RELATION BETWEEN SPLENECTOMY AND SUBSEQUENT INFECTION

A CLINICAL STUDY

BY

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Six years ago, in a treatise on 'Splenic Function', Hayhoe and Whitby (1955) stated as one of their conclusions that 'the spleen can be removed with relative impunity and low mortality and is not in any way essential to life'. The present study, however, provides evidence to prove that the spleen may be essential to life; that its absence, in infancy particularly, may result in serious and overwhelming infection. Such a relation was suggested first by King and Schumacker (1952), and later by Smith and his colleagues (Smith, Erlandson, Schulman and Stern, 1956; Smith, Erlandson, Schulman and Stern, 1957; Smith, Erlandson, Stern and Schulman, 1960), Gofstein and Gellis (1956), Robinson and Sturgeon (1960) and Lucas and Krivit (1960). On the other hand, this view has been opposed by certain authors, particularly by Gross (1953), and Laski and MacMillan (1959). When the present study was commenced, a critical review of the relevant English and French literature indicated that the essential problem remained unsolved: does splenectomy itself significantly increase the susceptibility of the child to serious infection?

To the clinician there seem to be very important reasons for obtaining a definite answer to this question. One is that the recent developments in anaesthetic and surgical techniques and in antibiotic therapy have made the operation of splenectomy far safer than it was a generation ago, when the operative mortality was three or four times as high as it is today. As a result, splenectomy may appear to be justifiable far more often nowadays, even in the neonatal period. Another reason is that in certain disorders, for which splenectomy in infancy was hitherto advocated in some centres, medical treatment has now been developed to the stage where it may effectively replace splenectomy, at least until the later years of childhood when the operation carries less surgical risk. For such cogent and practical reasons it was decided to assess critically the evidence in the literature and to investi-

gate further the problem of the relation between splenectomy and subsequent serious infection.

The present study involved a follow-up of 142 patients in whom splenectomy had been performed in childhood. The purposes were first to determine whether there was a significant incidence of serious infections following this operation, secondly to determine whether the incidence of such infections was influenced by the age of the patient at operation, and thirdly to determine whether the incidence was influenced by the nature of the condition for which splenectomy was performed. The incidence of serious bacterial infections following splenectomy in this series was 12.0%. A statistically significant relation of infection to age was shown in infancy: of 10 infants aged 8 months or less at the time of operation, five developed serious infections, three of which were fatal. The findings suggested also that when splenectomy was performed for an underlying disease, it carried a greater risk of subsequent infection than when it was performed for traumatic rupture.

Review of Published Work

In Table 1 are outlined some important features of previously reported surveys of the incidence of serious infection following splenectomy in childhood. King and Schumacker (1952) recorded serious infections in five patients after splenectomy for hereditary spherocytosis. Each of these patients was less than 6 months of age at the time of operation, but unfortunately the remaining 95 cases were not adequately documented. These authors were impressed by the possibility that splenectomy in infancy might cause an increased susceptibility to infection. Gross (1953) 'found little evidence to support this view'. His data indicate, however, that the minimum period of follow-up was very short, that 14% of his patients were not followed up at all and that two of the remaining 51 children died of acute infections within a year of operation.

His cases were included in the larger series reported by Gofstein and Gellis (1956). Walter and Chaffin (1955) found three fatal infections within 13 months of operation—in cases of splenic neutropenia, of splenic haematopenia and of Gaucher's disease. In 37 cases of hereditary spherocytosis, 10 of them with splenectomy before the age of 8 months, these authors recorded no serious infections at all; a finding that may be related to the relatively short minimum period of follow-up. Smith and his colleagues in a series of papers (Smith *et al.*, 1956, 1957) found a high incidence (28%) of serious infections, and 8% were fatal. Unfortunately relevant clinical details and other factors were not published for all the cases in this survey.

Gofstein and Gellis (1956) reviewed 206 cases, of which they excluded 100 cases of tumour, leukaemia, portal hypertension and storage disease, because these conditions might themselves cause an increased susceptibility to infection. Pneumococcal meningitis developed in four of their remaining 106 cases—a group that may have included those reported by Gross (1953). One of the fatal cases of meningitis occurred in a 6-year-old child a few months after splenectomy for hereditary spherocytosis; yet of 16 infants having splenectomies for the same disease none had developed serious infection within the follow-up period which appears to have been less than 12 months in some cases. These authors concluded that there was some correlation between splenectomy and sepsis, but that they were unable to find any relation to the age at operation. Reemtsma and Elliott (1956) reported no infections in 13 children with thalassaemia, but their paper makes no mention of any specific inquiry concerning infections nor of any autopsy in three of the children who died. Huntley (1958) recorded a high incidence of serious infection; in 15% of 46 patients, it was fatal in no less than 11%. Of seven infants less than 1 year old at operation, five developed severe infections, three of them fatal. These figures, however, are weighted by the inclusion of three infants with Aldrich's syndrome of eczema, thrombocytopenic purpura and otorrhoea. Each of these contracted a fatal infection, as is usual in this condition even without splenectomy.

It can be seen, therefore, that when the present study was begun in 1959, the answer to the question of whether splenectomy is related to subsequent serious infections had been only vaguely outlined. Seven additional papers have been published since then, but they have done little to clarify the problem. Laski and MacMillan (1959) followed up and evaluated only 81 of a total of 135 children who had had their spleens removed and the minimum period

of follow-up was as short as one month. Five of these 81 children subsequently died, two with meningitis, two with respiratory infection complicating other conditions and one with an undiagnosed sudden illness that may well have been infective. These authors attempted to obtain controls from a series of children who had undergone appendectomy during the same period. Of these children 40% were studied as the controls; one of them developed a serious bacterial infection (meningitis), and that child recovered. The conclusion drawn by these authors was that serious infection occurred no more frequently after splenectomy than after appendectomy, but careful appraisal of their data shows that if any conclusion is justifiable it seems to be that splenectomy does produce the greater risk of infection. The authors' own conclusion has since been quoted uncritically by several writers, so it is appropriate to draw attention to Greenberg's comment in the *Year Book of Pediatrics* (1960-61) that this paper 'violated epidemiological principles both in the design of study and in the conclusions'.

It can be seen in Table 1 that most of the remaining surveys also suffered from one or more defects, of which the more serious were the use of an unduly short minimum follow-up period and the exclusion of a high proportion of the total number of cases from evaluation. In the survey by Forward and Ashmore (1960) the method of follow-up was not stated, but the incidence of fatal infections (10%) was high, including septicaemia or meningitis in two older children. Robinson and Sturgeon (1960) carefully studied a large series and analysed the literature in an endeavour to reach definite conclusions. They too reported a high incidence of septicaemia and meningitis, both fatal and non-fatal, but their 110 evaluated cases included 12 of reticulo-endothelial malignancy and many others of conditions likely to cause an increased susceptibility to infection. They emphasized the fulminating character of many of the infections and introduced the term 'life-threatening infections' for non-fatal attacks of septicaemia and of meningitis. These authors thought their findings indicated that the incidence of infections was related to the nature of the underlying disorder though not apparently to the age at operation. Their data suggest, however, that infections which do follow splenectomy may more often prove fatal if the operation has been done early in childhood. The survey by Lucas and Krivit (1960) was one of the few with an adequate period of follow-up for all cases. The sources of information were hospital records, supplemented in some cases by questionnaires sent

TABLE 1
PREVIOUSLY REPORTED SPLENECTOMY SURVEYS

Authors	Cases Evaluated	Number Developing Infections		Minimum Follow-up Period	Special Remarks
		Fatal Infection	Non-fatal Sepsis or Meningitis		
King and Schumacker, 1952	100	2	3	?	Adults included; age and indication for operation not stated in 95 cases
Gross, 1953	51	2	?	'A few months' 10 months ?	HS cases only
Walter and Chaffin, 1955	72	3	?		
Smith <i>et al.</i> , 1956	50	4	10		Indication for operation not stated in cases without infection
Gofstein and Gellis, 1956	106	2	2	<2 years in some cases 6 years in survivors 6 months	HS, ITP, TR and TH cases only; includes series reported by Gross
Reemtsma and Elliott, 1956	13	0	?		TH cases only
Huntley, 1958	46	5	2	1 month	Includes three cases of Aldrich's syndrome
Laski and MacMillan, 1959	81	2(?)	?		Only 60% of total series was evaluated
McKinnon, Boley and Manpel, 1959 ..	26	0	0	2 months	TR cases only; 79% of total series evaluated; no cases under 2 years at operation
Forward and Ashmore, 1960	30	3	20	6 months	HS, ITP and TR cases only; 85% of total series evaluated
Robinson and Sturgeon, 1960	110	7	6	12 months	74% of total series evaluated; includes series of Walter and Chaffin
Lucas and Krivit, 1960	74	3	?	2½ years	HS, ITP and TR cases only; 95% of total series evaluated
Wolff <i>et al.</i> , 1960	18	0	1	5 months	TH cases only; no cases under 2 years
Broberger <i>et al.</i> , 1960	42	0	1	3 months	HS, ITP and TR cases only; one case under 2 years

TR = trauma; HS = hereditary spherocytosis; ITP = idiopathic thrombocytopenic purpura; TH = thalassaemia.

to the family doctor or to the parents. Their reported findings were limited to fatal infections. Of particular interest is the fact that two of the three children who developed fatal septicaemia following splenectomy for hereditary spherocytosis were 6 and 7 years of age at operation. In the small survey of patients with thalassaemia reported by Wolff, Sitarz and Von Hofe (1960), no details were given of the method of inquiry for infections, but one patient did develop septicaemia due to *Salmonella typhimurium*. Finally, in the series studied by Broberger, Gyulai and Hirschfeldt (1960) there was only one severe infection (*H. influenzae meningitis*); however, the significance of this finding may be affected not only by the paucity of infants included and by the short minimum follow-up period, but also by the fact that in more than half of those cases that were followed for at least two years the indication for splenectomy was traumatic rupture of the spleen.

In addition to these papers describing series of cases, the literature contains reports of a number of isolated cases of serious infection following splenectomy in childhood (Bertoye, Monnet, Pinel and Carron, 1950; Newns, 1951; Gruber, Redner and Kogut, 1951; Simpkins and Cathie, 1954; Evans, Waters and Lowman, 1954; Hoefnagel, 1956; Robinson, 1957; Burman, 1958; Macpherson,

1959; Wunderlich, 1959; Smith *et al.*, 1960; Gordon, 1960). Although these isolated case reports are of no help in clarifying the relation between splenectomy and infection, they do provide data that can be usefully analysed in the study of certain features such as the type and the bacteriology of these infections and the interval between splenectomy and infection.

The literature on this subject obviously contains a large amount of material for analysis. Up to 1960 the published reports of series of splenectomies in children included altogether more than 600 cases studied in 12 independent centres. However, the views expressed have been conflicting in many respects, and none of the authors submitted proof of any clear-cut relation between splenectomy and subsequent serious infection.

Material and Methods

The present survey covers a period of 20 years, from 1938 to 1958, during which time splenectomy was performed on 141 children at the Royal Children's Hospital and on four at the Queen Victoria Memorial Hospital, Melbourne. With the assistance of the Almoner's Department it was possible to trace 142 of these cases, over 98% of the total. In some instances this necessitated personal visits by the authors to the patients' homes, and two patients were visited in another State of Australia.

Of the 142 patients, 123 were interviewed personally, mostly in the Haematology Research Clinic at the Royal Children's Hospital. Of the remainder, eight were not able to attend, and information about them was obtained by means of a questionnaire; and 11 patients were found to have died before the survey was begun. Adequate histories were obtained concerning all patients whether they attended the Clinic or not. All those who did attend had a physical examination and a blood examination, consisting of estimation of haemoglobin, reticulo-cyte count, white cell and differential white cell count, platelet count and blood film.

Criteria accepted for a satisfactory follow-up in the surviving patients were two: (a) an interval of at least two years between splenectomy and the time of review, (b) an adequate history, particularly relating to infections before and after splenectomy. The shortest period of follow-up in the present series was two years, the longest 19 years. The time interval between splenectomy and review was two years in 30 cases, three to four years in 23 cases, five to 10 years in 50 cases, and more than 10 years in the remainder.

In obtaining an adequate history, inquiry was made for septicaemia, meningitis, pneumonia and other serious bacterial infections. Pneumonia was accepted only if it was severe enough to require at least one week in bed and

if it was not a terminal event in the course of another major disease. The other serious bacterial infections that were regarded as acceptable were suppurative endocarditis, pericarditis, osteomyelitis, arthritis, peritonitis, subphrenic abscess, empyema, lung abscess, mediastinitis, mastoiditis and miliary or meningeal tuberculosis. All infections manifested within two weeks of splenectomy were specifically excluded. Viral infections were not included in the tabulation of serious infections because of the generally benign nature of such infections and because it was considered almost impossible to make a satisfactory estimate of the incidence of virus infections in a retrospective study.

Results of Present Study*

Analysis of Material. The age distribution of 142 cases at the time of splenectomy is shown in Fig. 1. Ages ranged from 14 weeks to 16 years. In 112 cases (approximately 80%) the operation was performed between 4 and 13 years of age; in

* A preliminary paper presenting most of these results has already been published in abstract (Horan, 1960).

FIG. 1.—Distribution of 142 splenectomies (Royal Children's Hospital Survey, 1938-1958).

TABLE 2
INCIDENCE OF SERIOUS POST-SPLENECTOMY INFECTIONS: COMPARISON OF TRAUMA
WITH UNDERLYING DISEASES
(Royal Children's Hospital Survey)

Indication For Splenectomy	Number of Cases	Serious Bacterial Infections			
		Non-fatal	Fatal	Total Infections	Percentage Incidence
Trauma	64	4	0	4	6.3
Disease states	78	8	5	13	16.7
Total	142	12	5	17	12.0

TABLE 3
TYPES OF SERIOUS POST-SPLENECTOMY INFECTION RELATED TO UNDERLYING CONDITION
(Royal Children's Hospital Survey)

Primary Condition	No. of Cases	Serious Bacterial Infections					
		Menin- gitis	Septi- caemia	Pneu- monia	Subphrenic Abscess	Others	Total
Trauma	64	0	0	3	0	1	4
Hereditary spherocytosis	40	1	2	2	0	0	5
Acquired haemolytic anaemia	3	0	0	0	1	0	1
Thrombocytopenic purpura	14	0	0	0	0	0	0
Portal hypertension	10	2	0	1	1	1	5
Thalassaemia	4	0	0	0	0	0	0
Miscellaneous	7	0	1	0	1	0	2
Totals	142	3	3	6	3	2	17

a small but significant number (17 cases) the operation was performed in infants under 2 years of age.

In patients with an underlying disease the ratio of males to females was 43 to 35. In patients with traumatic rupture of the spleen the ratio of males to females was 51 to 13.

Traumatic rupture accounted for 45% of all cases, and a comprehensive range of indications accounted for the remainder.

Incidence of Serious Bacterial Infections

Infections before Splenectomy. In 17 of 142 cases serious non-fatal infection occurred before splenectomy. There were 12 cases of pneumonia, four of meningitis and one of osteomyelitis. One of the children who contracted pneumonia before splenectomy for traumatic rupture of the spleen, developed pneumonia afterwards (Case 133). No other child who developed a serious infection before, developed one after splenectomy.

Infections after Splenectomy. In 142 cases there were five patients with fatal, and 12 with non-fatal infections following splenectomy, an incidence of 12.0% (Table 2). There was a fairly even distribution in all age groups of non-fatal infections following splenectomy. Two fatal infections occurred in 132 older children; three fatal infections occurred in 10 children who were under 1 year of age at splenectomy.

In 64 cases of trauma, the incidence of serious infection was four (6.3%) and there were no fatal cases (Table 2). In contrast, in 78 cases with an underlying disease, the incidence of serious infections was 13 (16.7%) and five of these infections proved fatal.

Type of Bacterial Infection. Table 3 indicates the type of infection related to the underlying condition.

Meningitis occurred in three patients, all of whom recovered. One was a case of hereditary spherocytosis (Case 144). Two were cases of portal hypertension (Cases 13 and 53). **Septicaemia** occurred in three patients, all of whom died. Each had an underlying disease and was less than 6 months at the time of splenectomy. Two were cases of hereditary spherocytosis (Cases 1 and 132). One was a case of neonatal staphylococcal sepsis (Case 140). **Pneumonia** occurred in six patients, none of whom died. Three of the patients had had splenectomy performed for traumatic rupture (Cases 102, 110, 133); two patients were twin brothers with hereditary spherocytosis (Cases 47 and 51); one patient was a case of portal hypertension (Case 39). **Subphrenic abscess** occurred in three patients and in each case it was related to upper abdominal surgery. One patient, a case of acquired haemolytic anaemia, died (Case 32). One patient with

portal hypertension (Case 40) and one with hydatid disease (Case 31) recovered. *Osteomyelitis* occurred in one patient in whom splenectomy was performed for traumatic rupture (Case 34). Recovery followed. *Tuberculosis* of the genito-urinary tract with miliary dissemination was found at autopsy to be the cause of death in a patient with portal hypertension (Case 4).

Cultures were made and a pathogenic organism grown in eight of the 17 cases of infection. *Staphylococcus* was grown in three cases, and *Streptococcus*, *Pneumococcus*, *Meningococcus*, *Haemophilus influenzae* and *M. tuberculosis* each in one case.

Infections in Relation to Age at Splenectomy. At the time of splenectomy (Table 4) 10 infants were aged between 14 weeks and 8 months. Serious infections occurred in five of these infants and three of these infections were fatal. All five infections occurred within 22 months of operation (Cases 1, 53, 132, 140, 144).

At the time of splenectomy 132 children were over 1 year of age. Serious infections occurred in 12 of these children (see Appendix) and two of the infections were fatal (Cases 4 and 32).

Infections in Relation to Underlying Disease. Table 3 shows the incidence of serious bacterial infections in relation to the primary condition for which splenectomy was performed in this series.

In 64 cases of *traumatic rupture* of the spleen, four developed serious, but not fatal infections (Cases 34, 102, 110, 133). Of 40 cases of *hereditary spherocytosis* five developed serious infections. Two of these infections were cases of fatal septicaemia and occurred in infants who were under 6 months of age at the time of operation (Cases 1 and 132); one was a case of non-fatal influenzal meningitis in an infant aged 8 months at operation (Case 144). Two cases of non-fatal pneumonia occurred in twin brothers (Cases 47 and 51). Of three cases of *acquired haemolytic anaemia* one developed a serious infection, fatal subphrenic abscess (Case 32). Of 10 cases of *portal hypertension* five developed serious infections, two following later thoraco-abdominal operation (Cases 39 and 40); two were cases of meningitis (Cases 13 and 53), and one was a fatal case of miliary tuberculosis (Case 4). In 14 patients with *idiopathic thrombocytopenic purpura*, all over 4 years of age at the time of operation, no serious infections followed splenectomy. In four patients with *thalassaemia*, aged 15 months, 22 months, 3 years and 4 years at the time of splenectomy, no serious infections occurred.

Serious infections followed splenectomy in two

TABLE 4
SERIOUS POST-SPLENECTOMY INFECTIONS RELATED TO
AGE AT OPERATION
(Royal Children's Hospital Survey)

Age at Splenectomy	Number of Cases	Number with Serious Bacterial Infections
0-11 months	10	5
12-23 months	7	0
2-5 years	35	3
6-16 years	90	9
1-16 years	132	12

patients in the group with *miscellaneous diseases*. This group consisted of one infant with neonatal staphylococcal sepsis who died of septicaemia 10 months after splenectomy (Case 140); one infant aged 6 months with a thoracic tumour of undetermined pathology; one infant aged 15 months with myofibroma of the stomach; one child aged 5 years with pancreatic cysts; one child aged 7 years with hydatid of the spleen who developed a non-fatal subphrenic abscess following operation for hydatid of the liver, 20 months after splenectomy (Case 31); one child aged 9 years with perisplenitis of undetermined aetiology.

Discussion

Previously reported surveys have made useful contributions to knowledge on this subject but they have not provided statistically valid answers to the important questions of whether splenectomy produces an increased risk of serious infections and whether this risk is affected by the age of the patient or by the nature of the underlying disorder. One reason for this lack of convincing conclusions is that no one series has been large enough to provide adequate data. The present series of 142 cases is materially greater than any previously reported, and it has produced at least one finding that is highly significant statistically. Greater numbers of cases are needed, however, to provide complete answers to all three of the questions posed, so in this discussion data from the present series will be combined wherever justifiable with those from similarly studied series in the literature.

The task of consolidating the findings in previously reported surveys is made difficult by the fact that these surveys differ from each other in a number of ways. The major differences occur in respect to (i) the method of follow-up, which varied from a mere perusal of hospital records to a personal interview and examination of each patient; (ii) the percentage of cases successfully followed up, which ranged from 60% to almost 100%; (iii) the length

of the minimum period of follow-up, which ranged from one month to two and a half years; (iv) the age distribution of patients at the time of operation—in some series there were few or none at all in the important age-period of infancy; (v) the relative frequency of the various disorders for which splenectomy was performed, some series for example containing a high and others a low proportion of conditions as immunologically different as malignant reticulosis and traumatic rupture; and (vi) the exclusion of all infections other than fatal septicaemia and meningitis in certain surveys. It may well be that infections such as acute suppurative arthritis, endocarditis and pericarditis and severe pneumonia are of significance in relation to splenectomy, particularly when they are pneumococcal and prove fatal, but most authors have made no record of such infections. In order to obtain a common basis for comparison in this discussion it will be necessary to concentrate on septicaemia and meningitis. The term 'life-threatening infection' coined by Robinson and Sturgeon (1960) will be used for non-fatal attacks of septicaemia or meningitis.

Incidence of Infections. The total incidence of serious bacterial infections in the present series was 17 in 142 cases or 12%. When the analysis was limited to fatal and life-threatening infections, the incidence was eight in 142 or 5.6%. Of fatal infections alone, the incidence was five in 142 cases or 3.5%. In those previously reported series each containing at least 50 cases, the incidence of fatal infections ranged from 3% to 8%. In those previously reported series that were sufficiently comprehensive to include four or more types of underlying disorder, the incidence of fatal infections was 5.5% in a total of 363 cases. Observations to be discussed later indicate that these reported figures may understate the true incidence.

Some workers question whether such figures for the incidence of fatal and of life-threatening infections in the splenectomy population are really higher than would be found in a control population. There is certainly a paucity of evidence to prove it. To obtain an adequate control series for this purpose the controls would need to be matched as to age, to the nature of the underlying disorder and to its severity—a set of conditions that could seldom be obtained in actual practice. A comparison of the incidence of fatal and life-threatening infections in the general child population of appropriate age with the incidence in children who have had their spleens removed might give some helpful information on this question. Robinson and Sturgeon (1960) considered it a reasonable

assumption that in a normal child population the incidence of septicaemia and meningitis would be 'substantially less than 1% over the length of time the post-splenectomy population has been followed'. In many of the reports of surveys the mean length of the follow-up period has been only vaguely indicated, but in general it seems to have been of the order of five years; in the present series it was almost six years. Pertinent information therefore has been provided by the recent report of the first five years of the continuing study of 1,000 families in Newcastle upon Tyne, England (Miller, Court, Walton and Knox, 1960). Of 847 children followed for five years from the time of their birth in May-June (1947), only six developed pyogenic meningitis or septicaemia, an incidence of 0.7%. It might reasonably be assumed that if one took instead a five-year period beginning a year or two later in childhood (to make it more closely related to the age range of the children under discussion), the incidence of such infections would be less than 0.7%. By contrast, in children who had had splenectomies the incidence of such infections was 5.6% in the present series and 8.7% in the total of 540 adequately documented cases on record. The difference is a striking one, but its significance is limited by the fact that an apparently normal population is being compared with children without spleens, many of whom have an underlying disease.

To summarize, the general incidence of such serious infections as septicaemia and meningitis during the years following splenectomy in childhood is of the order of 8% and the incidence of fatal infections is close to 5%. The available evidence strongly suggests that these figures for the total population of children who had had splenectomies are much higher than occur in the general child population. Evidence discussed later indicates that certain factors may materially increase the susceptibility of this child to infection; for example, in infants and in those who have undergone splenectomy for certain disease states the incidence of such infections is considerably higher.

Clinical Features. In the present series the 17 serious infections included fatal septicaemia in three cases and non-fatal meningitis in three cases. In addition, miliary tuberculosis and ruptured subphrenic abscess caused another two deaths. In the literature, of all the recorded fatal and life-threatening infections, 40 were diagnosed as septicaemia, often with meningitis, and 31 of these were fatal; 39 were cases of meningitis alone and six of these were fatal. In addition there were eight fatal infections of other kinds, six of them being pneumonia.

A most important feature of the infections as recorded was their fulminating character. In more than half of the fatal cases of septicaemia, the total length of the illness was less than 18 hours or was described as 'very brief', and in a third of them the patient was dead within as few as 10 hours of the onset of symptoms. In several of the cases of meningitis, death occurred within 16 hours of the onset, suggesting the possibility of an unrecognized septicaemia in these cases. As one author remarked with regard to infection following splenectomy for underlying disease states, 'a striking feature was the rapidity with which the patients . . . became moribund', two of them having died in spite of excellent medical care while under his immediate clinical supervision. As the explosive nature of these infections can cause the child to be overwhelmed with such great rapidity, despite early and intensive treatment, the need for prophylactic therapy has been advocated by Smith *et al.* (1957).

Another significant feature of the case histories is the number with repeated attacks of infection. Of all children recorded as having survived the first attack of serious bacterial infection following splenectomy, 40% subsequently had one or more further episodes of serious infection and 20% had more than one attack of septicaemia or meningitis. In seven of the case reports, the patient had a succession of from three to seven episodes of serious infection within three years of splenectomy, culminating in five of these cases in septicaemia or other fatal infection. Both the tendency of these infections to be fulminating, and the frequency of recurrent attacks if the first one is not fatal, strongly suggest that after splenectomy the child may react less favourably than the normal child to acute bacterial infection.

Bacteriology. Early reports drew attention to the predominance of pneumococci amongst the bacteria responsible for these fatal and life-threatening infections. In the present series, six different organisms including pneumococci were cultured from eight of the children with serious infections. When these results are combined with those reported in the literature, it is found that positive cultures were obtained in a total of 65 fatal or life-threatening infections contracted by 57 children who had had splenectomies and that the organisms cultured were the *Pneumococcus* in 36 of these infections (55%), *E. coli* in eight, *H. influenzae* in six, *Meningococcus* in four, *Streptococcus haemolyticus* in three, *Staphylococcus pyogenes* in three, *Salmonella typhimurium* in two and miscellaneous organisms in the remaining three infections. There was thus an overwhelming

predominance of pneumococcal infections. This may be explained by the work of Kerby (1950) who showed that the reticulo-endothelial system of animals is less efficient in removing encapsulated bacteria from the blood stream than in removing non-encapsulated bacteria. These bacteriological findings have an important bearing on prophylactic therapy, for penicillin might have been effective in preventing about 70% of these infections.

Interval Between Splenectomy and Infection. Some authors appear to believe that if splenectomy does predispose the child to serious infection, this will necessarily be manifested within a few months of operation. Were this true, it might be held to justify the inclusion in published surveys of those cases that have been followed up for short periods—12 months in many cases, six months in a number and only one to two months in some. It is not possible, however, to hold this view in the face of the facts recorded in the literature and in the present series (Fig. 2).

The interval between splenectomy and infection has been recorded concerning a total of 93 attacks of septicaemia or meningitis contracted more than two weeks after operation by 82 children; 13 of these infections were second or third attacks. Of the 47 fatal infections, 41 (87%) occurred within two years of splenectomy, while only 31 (66%) occurred within the first year and only 20 (43%) within the first six months. Likewise, of the 46 non-fatal life-threatening infections, 30 (65%) occurred within two years of operation, 21 (46%) within one year and only 11 (24%) within six months. Of the 93 recorded infections 18 occurred more than two years after splenectomy and the true incidence of late infections must be higher than this as many of the reported cases were followed for less than two years. Of the 18 recorded late infections, seven were attacks of septicaemia of which at least three overwhelmed the patient within 10 hours of the onset; five of the attacks of meningitis were in patients who suffered recurring attacks of serious infection following splenectomy; and in nine of the 16 infections of which the bacteriology was known, the organism was the pneumococcus. Thus it is clear that fatal and life-threatening infections that occur more than two years after splenectomy show the same characteristics as do those that occur earlier—fulminating course, with pneumococci the predominant organism, high mortality, and a tendency to recur if not fatal—and so it is reasonable to assume that they bear the same relation to splenectomy.

The following conclusions are justified concerning

FIG. 2.—Interval between splenectomy and infection with septicaemia or meningitis.

the interval between splenectomy and subsequent fatal and life-threatening infections: (i) that about half of all such infections will occur the first year after operation, perhaps a quarter will occur in the second year and at least one-fifth will occur later; (ii) that these later infections follow the same clinical and bacteriological pattern as do the earlier infections. An important corollary is that almost half the infections will be missed in cases followed up for only one year and at least one-fifth will be missed in those followed up for two years.

Incidence of Infection in Relation to Age. In the 142 cases of the present series the relative incidence of serious infections at different ages was subjected to statistical analysis. There was a higher incidence of such infections in infants under 1 year of age compared with older children (Table 4). This difference was just statistically significant.

When the analysis was confined to fatal infections and life-threatening infections such as septicaemia and meningitis, the higher incidence in infants compared with older children was highly significant statistically (Table 5). The likelihood against such a difference being due to chance is approximately 1,000 to one. In the 40 cases of hereditary spherocytosis a similar but less strikingly significant difference in the age

incidence of fatal or life-threatening infections was recorded (Table 6). The likelihood against this difference being due to chance is about 140 to one.

In cases of trauma and of other underlying disease states there were insufficient infants in the series to allow statistical comparison of the incidence of infection in infancy and in older children.

Analysis of comparable material in the literature supplied additional evidence of the higher risk of serious infection following splenectomy in infancy. Table 7 shows the incidence of infection in the few series in which the number of infants under 1 year of age was stated and in which the follow-up period after splenectomy was at least two years. Statistical analysis showed a significantly higher incidence of serious infections in infancy in all cases. Where analysis was confined to the two underlying diseases, hereditary spherocytosis and thrombocytopenic purpura, there was a higher incidence of serious infections in infants compared with older children, but the difference was not statistically significant.

Analysis of the material in the present survey has established beyond question a greater risk of fatal or life-threatening infections following splenectomy in infants under 1 year of age compared with splenectomy in the older child. These findings are statistically significant only with regard to age and

TABLE 5
INCIDENCE OF INFECTIONS IN ALL CASES IN RELATION TO AGE,
LIFE-THREATENING AND FATAL INFECTIONS ONLY
(Royal Children's Hospital Survey)

Age at Splenectomy	Number Without Infection	Number With Infection	Total	
0-11 months	5	5	10	$\chi^2 = 24.7$
1-16 years	129	3	132	Significant at 0.1% level

TABLE 6
INCIDENCE OF INFECTIONS IN HEREDITARY SPHEROCYTOSIS IN RELATION TO AGE
LIFE-THREATENING AND FATAL INFECTIONS ONLY
(Royal Children's Hospital Survey)

Age at Splenectomy	Number Without Infection	Number With Infection	Total	
0-11 months	4	3	7	
1-16 years	33	0	33	Significant at 0.7% level

TABLE 7
INCIDENCE OF INFECTIONS IN RELATION TO AGE: CERTAIN SPECIFIED DISORDERS*
LIFE-THREATENING AND FATAL INFECTIONS ONLY
(Relevant Surveys in Literature)†

Age Groups	Total Number of Cases	Number With Infection	Number Without Infection	
0-11 months	29	6	23	$\chi^2 = 15.60$
1-16 years	211	5	206	Significant at 0.1% level

* Traumatic rupture, hereditary spherocytosis, thrombocytopenic purpura and miscellaneous conditions.

† Gofstein and Gellis (1956); Lucas and Krivit (1960); Huntley (1958), excluding Aldrich's syndrome.

give no indication of the part played by other possible contributing factors. In infants, is the incidence of fatal or life-threatening infections following splenectomy significantly greater than in the normal infant population? A matched control series of normal infants was not available for comparison. The nearest approach to a control series is provided in the 'Thousand Families' study made by Miller and his colleagues (1960) in Newcastle upon Tyne. The incidence of septicaemia and meningitis in this large group of normal infants was in the region of 0.5% in the first year of life and no such infections were recorded in the second year. Admitting the obvious dissimilarity between this Newcastle series and the present one, the incidence of these infections was very much higher in the present series (Table 8). Four of the five affected infants developed serious infections in their second year of life at an age when in the normal infant population of Newcastle upon Tyne the susceptibility to such infections appeared to be declining. This difference in the incidence of infection between normal infants and infants after splenectomy in the present series is highly significant

statistically and indicates that susceptibility to infection is not a function of age alone.

Material in the present survey was insufficient to establish to what extent the susceptibility to serious infection diminishes with increasing age. In the present series fatal infections did occur in two children who had their spleens removed at 12 and 13 years of age, the causes of death being ruptured

TABLE 8
FATAL OR LIFE-THREATENING INFECTIONS IN NORMAL INFANTS AND INFANTS AFTER SPLENECTOMY

Series	Number of Infants in Series	Number of Infants Developing Infection	Age at Time of Infection	
			0-11 months	12-23 months
Newcastle upon Tyne: normal infants ..	967	5	5	0
Royal Children's Hospital Survey: infants having splenectomy in first year of life ..	10	5	1	4

subphrenic abscess (Case 32) and miliary tuberculosis (Case 4).

Further evidence on the relation of age to the incidence of infections was sought in the literature. Of 73 patients with serious infection in whom the age at splenectomy was recorded, 25 were under 1 year, 43 were 1 to 8 years, and five were at least 9 years of age at the time of splenectomy. It would be unjustifiable to draw conclusions from such evidence, but the figures do suggest that a heightened susceptibility to infection following splenectomy may not be confined to infancy, but may also be found to a lesser degree in the older child.

Incidence of Infection in Relation to Underlying Condition. The present series has established that in infancy there is a significantly higher incidence of infection in children subjected to splenectomy compared with normal children. Could it be that the present series of children had an undue susceptibility to infection as an inherent characteristic? This possibility is difficult to disprove, but the relevant data do not support it. In the present series a number of infections had occurred before splenectomy, four of the infections being meningitis. None of these four patients developed serious infections after splenectomy. In the 142 cases of the present series there were no examples of Aldrich's syndrome in which an increased susceptibility to infections is a known characteristic; there were two cases of tumour and one case of leukaemia presenting as acquired haemolytic anaemia and in none of these did serious infection occur after splenectomy.

Do other underlying diseases by themselves carry an increased risk of infection? The present survey cannot supply the answer. Some authors have assumed that certain underlying diseases do predispose to infection. For this reason Gofstein and Gellis (1956) did not publish figures for the incidence of infection in cases of tumour, leukaemia, portal hypertension and storage disease. Robinson and Sturgeon (1960), on the other hand, did record the incidence of infections in patients in such a group of diseases and compared it with the incidence in a group consisting of patients with traumatic rupture of the spleen, with hereditary spherocytosis or with thrombocytopenic purpura. These authors assumed that these three conditions did not themselves predispose to infection. In the case of traumatic rupture of the spleen this assumption is upheld by reports in the literature (Gofstein and Gellis, 1956; Laski and MacMillan, 1959; Lucas and Krivit, 1960) and by the present series. In none of these reports of traumatic rupture were any life-threatening infections recorded, but the series did

not contain any cases in the highly susceptible age period of infancy. However, there are isolated reports of three cases of life-threatening infections following splenectomy for trauma (Smith *et al.*, 1957; Forward and Ashmore, 1960). In spite of these reports the incidence of such infections in cases of traumatic rupture over the age of 1 year at operation still appears very low—in the region of 1% or less. In the case of hereditary spherocytosis the reported incidence of such infections for all ages varies from approximately 1.6% (Gofstein and Gellis, 1956) to approximately 7.7% (Lucas and Krivit, 1960) and in the present survey it was 7.5%. In the case of thrombocytopenic purpura the reported incidence of infections showed a similar wide variation and in the present series there were no serious infections in 14 cases. In thalassaemia and portal hypertension the reported incidence is very much higher. In considering the incidence of post-splenectomy infection in each underlying condition, few authors have taken into account the variable number of infants with each condition—in traumatic rupture there were none under 1 year of age at the time of splenectomy, in hereditary spherocytosis there were many. In an attempt to reach a conclusion on the influence of the underlying condition on the incidence of infection we have combined our figures with comparable material in the literature, have confined the analysis of infections to septicaemia and meningitis and have separated infants from older children (Table 9). Over 1 year of age statistical analysis did not show a significant difference between the incidence of infection in cases of trauma compared with hereditary spherocytosis and thrombocytopenic purpura; it showed a significant difference between hereditary spherocytosis and thrombocytopenic purpura on the one hand compared with thalassaemia and portal hypertension on the other; and it showed a highly significant difference between the incidence in trauma compared with thalassaemia and portal hypertension.

More data are required before it can be stated categorically that hereditary spherocytosis and thrombocytopenia do not themselves carry a greater risk of infection following splenectomy than does traumatic rupture of the spleen. The high incidence of infection following splenectomy in thalassaemia may be related to the necessity for repeated transfusion with consequent development of haemosiderosis; in addition, in thalassaemia and in portal hypertension, repeated admissions to hospital increase the risks of exposure to infection.

The combined figures thus strongly suggest that the underlying disease either *per se*, or in respect

TABLE 9
INCIDENCE OF INFECTION IN RELATION TO AGE
LIFE-THREATENING AND FATAL INFECTIONS ONLY
(Combined Series)

Underlying Condition	Age at Splenectomy					
	0-11 Months			1-16 Years		
	Number of Cases	Number Developing Infection	%	Number of Cases	Number Developing Infection	%
Trauma	0	—	—	181	0	
Hereditary spherocytosis	29	3	10.4	120	3	2.4
Thrombocytopenic purpura	4	3	75	101	2	2
Thalassaemia	0	—	—	70	7	10
Portal hypertension	2	2	100	14	3	21.4

of the treatment it requires, does affect the incidence of serious infection following splenectomy.

Infection in Relation to Absence of Spleen. It has been established that following splenectomy the child in the circumstances described runs greater risk of developing fatal or life-threatening infections in future years, and it remains to be determined whether this is due to the absence of the spleen *per se*. This question may be approached in several ways.

(a) Regarding any one underlying disease the incidence of infection in non-splenectomized may be compared with that in splenectomized patients, providing that strict matching of the two groups can be achieved. Studying cases of thalassaemia major, Smith and his colleagues (1960) found a high incidence of infection in children after splenectomy and none at all in the non-splenectomized group. This might be taken to indicate that splenectomy is a factor in increasing susceptibility to infection, but the two groups were not matched in regard to age and to the severity of the disease.

(b) The incidence of infection following splenectomy may be compared with the incidence following other comparable abdominal operations. Laski and MacMillan (1959) compared the incidence of infection following appendectomy with that following splenectomy, but as has been indicated earlier, the data in their report did not justify drawing conclusions. For purposes of comparison, carefully matched series large enough to allow statistical analysis are essential. Because the importance of the age factor has been clearly established in infancy and because certain underlying diseases are of significance, the most suitable groups for comparison would be infants subjected to splenectomy for traumatic rupture and infants who have had other comparable abdominal operations. But rupture of the spleen at this age is so rare that sufficient cases

for comparison are unlikely to be forthcoming. In the present series the youngest infant with traumatic rupture of the spleen was aged 15 months.* In the Haematology Research Clinic at this hospital the incidence of infection is now being studied in patients operated on under 1 year of age for intussusception. The incidence of infection in this group of infants will be compared with that in the Newcastle series of normal infants and with that in infants in the present series.

(c) The incidence of infection may be studied in cases of congenital absence of the spleen. In the period covered by the present survey two cases of asplenia have been recorded at this hospital. Both had associated cardiac and other abnormalities leading to death in the neonatal period. Signs of infection were not found at autopsy. The majority of cases of asplenia reported in the literature had similar cardiac defects leading to early death, but in two of 11 cases surviving the neonatal period and analysed by Ivemark (1955) and in three of 30 similar cases analysed by Putschar and Manion (1956) death was due to meningitis or to Waterhouse-Friderichsen syndrome.

Asplenia as the sole congenital abnormality has been recorded at autopsy in children only seven times. Meningitis or Waterhouse-Friderichsen syndrome associated with pneumonia was the cause of death in four of the seven children. Infection was noted in two others and Waterhouse-Friderichsen syndrome associated with burns was reported in the seventh case (Table 10).

In adults asplenia as the sole congenital abnormality has been recorded at autopsy 17 times, only six cases having been reported since 1918. In three of these six cases no evidence of infection was noted

* Since this survey was carried out, splenectomy for traumatic rupture has been performed at this hospital in an infant aged 4 days. This child is now 1 year old and has been receiving prophylactic penicillin since the operation and has not had any serious illnesses during that time.

TABLE 10
CONGENITAL ABSENCE OF THE SPLEEN REPORTED IN
CHILDREN

Author	Sex	Age at Death	Autopsy Findings
Ivemark, 1955 ..	F	9 months	Meningitis
Pana, 1934 ..	F	12 months	Meningitis
Murphy and Mitchell, 1957 ..	F	15 months	Meningitis
Nelson and Venable, 1941 ..	M	14 months	Bacterial endocarditis
Beyer, Stoessie and Kober, 1959 ..	F	14 months	Minor burns; Waterhouse-Friderichsen syndrome
Muir, 1959	F	4 years	Pneumonia; Waterhouse-Friderichsen syndrome
Varma, 1922	F	13 years	Injuries; broncho-pneumonia

at autopsy (Putschar and Manion, 1956), and in the other three cases infection was the cause of death. Bacterial endocarditis was recorded in a female (Titoff, 1925), ulcerative colitis and lung abscess in a male (Alexander, 1958) and Waterhouse-Friderichsen syndrome in a male (Myerson and Koelle, 1956). This last report is of particular interest as the type of infection noted was of the same character as many described following splenectomy. This patient was a 36-year-old man who had two attacks of pneumonia, then one of pneumococcal meningitis associated with circulatory collapse. He recovered from this but died six months later of a septicaemic illness. At autopsy there was evidence of acute and healed meningitis, bilateral adrenocortical haemorrhage, pneumonia and purulent cystitis.

These overwhelming illnesses associated with Waterhouse-Friderichsen syndrome, life-threatening pneumococcal infections and recurrent attacks of pneumonia and meningitis reported in cases of asplenia are strikingly similar to the infections recorded following surgical removal of the spleen.

Such reports lend considerable additional weight to the hypothesis that absence of the spleen *per se* does lead to increased susceptibility to serious infection.

Conclusions

Results of the present study and analysis of relevant reports in the literature indicate that splenectomy in childhood does increase the incidence of serious bacterial infections in subsequent years; congenital asplenia seems to produce a similar result. Some children are more susceptible than others to this effect of splenectomy. Two factors that influence this susceptibility are the age of the child at operation and the nature of the underlying disorder. Infections that follow splenectomy tend to be

fulminating, and many of those recorded have been fatal in spite of treatment.

What then should be the clinician's approach to the question of splenectomy in childhood? In infancy splenectomy carries a particularly high risk of subsequent serious infection (at least 20%) which has to be weighed most carefully against the possible benefits that the operation may confer. At any age, children with certain underlying diseases are more susceptible to serious infections following splenectomy, and this fact must be considered when weighing the benefits of the operation against those of more conservative measures.

In the case of traumatic rupture of the spleen, the incidence of post-splenectomy infection in children over 1 year of age is so low that it may be considered negligible for practical purposes. In the case of hereditary spherocytosis the risk of post-splenectomy infection is appreciable, but rarely if ever is it necessary to remove the spleen in early childhood. Recent experience in this hospital shows that even in severe cases splenectomy can reasonably be deferred until after the pre-school period if sufficient attention is paid to providing good general paediatric care with prompt and adequate treatment of infections. In the case of thrombocytopenic purpura similar measures together with early administration of steroids in adequate dosage will in the vast majority of cases result in remission leading to cure, thus obviating the necessity for splenectomy. In the cases of portal hypertension, thalassaemia major and many of the other indications for splenectomy, the incidence of serious infections is certainly greater (10% or more), but a calculated risk often has to be taken. Even so, conservative measures including good general paediatric care may do much to justify deferring splenectomy well beyond the dangerous period of infancy.

In each child a complete assessment is obviously required before recommending splenectomy. Due consideration should be given to the influence of age and of the underlying condition. The advantages of splenectomy over more conservative measures need to be weighed carefully not only against the small risk of immediate surgical complications but also against the greater risk of serious bacterial infections occurring later. Finally, when splenectomy is undertaken, particularly in early childhood, the use of antibiotics prophylactically for perhaps two years after operation should be seriously considered. Penicillin is the antibiotic of choice as almost three-quarters of the recorded infections have been due to organisms ordinarily sensitive to this drug.

Summary

The literature has been reviewed, revealing a lack of proof hitherto of any clear-cut relation between splenectomy and subsequent serious infections.

A careful follow-up has been made of 142 patients on whom splenectomy was performed in childhood, and the figures for the incidence of infections have been statistically analysed.

The incidence of septicaemia and meningitis in infants after splenectomy was much higher than occurs in a normal infant population.

A significant relation was found between the incidence of serious post-splenectomy infections and the age of the patient at operation. The greater susceptibility of infants was particularly striking when the analysis was confined to fatal and life-threatening infections such as septicaemia and meningitis.

In children over 1 year of age the risk of serious infections following splenectomy is still appreciable, except perhaps in the case of traumatic rupture of the spleen.

Certain underlying diseases, including thalassaemia and portal hypertension, themselves carry an increased risk of serious infection.

Of all serious infections recorded following splenectomy, 80% occurred within two years of operation.

Post-splenectomy infections tend to follow a characteristic pattern. The course is fulminating, the mortality high, the infecting organism is predominantly pneumococcal and there is a tendency to recurrent attacks.

In the few cases recorded of uncomplicated congenital absence of the spleen, infections strikingly similar to those following surgical removal of the spleen were the commonest findings noted at autopsy.

A careful assessment of all the factors involved should be made before advising splenectomy in childhood. Following splenectomy long-term prophylaxis, preferably with penicillin, is considered advisable.

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Appendix

Case 1. M.L., male, was born on August 18, 1938. At the age of 1 month he was found to be anaemic, and a diagnosis of *familial haemolytic anaemia* was made on the basis of a strong family history of the disease, a haemoglobin of 46% and increased osmotic fragility of the red cells. Blood transfusion was given and splenectomy was performed two months later, on November 25, 1938, when he was aged 14 weeks. He remained well until September 14, 1940, when he was admitted in a moribund condition with clinical signs of pneumonia and died within 10 hours of the onset of symptoms. At autopsy the upper lobe of the right lung was in a state of red hepatization and there was haemorrhage in both suprarenal glands. The interval between splenectomy and death from overwhelming infection was 22 months.

Case 4. N.N., male, was born in 1927. Following several haematemeses in 1938 a diagnosis of extrahepatic *Banti's Disease* was made and splenectomy was performed on February 9, 1940, when he was aged 12 years. Haematemeses continued, necessitating transfusion at intervals. In August 1945, in spite of transfusions following melaena, he did not respond and died on August 24, 1945. At autopsy he was found to have tuberculosis of the kidney, ureter, and prostate and related lymph gland, miliary tuberculosis and tuberculous meningitis. The interval between splenectomy and death from tuberculosis was five years and six months.

Case 13. L.L., male, was born in June 1937. Following several haematemeses in 1942, a diagnosis of extrahepatic *Banti's Disease* was made and splenectomy was performed on June 27, 1943, when he was 6 years of age. In March 1945, he developed meningococcal meningitis from which he made a complete recovery. Gastro-intestinal haemorrhage continued at intervals necessitating transfusion on several occasions. When interviewed by telephone he stated that he was well, was working in an office full-time, and had not had any serious infections since his illness in 1945. The interval between splenectomy and meningitis was one year and nine months.

Case 31. D.B., male, was born in 1941. In 1945 a diagnosis of *hydatid disease* was made, and three

hydatid cysts were removed from the liver in July of that year. In January 1947 the right kidney was removed. On July 8, 1948, when he was 7 years the spleen was removed for hydatid disease. On March 23, 1950, another hydatid cyst was removed from the liver after which he developed a subphrenic abscess. This was drained on April 6, 1950, and *Staph. aureus* was obtained on culture from the contents. When the patient was interviewed on March 2, 1960, he stated that he was well and had not had any other serious infections. Physical examination did not reveal any other abnormality. The interval between splenectomy and subphrenic abscess was one year and eight months.

Case 32. K.McD., female, was born in 1935. On August 19, 1948, she was admitted to hospital with a few weeks' history of pallor. Her haemoglobin was 20%, the Coombs' test was positive and a diagnosis of *acquired haemolytic anaemia* was made. In spite of repeated simple transfusions a satisfactory haemoglobin level could not be maintained and splenectomy was performed on August 26, when she was 13 years of age. Further frequent transfusions were required and on September 7, exchange transfusion was carried out. She then slowly improved and during convalescence had attacks of upper abdominal pain. These subsided and she was discharged from hospital on November 12, 1948. She remained well for three months, and then on January 5, 1949, had an acute illness of sudden onset ending in death within 10 hours. At autopsy a fibrous-walled left subphrenic abscess of about 300 ml. capacity was found adherent to the stomach with a small slit-like perforation into the stomach. There was discoloration of lung tissue probably due to inhalation of stomach contents. The interval between splenectomy and rupture of subphrenic abscess was five months.

Case 34. J.A., male, was born on August 11, 1944. Splenectomy was performed for *traumatic rupture* of the spleen on January 21, 1949, when he was aged 4 years. In May 1954 he was admitted to hospital with osteomyelitis of the ileum. He responded to antibiotics and operation was not required. He was interviewed on August 20, 1958, at which time history and examination were otherwise normal. The interval between splenectomy and osteomyelitis was 5 years and 4 months.

Case 39. P.P., female, was born on January 1, 1938. Following several haematemeses in 1948 a diagnosis of *portal hypertension* was made and splenorenal anastomosis and splenectomy were performed on May 13, 1949, when she was aged 11 years. Haematemeses continued and oesophago-gastrectomy was carried out in August 1956. In the post-operative period of this operation she developed staphylococcal mediastinitis and empyema, from which she recovered. In November 1957 and August 1958 she had melaena. When interviewed on November 21, 1958, she was doing clerical work and home duties and considered her general health to be excellent. Clinical examination confirmed this statement. The interval between splenectomy and staphylo-

coccal mediastinitis and empyema was seven years and three months.

Case 40. A.D., male, was born in December 1946. Following haematemesis, melaena and ascites in 1948 a diagnosis of *portal hypertension* was made and splenectomy performed on July 23, 1949, when he was aged 2 years and 8 months. Cavernous malformation of the portal vein was found. In October 1955, transgastric portal phlebectomy with ligation of varices was carried out. Subphrenic abscess followed this operation and was treated by drainage. Haematemesis and ascites continued and he died in March 1956. The interval between splenectomy and subphrenic abscess was five years and nine months.

Case 47. (Twin of Case 51.) J.D., male, was born on November 19, 1940. An illness in 1949 in which he became pale and jaundiced was diagnosed as *hereditary spherocytosis* on the basis of microspherocytosis in the blood film, increased osmotic fragility of the red cells and a history of the disease in his father. Splenectomy was performed on November 12, 1949, when he was 9 years of age. In 1954, appendectomy was performed for gangrenous appendicitis and in 1956 he was ill for two weeks with pneumonia. When interviewed on September 17, 1958, he said that his health was good. Physical and haematological examination confirmed his statement. The interval between splenectomy and pneumonia was six years.

Case 51. (Twin of Case 47.) T.D., male, was born on November 19, 1940. In 1949 he was found, like his brother, to have *hereditary spherocytosis*. Splenectomy was performed on December 3, 1949, when he was 9 years. In 1952 appendectomy was performed for acute appendicitis. In 1954 and 1957 he had pneumonia and on each occasion was ill for two weeks. When interviewed on December 10, 1958, he said that his health was good. Physical and haematological examination confirmed this statement. The intervals between splenectomy and the two attacks of pneumonia were five years and eight years.

Case 53. D.D., female, was born in July 1949. A diagnosis of *portal hypertension* was made following haematemesis in October 1949. Splenectomy was performed on February 15, 1950, when she was 6 months. Haematemesis continued. She developed pneumococcal meningitis in May 1950 and recovered. She died on September 20, 1950, following repeated haematemesis. The interval between splenectomy and meningitis was three months.

Case 102. S.G., female, was born on February 25, 1947. Splenectomy was performed following *traumatic rupture* of the spleen on August 23, 1955, when she was 8 years. In 1958 she developed pneumonia which necessitated one week in bed. When seen on February 25, 1959, she gave a history of occasional attacks of spasmodic bronchitis, and apart from a mild allergic

bronchitis, physical and haematological examination were normal. The interval between splenectomy and pneumonia was three years.

Case 110. T.K., male, was born on November 13, 1943. Splenectomy was performed following *traumatic rupture* of the spleen on September 14, 1956, when he was aged 12 years. On March 24, 1957, he developed streptococcal pneumonia which responded to antibiotics. When seen on March 18, 1959, his general health was said to be good and physical and haematological examination were normal. The interval between splenectomy and pneumonia was six months.

Case 132. B.P., male, was born on August 30, 1957. In February 1958, he was found to be anaemic and a diagnosis of *hereditary spherocytosis* was made on the basis of microspherocytosis in the blood film, increased osmotic fragility of the red cells, negative Coombs' test and history of a similar disease in his brother. Transfusion was required and splenectomy was performed on March 4, 1958, when he was 5 months. He was sent home to the country and had a series of pneumonic episodes after the operation necessitating a period in hospital in the country on four occasions. In February 1959, he had another severe pneumonia, responded to treatment in hospital and was sent home. Two days later he developed an overwhelming septicaemia and died within six hours of the onset of the illness. No autopsy was performed. The interval between splenectomy and death from septicaemia was 11 months.

Case 133. M.DeO., male, was born on May 17, 1951. He had pneumonia in 1956. Splenectomy was performed for *traumatic rupture* of the spleen on March 7, 1958, when he was 6 years. In July 1958 he developed pneumonia and was ill for three weeks. When seen on August 12, 1959, his general health was said to be good apart from frequent colds. Physical examination disclosed a mild degree of bronchitis and an eosinophilia. The interval between splenectomy and pneumonia was four months.

Case 140. S.H., male, was born in April 1953. In the neonatal period he had atelectasis, and pneumonia supervened. At the age of 10 days he developed a *staphylococcal infection* of the skin, later he developed staphylococcal otitis media and at 8 weeks of age *Staphylococcus aureus* was obtained on blood culture. At this time signs suggested an intraperitoneal collection, and laparotomy was performed on July 30, 1953. At this operation uncontrollable oozing from an enlarged friable spleen necessitated splenectomy. Within two weeks of splenectomy he required mastoidectomy for staphylococcal mastoiditis. After a series of episodes of respiratory infections he developed staphylococcal septicaemia and multiple abscesses in January 1954. Agranulocytosis followed and death occurred on May 13, 1954. The interval between splenectomy and death from septicaemia was 10 months.

Case 144. C.U., female, was born on April 10, 1958. At the age of 3 weeks she required transfusion for anaemia. At the age of 3 months a diagnosis of *hereditary spherocytosis* was made on the basis of the blood film, increased fragility of the red cells and a negative Coombs' test. There was no family history of hereditary spherocytosis. Further transfusions were

required and splenectomy was performed on December 30, 1958, when she was 8 months of age. In November 1959 she developed influenzal meningitis and recovered with treatment. She was seen one year later and had made an apparently complete recovery. The interval between splenectomy and meningitis was 10 months.