., L.A.), there was evidence of a viral infection superimposed on a streptococcal infection. One child (G.A.), had a remitting fever for 28 days. The fourth child (A.P.), (ASL > 800 U/ml; marked leucocytosis), was referred because she had been ill for 10 days. Twenty-four hours after starting treatment with i.m. penicillin her temperature was normal and she was much better. She was followed up by her own doctor.

In the child with infected varicella the spleen was palpable only while a streptococcal abscess was present:

M.St., female aged 5, became very ill 2 days after developing varicella. The rash was infected. The spleen was not palpable. Swabs from throat and from infected areas yielded group A streptococci. Penicillin i.m. was started. Two days later she was greatly improved and afebrile but an abscess was developing on her back and the spleen was palpable. Three days later the abscess was drained; she was then well and the spleen was no longer palpable. The ASL titre was over 800 U/ml at the onset of varicella, falling to 205 U/ml 4 weeks later.

Duration of splenomegaly

The exact duration of splenomegaly is not known for all episodes since only a few patients were seen daily. In 32 episodes it was possible to identify whether splenomegaly lasted less or more than 5 days.

In 7 episodes of pharyngitis (3 with evidence and 4 with no evidence of streptococcal infection) the spleen is known to have been enlarged for more than 5 days; in 5 atypical white cells were found in the blood.

In 14 episodes of pharyngitis the spleen is known to have been enlarged for less than 5 days. In 6 episodes swabs yielded group A streptococci and in 3 a virus; in 5 no evidence of the aetiology was found. In none were atypical white cells found in the blood.

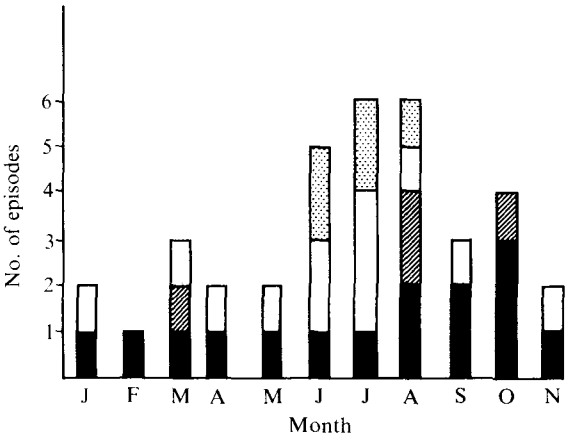

Fig. 1. Splenomegaly: seasonal incidence by probable aetiology. ■, Probable streptococcal infection; □, virus isolated; ▨, atypical white cells present; □, aetiology unknown.

One of the six patients with lymphadenitis, (G.A.), had remitting fever and remitting splenomegaly over a period of 28 days. In two (L.A. and M.W.), both with atypical cells in the blood, the spleen was palpable for less than 5 days. In three (S.M., G.C., A.P.), the spleen was palpable for 13–30 days; in the first there was evidence of both viral and streptococcal infection and in the second of a viral infection following a streptococcal infection.

In G.Ha. who had a 'flu-like illness the spleen was palpable for 35 days after the onset of the illness but not 15 days later. In R.I. who had a feverish cold the spleen was palpable for 8 days.

The spleen was palpable for 1–3 days in both patients with varicella and in the one patient with rubella.

Seasonal incidence

Four episodes are excluded from Figure 1 because in each the principal condition has its own seasonal variation: measles, varicella (two patients) and rubella. 'Probable streptococcal infection' includes two patients with evidence of virus infection also (L.A. in January, M.H. in February) but not S.M. who yielded adenovirus and is included in the 'virus isolated' group.

The number for September represents my experience in only a third of that month since for most of these years I was on leave for 21 days at that time. Allowing for this, there is a peak in the distribution of cases beginning in June and ending in October. This peak is almost entirely due to episodes associated with a positive culture for viruses plus an increased number of episodes for which no evidence of a possible aetiology was found. Episodes with evidence of streptococcal infection are scattered fairly evenly throughout the year with a peak in October. The picture is similar if only patients with temporary splenomegaly are considered.

https://doi.org/10.1017/S0950268800050160 Published online by Cambridge University Press

DISCUSSION

These cases were studied in the course of ordinary general practice and it is not surprising that information is incomplete. Some conclusions can however be drawn.

It is clear that the spleen may be temporarily enlarged in acute infections of the upper respiratory tract even in patients with little or no swelling of lymph glands. Such cases were not rare in the two populations with a high incidence of streptococcal infections (and possibly also of virus infections). The average general practitioner could expect to see 2 or 3 cases a year if working in a similar population.

Five of the patients described had recurrent splenomegaly. In such cases the aetiological factor may reside in the patient rather than in an infectious agent. However the results of various analyses were similar whether all cases or only those with temporary splenomegaly were considered. It is of course possible that more of the latter might have been found to have recurrent splenomegaly if followed up for long enough.

Viruses were isolated in 5 episodes (adenoviruses in 3, coxsackie B in 2) and the seasonal incidence suggests that they might have been responsible for others for which no possible cause was identified. In five episodes with more than just occasional atypical white cells the probable cause was Epstein–Barr virus or cytomegalovirus [7]. In 2 of these 10 episodes there was also evidence of streptococcal infection.

In nearly half the episodes there was evidence of streptococcal infection. In the first practice isolation of group A streptococci was highly correlated with serological evidence of streptococcal infection [8] and in this series, in 6 of the 7 patients for whom ASL titres both in the acute phase and in convalescence are known there were significant changes in titre.

The age distribution for pharyngitis associated with splenomegaly in this series follows the bimodal age distribution for pharyngitis due to group A streptococci found in the first practice [8].

Splenomegaly was of short duration in most episodes of pharyngitis followed up; in these cases splenomegaly lasting more than 5 days was found only in patients whose blood contained atypical white cells. In five episodes there was evidence of dual infection with both group A streptococci and a virus.

It appears that temporary splenomegaly may result from infections of the upper respiratory tract with adenovirus or coxsackie virus alone, although streptococcal infection was not excluded in such cases in this series, and from dual infection with both a virus and group A streptococci. The question is whether streptococcal infection alone may be responsible in some cases. A conclusive answer to this question is not possible – and may never be possible; it will always be difficult to rule out another contributing infection.

However if viruses were the only and sufficient cause one would expect the age distribution to be weighted more heavily in favour of children under 5. The clinical picture in some of these cases and the differences in seasonal incidence and in the duration of fever as between those with evidence of streptococcal infection alone and those with no evidence of streptococcal infection suggest that streptococcal

infection of the upper respiratory tract may in some instances cause splenomegaly without the involvement of any other infectious agent.

ACKNOWLEDGEMENTS

I am grateful to Professor C. A. Mims, Dr R. M. Turner and Mr M. P. Curwen for helpful comments and to Mr A. Fitzgerald for statistical advice.

REFERENCES

1. Pochedly C, Sills RH, Schwartz, et al. Disorders of the spleen. Pathophysiology and management. New York: Marcel Dekker, 1989; 229
2. McCrae J. A study of eight hundred and fifty cases of scarlet fever with a more particular consideration of seventy-one fatal cases. Canad Med Ass J 1911; **1**: 293–310.
3. Sutton RNP, Pullen HJM, Blackledge P, Brown EH, Sinclair L, Swift PN. Adenovirus type 7 1971 -4. Lancet 1976; ii: 987–91.
4. The Influenza Committee of the Advisory Board to the D.G.M.S. France. A report on the influenza epidemic in the British Forces in France 1918. Br M J 1918; ii: 505–9.
5. McIntyre OR, Ebaugh FG. Palpable spleens in college freshmen. Ann Int Med 1967; **6**: 301–6.
6. Lawy HS. Use and interpretation of the antistreptolysin test. Ann Rheumat Dis 1960; **19**: 42–7.
7. Klemola E, von Essen R, Henle G, Henle W. Infectious mononucleosis-like disease with negative heterophil agglutination test. Clinical features in relation to Epstein-Barr virus and cytomegalovirus antibodies. J Infect Dis 1970; **121**: 608–14.
8. Higgins PM. Streptococcal pharyngitis in general practice 1. Some unusual features of the epidemiology. Epidemiol Infect 1992; **109**: 181–9.