Schnlein-Henoch syndrome (Anaphylactoid purppura) in childhood

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THE SCHÜENLEIN-HENOCH SYNDROME
(ANAPHYLACTOID PURPURA)
IN CHILDHOOD

by

IAN C. LEWIS, M.B., Ch.B., M.R.C.P., D.G.H.

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INTRODUCTION

In children, purpura may be the symptom of a serious or even fatal disease. There are numerous conditions, some very rare, in which it may occur, but one of the commonest is the Schönlein-Henoch Syndrome or anaphylactoid purpura. It does not occur infrequently; for instance, there were 14 cases investigated at the Royal Hospital for Sick Children, Edinburgh, during 1955, compared with 13 cases of acute rheumatism and 9 cases of acute nephritis. Yet the condition is frequently mis-diagnosed and it may even be regarded as somewhat of a rarity by general practitioners.

It must be one of the most fascinating conditions in medical practice for what other disease may present as a problem to the dermatologist, to the rheumatologist, to the surgeon or to the physician? It may be so mild as to almost escape notice or so severe as to cause the patient excruciating pain. Its duration may be only days or its course with exacerbations extend over many years, and at any stage, life may be imperilled by renal or alimentary
complications.

It is, therefore, surprising that so little attention has been paid to the Schönlein-Henoch Syndrome. There are indeed a number of accounts of either special aspects of the condition or studies of cases so few in number as to preclude reliable conclusions. Many papers have drawn tentative conclusions of a conflicting nature and, therefore, it is the author's aim to record the natural history of this most interesting disease paying particular attention to the aetiology and pathogenesis as well as the prognosis and basing deductions on a large series of cases.
The Schönlein-Henoch Syndrome is also termed "anaphylactoid purpura" or again "allergic purpura". The first two titles are very widely recognised, but they are both far from satisfactory. The eponymous combination, like so many such titles, ignores excellent descriptions published prior to the works of Schönlein and Henoch.

The term "purpura" itself is not good when applied to the multiform exanthem. There are reasons why the term "anaphylactoid" should not be used and these will be discussed later. Allergic purpura is an inclusive term which is more acceptable, but as it covers other forms of purpura having no bearing on this thesis, it will not be used.
DEFINITION

The term Schönlein-Henoch Syndrome or anaphylactoid purpura is used to denote a collagen disorder characterised by a rash, pleomorphic in type and of a typical distribution with additional inconstant features, such as gastro-intestinal symptoms (colic, vomiting, melena, haematemesis), joint symptoms (pain, swelling), oedema, haematuria or nephritis. The condition is liable to relapse over an indefinite period and may cause permanent renal damage.
MATERIAL AND METHODS

The cases described and studied hereafter, have occurred in records of the Royal Hospital for Sick Children, Edinburgh, between the years 1944 and 1955 inclusively, and in the paediatric units of the Western General Hospital, Edinburgh, and Leith Hospital between 1950 and 1955 inclusively. They have been accepted only where the rash and its distribution have been characteristic and where, in addition, arthralgia or abdominal colic or both have occurred. In the war years many records were scanty or incomplete and these have been excluded together with the cases in which the typical exanthem was not accompanied by any other symptom, or where there were such atypical features as to leave some dubiety as to the true nature of the condition. The upper age limit for the cases was 12 years (the age limit of the units concerned). A brief summary of the details of the patients selected for the review has been included at the end of this thesis.

In the more recent years many of the cases have been studied personally while in their acute phase and all but 5 have been seen and examined by the author in his follow-up.


HISTORY OF THE SCHÖNLEIN-HENOCH SYNDROME

The history of purpura commences with the famous German clinician, Werlhof who in 1735 recorded the details of an illness suffered by a 10-year-old girl which had the clinical features of a case of acute idiopathic thrombocytopenic purpura. A few cases of a like nature were reported later in the 18th century.

In 1808, however, an English physician, Robert Willan, published a dermatology textbook in which he gave a classification of purpuras, but more important he reported a case of Schönlein-Henoch syndrome as well as describing the exanthem as follows:

"This form of the Purpura (PURPURA URTICANS) begins with hard reddish and rounded elevations of the cuticle of the size and appearance represented plate 30, figure 1. (see reproduction page 7). These small tumours gradually dilate, but within 24 hours they subside to the level of the surrounding cuticle. They are then succeeded by livid spots of the same extent. During the night the spots are somewhat elevated, and exhibit a little redness intermixed with the livid colour; towards morning, they constantly resume their former state being dark-coloured and without elevation.

The tumours are not permanent, but succeed each other in different places, chiefly on the legs, but sometimes on the thighs, arms, breast, etc. On the legs and arms, they are frequently intermixed with petechiae. The most distressing symptoms are a sensation of great languor and debility and a loss of appetite. I have
ILLUSTRATION 1

The first known drawing of the exanthem of the Schönlein-Henoch syndrome reproduced from "On Cutaneous Disorders" by Robert Willan, published in 1806.
not, in any case, observed haemorrhage or fever.

The Purpura Urticans generally appears in the summer and autumn ........."

He goes on to say that it affects children and females.

The case report occurred in Willan's section on Purpura Haemorrhagica, and it is quoted verbatim again:

".........I will here describe the progress of one case which exhibited some striking appearances. A lady, aged thirty-six, of the sanguine temperament, after experiencing for several days a painful inflation of the stomach, was seized, on the 17th of June 1792, with violent vomiting which continued almost incessantly through 18th. and 19th. was accompanied with excruciating pains in the bowels. The fluid discharged was clear, and strongly tinged with green bile, the quantity of it being not less than three or four quarts every day. By the 20th. the vomiting abated and she had several loose stools of a green colour and mixed with black coagulated blood. The diarrhoea continued in this form until the 25th. producing great languor and faintness. During this time the pulse was remarkably slow, and the skin cool; the urine was of a straw colour and deposited a white mucus sediment; the tongue was moist but covered with a yellowish fur. She was always very thirsty, and restless. On the evening of the 25th. her extremities became suddenly cold, her pulse was scarcely discernible, a cold sweat trickled down in streams from every part of the body, her voice was indistinct and her breathing very laborious. From the alarming state she recovered in the course of the night and on the following day a rash appeared over the whole of the body, in small red patches, confluent on the neck, shoulders and nates but in other places distinct. On the 27th. and 28th. the eruption was less extensive but of a livid colour; her hands swelled and was faint and languid but free from internal pain. The discharge of blood ceased at this time. On the 29th. and 30th. she was in better spirits but complained much of pains in the limbs, particularly near the knee joints.

July 1st. and 2nd. she was sick, weary and restless but had not any disorder of the bowels; her tongue was brownish and clammy, and she felt considerable
pain in the wrists. The rash began to fade on the following day. On the 4th, she was easy and able to sit up in bed. Slight vestiges of the livid spots remained on her arms only. Two spots on the back of the left hand terminated with gangrenous sloughs. The complaint was succeeded by large amasarous swellings of the legs, thighs and hands, which were not reduced till the latter end of August, and during that time she continued in a weak irritable state."

This patient exhibited the symptoms of a severe attack of the Schönlein-Henoch syndrome, although there was no macroscopic haematuria. The skin lesions on the back of the left hand resulted in local gangrene, a rather uncommon finding, but it occurred in the present series on occasion. (see illustration No. 28 P. 114).

Willan did not differentiate between haemorrhagic purpuras but a much neglected Frenchman, Ollivier (1927) gave an excellent account entitled "Spontaneous development of ecchymoses with oedema and gastro-enteritis" of a severe case of Schönlein-Henoch syndrome which occurred in a 3-year-old girl. She suffered limb pains, oedema, severe intestinal colic and melena and recurrent crops of the rash. He described not only the site of the exanthem but the characteristics of the lesions at the various stages. For instance,
he noted that they did not blanche on pressure.

"............. The back of the two hands and the lower half of each forearm are oedematous and covered with numerous ecchymoses of a reddish violet, more intense in the centre of the spot, irregularly shaped, being between the diameter of a lentil and \( \frac{1}{2} \) inches; in some of them the violet hue is less deep, more red, the spots diminishing in numbers towards the shoulders. The lower limbs have a somewhat similar aspect, only the oedema is partly absorbing, and among these spots which are generally larger are several the colour of which is greenish yellow similar to that seen in traumatic bruising. They are less numerous on the thighs. ............."

He traced the lesions until they finally disappeared and he noted that a bandage applied just above the knee caused a band of ecchymoses at its edge. The child was at first constipated but later following severe colic she had loose motions partly the result of calomel and enemata. After following the case to complete recovery, he then discussed the condition which he thought was being recorded for the first time. He noted the points which differentiated it from Werlhof's disease. He noted the skin lesions, anorexia, gastro-enteritis and abdominal pain were not features of the latter condition, which frequently presented with haemorrhages and was a pyrexial. In his final paragraph he stated that he did not wish to be carried away by
conjectures, based on an isolated case, which would be open to disputation. If it is argued that Willan did not realise he was describing a new condition and therefore that it is justifiable not to include his name in an eponym, one should grant Ollivier his place in medical history and term the condition "Ollivier's Disease".

Professor J.L. Schönlein's medical lectures delivered in Berlin were collected and published by some of his students. Under the heading "Papulas Rheumatica" he stated that the spots never coalesced as they often did in Werlhof's disease.

A translation of the description is as follows:

"The patients have either previously suffered from rheumatic pains or at the time of the attack rheumatic pains develop in the joints, particularly the knees and the hands which become swollen and tender. The erythematous spots appear in the majority of cases first on the extremities, usually the legs, and only as high as the knees. The spots are small, varying from the size of a lentil to a millet seed, not raised above the surface, and they blanche on pressure. At first bright red, they become dirty brown then yellowish. There is some desquamation. Repeated outbreaks of the eruption occur often for several weeks. Slight changes in temperature such as walking around in another and slightly cooler room may produce fresh eruptions. The disease is usually accompanied by a remittant fever. The symptoms are usually worse in the evening being better in the morning. The urine frequently contains a deposit."

He proceeded to differentiate the condition from
Werlhof's disease remarking that purpura of the mouth mucosa and oral bleeding did not occur.

Schönlein taught that delicately-skinned individuals who had either had rheumatism previously or had had rheumatic arthritis and peliosis together with a cold were more liable to develop the condition. He gave a good prognosis but it is interesting that whereas in his treatment of peliosis rheumatica he paid great attention to the diet and to the bowels, he nowhere mentioned alimentary upsets such as colic, vomiting, melena, etc. He also stated that the skin lesions blanched on digital pressure which was incorrect except in the earliest stage of the rash.

In these accounts of the Schönlein-Henoch syndrome no mention had been made of renal disease or haematuria, but Johnson (1852) in his textbook on "The Diseases of the Kidney" stated -

"Disease of the kidney, with albuminous urine, is very common in connexion with purpura. I have observed this in several instances............"

Johnson proceeded to describe the illness suffered by
In Johnson's own words:

".....When I first saw him on the 19th. (July 1847), the eruption which was then subsiding, consisted of irregular diffused patches, somewhat raised, and of a rather bright red colour; they were chiefly on the outside of the calf, as low down as the ankle, they appeared to be getting well in the centre, where they were elevated and of a fainter colour than at the margins. It appeared to me that purpura would be the name most applicable to the appearance. He appeared well-nourished, complexion clear, gums sound, tongue clean, his habits were regular, his family were all healthy, and there had been no offensive smells in his house. His supper the night before the sudden commencement of his illness consisted of cold meat with pickled cabbage .......

At this time he had no dropsy, but as I had more than once found a similar eruption associated with albuminous urine, I desired him to bring me some urine on the following day.

July 20th. - The urine had a sherry colour and was clear when first passed. After standing, it deposited a light cloud containing numerous epithelial casts with blood corpuscles. It was highly albuminous."

The patient had oedema of the limbs and face as well as limb pains and discomfort in the loins.

Dr. Johnson tried to persuade his patient to enter hospital, but he refused so on August 1st. Dr. Johnson decided to "discontinue his attendance". However he met the man in November and the patient claimed he was fit, attributing his cure to drinking three pints of broom tea daily on the advice of a neighbour. Johnston reported...
that Fox's urine was clear of albumin and abnormal deposit at this time.

Johnson's textbook was thus of considerable importance to those interested in the Schönlein-Henoch syndrome as it showed that the author was fully conversant with the association between this type of purpura and nephritis, that he had observed several cases and that he taught his views. Von Bamberger (1860) made similar observations stating in a treatise on nephritis that peliosis rheumatica was not uncommon in Bright's disease.

It was in 1868 that Henoch's name was first linked with the condition. He described a single case suffering from very severe colic, melaena, vomiting, as well as recurrent purpura and arthralgia. The patient, a 15-year-old boy, had five attacks of the conditions over a period of seven weeks. Six years later he reviewed the case stating that he was now a healthy man. In this paper entitled "About a Peculiar Form of Purpura" he gave full clinical details of three more cases, one being a 4-year-old boy with abdominal
pain and diarrhoea. His stools contained blood and he also had at least two attacks of the exanthem. The child recovered completely within three weeks. Another of Henoch's cases was that of a 12-year-old girl. She had arthralgia with oedema and in addition to the rash she had severe intestinal colic, vomiting and loose melaena motions. The disease ran a 4-week course, during which time there were four further exacerbations. The last case was an 11-year-old doctor's daughter and the description given was most interesting:

"The girl was an absolutely healthy child, although her heart beat was slightly irregular, but no cause could be found for this. In the summer, 1872, she complained of rheumatic pains in both feet and later on in the right hip. These symptoms soon disappeared and the heart sounds remained pure. The first attack of our special disease did not occur until a year afterwards in July 1873. When I was consulted, the illness had already lasted for 5 weeks; at first the pains were rheumatic, occurring in the hand and foot joints without oedema, soon afterwards purpura appeared on the lower extremities, slight fever and at the same time intestinal symptoms such as anorexia, vomiting, colic, melaena; the urine was normal. In 5 weeks there were three more attacks with intervals of 8-9 days between each .........."

He described his initial treatment, but after early improvement:

"the pains recurred suddenly and severely involving the right elbow joint and the left arm. During
the following night (23-24th. July) the child suffered from severe colic accompanied by several greenish vomits and she passed four orange-coloured stools containing many blood clots. The pulse was steady next day ..........

The child improved and appeared to recover completely until September when she had a fifth attack following which she remained well.

Henoch pointed out the salient features of these four cases and added brief notes on three more which he found in the literature. He described the exanthem and its distribution. He did not think they came into the category of purpura, or yet of peliosis rheumatica. He considered that he was describing a new clinical entity.

Here, in Edinburgh, John Thomson translated Henoch's textbook of paediatrics into English in 1889. Henoch by then had recognised the connection with peliosis rheumatica. Henoch gave details of the four cases mentioned above, and added two more, a 7 and an 8-year-old boy, but stated he had seen other cases. He made some important observations; for instance he realised the disease varied from case to case stating :-
"...we see that one of the links in the chain of symptoms may be absent".

He mentioned that characteristically the disease relapsed over days, weeks, or even a year. He warned against giving a favourable prognosis because of the danger of nephritis which had occurred in two of his cases, one dying of this complication.

In 1890, Von Dusch and Hoche, in honour of Henoch's 70th birthday, collected from a survey of the world's literature some 40 cases of "Henoch's purpura" only 13 of which were aged 12 or under. In a lengthy article they reviewed the pathological details and the clinical course.

This historical review of the Schönlein-Henoch syndrome would be incomplete without reference to the work of Sir William Osler. We owe a great deal to his interest in purpura, not only for his studies of the blood platelet (1874), but also for four articles published between 1895 and 1914. These articles were written as a serial and each was entitled "The Visceral Lesions of Purpura and Allied Conditions" and each described an ever-growing number of
cases, finally totalling 28 in Article 4. Only 12 of the cases were examples of the Schönlein-Henoch syndrome, and 9 of these were under 12 years of age. He made important observations; for instance he pointed to similarities between the Schönlein-Henoch syndrome and angioneurotic oedema, urticaria and some forms of purpura and he noted the ability of serum sickness to reproduce the features of the erythematous skin diseases.

"........The local oedema, the urticaria, the purpura, the arthritis, the vomiting and the persistence for years of the sensitiveness are paralleled by the lifelong liability to recurrence in some cases of angioneurotic oedema and of purpura".

Osler thought "the anaphylactic key" would reveal the aetiology of the conditions.

In the years before Osler’s final paper on purpura, Macalister (1906) reviewed the cases of purpura which he had collected during his years of practice. Twenty-one of his cases were described as purpura rheumatica and he stated
death, when it occurred, was due to associated heart disease. He recorded 15 cases of "Henoch's Purpura" mostly between the ages of 6 and 14 years, and although none had died, he went on to say that "Henoch's Purpura" may really be considered a variety of Bright's Disease, and, therefore, the ultimate prognosis is usually unfavourable".

Pratt (1908) gave an excellent review of the disease stating that nephritis "is a serious and very common complication". The age distribution of his cases differed from more recent figures, but the sex ratio was similar to that given by Philpott (1952) and Lewis (1955). Pratt writing in a textbook edited by Osler and McGare expressed the same views given by Osler in his papers.

Osler's observation that the Schönlein-Henoch syndrome bore a close resemblance to certain conditions which had a possible anaphylactic pathogenesis, was reached independently by Frank (1915) and Glanzmann (1916), but as Gairdner (1948) pointed out it was not clear whether they considered anaphylacti-
syndrome or only that clinically this condition was somewhat similar to the picture of serum sickness. Glanzmann (1920) described cases following an upper respiratory tract infection and he suggested that both infection and subsequent sensitization was the explanation of the aetiology in many of the cases. Christian (1917) supported Osler's views and he added further cases of purpura with visceral disturbances. He regarded the condition as due to a disturbance of small blood vessels - capillaries or pre-capillary or post-capillary vascular group - from some cause unknown.

Mention has been made of John Thomson in connection with the translation of Henoch's textbook. In his own book entitled "Guide to the Clinical Examination and Treatment of Sick Children" published in 1898, Thomson made no mention of allergic purpura, but in the 4th. edition (1925) now called "The Clinical Study and Treatment of Sick Children", he gave a full description, going on to say "............occasionally the resemblance to intussusception is increased in a most perplexing way, owing to the occurrence of haemorrhage into
the intestinal wall which gives rise to a palpable tumour. Some cases have also been reported in which such an extrava-
sation has led to a secondary intussusception. The relations
of this form of purpura to such diseases as angioneurotic
oedema, urticaria and erythema multiforme are close and
interesting”.

Reference has been made to the preceding upper respira-
tory tract infection in many cases, but Alexander and
Eyermann (1927 and 1929) published 10 examples of what
appeared to be typical cases of the Schönlein-Henoch syndrome
which were all precipitated by a known food allergen.

In the last 25 years there have been important papers
written, on various aspects of the Schönlein-Henoch syndrome,
but these are so recent in origin that they will have a direct
bearing on sections of this thesis, and therefore they will
be discussed in the light of the findings in the 116 cases
in this review.
INCIDENCE OF THE SCHÖNLEIN-HENOCHE SYNDROME

Origin and Incidence.

In the 12 year period from January 1944 until October 1955 there were 116 cases selected as examples of the Schönlein-Henoch syndrome. The majority of the patients came from the one hospital (Table Ia. p.23). Only cases from 1950 onwards were used from the two other paediatric units, and two records were obtained from the Royal Infirmary, Edinburgh. It would appear from Table Ib. (p.24) that there has been a rapid increase in the incidence of the condition, and this is probably correct, but one should remember that case records in the 1944-1946 period were frequently incomplete or unsatisfactory owing to wartime conditions and staffing difficulties.

No accurate estimate of the incidence of the Schönlein-Henoch syndrome in the general population is possible unless the admission rate to all the hospitals serving the region and the numbers of cases treated solely by the general practitioners are known. This task has not been undertaken


<table>
<thead>
<tr>
<th>Year</th>
<th>R.H.S.C.E.</th>
<th>W.G.H.</th>
<th>Leith Hospital</th>
<th>R.I.E.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1944</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1945</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1946</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1947</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1948</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1949</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1950</td>
<td>7</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1951</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1952</td>
<td>11</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1953</td>
<td>13</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>1954</td>
<td>14</td>
<td>1</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>1955</td>
<td>14</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>
TABLE 1

Yearly Distribution of the 116 cases under review
by anyone as yet. Extensive studies have been made of all aspects of acute rheumatism and since it became notifiable in parts of Britain the epidemiology and other aspects have been recorded by Hewitt and Stewart (1952) based on statistics from the County Boroughs of Sheffield, Bristol, Grimsby and Lincoln. These authors gave the annual incidence of acute rheumatism as 69 new cases per 100,000 of the population. It is unlikely that these west country, midland and east coast areas would be strictly comparable with south-eastern Scotland as climate, industry and many other factors differ so widely. If these were by chance comparable figures, the incidence of the Schönlein-Henoch syndrome would be 94 per 100,000, this deduction being based on the ratio between the number of cases of acute rheumatism and the Schönlein-Henoch syndrome occurring in hospital. The hospital incidence for these two conditions and also for acute nephritis is given in Table 2. (p. 26) for the years 1952-1955. These figures show that nephritis and the Schönlein-Henoch syndrome have a
<table>
<thead>
<tr>
<th>Year</th>
<th>Total Hospital admissions</th>
<th>No. of cases of Sch. - H. syndrome</th>
<th>Incidence</th>
<th>No. of cases of rheumatism</th>
<th>Incidence</th>
<th>No. of cases of nephritis</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1952</td>
<td>1,537</td>
<td>11</td>
<td>1 in 140</td>
<td>4</td>
<td>1 in 384</td>
<td>12</td>
<td>1 in 128</td>
</tr>
<tr>
<td>1953</td>
<td>1,589</td>
<td>13</td>
<td>1 in 122</td>
<td>13</td>
<td>1 in 122</td>
<td>20</td>
<td>1 in 79</td>
</tr>
<tr>
<td>1954</td>
<td>1,776</td>
<td>14</td>
<td>1 in 127</td>
<td>8</td>
<td>1 in 222</td>
<td>12</td>
<td>1 in 148</td>
</tr>
<tr>
<td>1955</td>
<td>1,738</td>
<td>14</td>
<td>1 in 124</td>
<td>13</td>
<td>1 in 131</td>
<td>9</td>
<td>1 in 193</td>
</tr>
<tr>
<td>Average for the 4 year period</td>
<td>1,660</td>
<td>13</td>
<td>1 in 128</td>
<td>9.5</td>
<td>1 in 175</td>
<td>13</td>
<td>1 in 128</td>
</tr>
</tbody>
</table>
similar admission rate and these two conditions are more common than acute rheumatism.

Age of Onset.

The age of onset has been studied by previous authors, but usually they give the age extremes and the mean age. Two recent examples of such statistics are - 8/12 - 10 years, mean 5.2 years (Philpott, 1952); 11/12 - 10 years, mean 4.3 years (Oliver and Barnett, 1955). Gairdner (1948) added his 12 cases to those from earlier papers and the "under twelves" are recorded in Table 3 (p.29), together with those of Simkiss (1953) and Wedgwood and Klaus (1955). In the present series of 116 cases, the age of onset is shown in Table 4 (p.30). This shows that most cases occurred between 2 to 8 years of age with a tendency to peak about the age of 3 (if 2-year age groups are studied). The mean age was 5.5 years. These figures have been added to Table 3 (p.29) for comparison with those mentioned above. It is clear from this Table that there is some difference between Gairdner's figures which included many cases collected in the 19th.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Total</th>
<th>0-1</th>
<th>1-2</th>
<th>2-3</th>
<th>3-4</th>
<th>4-5</th>
<th>5-6</th>
<th>6-7</th>
<th>7-8</th>
<th>8-9</th>
<th>9-10</th>
<th>10-11</th>
<th>11-12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present Series</td>
<td>116</td>
<td>1</td>
<td>2</td>
<td>17</td>
<td>13</td>
<td>13</td>
<td>14</td>
<td>13</td>
<td>14</td>
<td>11</td>
<td>8</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Wedgwood and Klaus</td>
<td>26</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simplicius</td>
<td>51</td>
<td>2</td>
<td>3</td>
<td>15</td>
<td>5</td>
<td>5</td>
<td>8</td>
<td>6</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Von Busch, Hecbe, MacLister, Prent, Gairner</td>
<td>44</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>5</td>
<td>7</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>7</td>
<td>5</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>

*2 aged between 12 and 12½
TABLE 4.

Age of Onset
century and the first 10 years of the present century, and those of the 3 modern series, but there is no doubt that the overall picture is of a disease of childhood, although cases may occur at any age including the very elderly.

**Sex Ratio.**

The sex ratio for the Schönlein-Henoch syndrome has been recorded in several papers (Table 5. p. 32). The figures given are for children under 12 years of age and it is significant that the overall totals and the present series give almost an identical figure, namely 3 males to 2 females (approximately).

**Social Background.**

No previous study of the social background of the Schönlein-Henoch syndrome has been made. Therefore, the parental occupation was grouped according to the Registrar-General's classification and these figures are shown in Table 6. (p. 33), together with the overall hospital admission figures for parental occupation obtained by random sampling over the last 5 years. For comparison the figures for acute
### Table 5

**SEX RATIO M : F (UNDER 12 YEARS)**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Males</th>
<th>Females</th>
<th>Total No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macalister (1906)</td>
<td>0.4 : 1</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Osler (1895 and 1914)</td>
<td>1.5 : 1</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Gairdner (1948)</td>
<td>6 : 1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Philpott (1952)</td>
<td>1.07 : 1</td>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td>Simpkins (1953)</td>
<td>1.125 : 1</td>
<td>1</td>
<td>51</td>
</tr>
<tr>
<td>Oliver and Barnett (1955)</td>
<td>1.89 : 1</td>
<td>1</td>
<td>26</td>
</tr>
<tr>
<td>Wedgwood and Klaus (1955)</td>
<td>1.875 : 1</td>
<td>1</td>
<td>23</td>
</tr>
<tr>
<td>Present Series</td>
<td>1.7 : 1</td>
<td>1</td>
<td>116</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td>1.59 : 1</td>
<td>1</td>
<td>282</td>
</tr>
<tr>
<td>REGISTRAR-GENERAL'S OCCUPATION CLASSIFICATION</td>
<td>Schonlein-Henoch syndrome No.</td>
<td>%</td>
<td>Overall Hospital No.</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>-------------------------------</td>
<td>----</td>
<td>----------------------</td>
</tr>
<tr>
<td>I</td>
<td>2</td>
<td>18%</td>
<td>36</td>
</tr>
<tr>
<td>II</td>
<td>6</td>
<td>5.4%</td>
<td>61</td>
</tr>
<tr>
<td>III</td>
<td>65</td>
<td>58.0%</td>
<td>306</td>
</tr>
<tr>
<td>IV</td>
<td>21</td>
<td>18.8%</td>
<td>80</td>
</tr>
<tr>
<td>V</td>
<td>18</td>
<td>16.1%</td>
<td>55</td>
</tr>
<tr>
<td>TOTAL</td>
<td>112</td>
<td>100.1%</td>
<td>538</td>
</tr>
</tbody>
</table>
rheumatism produced by Hewitt and Stewart (1952) are also shown.

From these figures it would appear that the Schönlein-Henoch syndrome affects commonly the skilled and unskilled workers' families, but this proved to have no statistical significance when compared with the overall hospital figures. The condition is relatively uncommon in the professional classes. (Statistically, the probability of this having arisen by chance lies between 1% and 2%). Rheumatism on the other hand appeared most frequently in the semi-skilled and unskilled workers' families.

**Geographical Location.**

Reports show that the Schönlein-Henoch syndrome occurs in most countries of the world, although the larger series have appeared in temperate climates such as Northern U.S.A., Great Britain, Germany and France. In any one country the incidence may vary from one location to another depending on a number of factors such as population, density, industrialisation, economics and climate. In this review the cases
came mainly from the urban areas as shown in Table 7. P.37) and the map in Fig. 2 (p.38). In Table 7, county population (Census 1951) are included for interest, but it is not suggested that the hospitals concerned with this thesis admit all the paediatric material from the areas mentioned. For instance, many cases from Lanark will go to hospitals in that area, Glasgow or Ayr. It was evident that most patients with Schönlein-Henoch syndrome came from Edinburgh itself, or the mining townships of West Lothian, Midlothian and Fife. The figures in Table 7 revealed that statistically no greater proportion of cases of the Schönlein-Henoch syndrome came from Edinburgh than one would expect from the overall admission rate. In the section on aetiology, the significance of these findings will be discussed.

Summary of Incidence Findings.

There is probably a true increase in the incidence of the Schönlein-Henoch syndrome in this part of Scotland.

The condition has a similar hospital admission rate to that for acute nephritis, and it is more common than acute
rheumatism.

The age of onset is most commonly between 2 and 8 with slight peak at about 3 years.

The sex ratio is M : F 1.7:1

There was a statistically significant decrease in cases occurring in the professional classes.

The vast majority of cases come from densely populated urban communities.
<table>
<thead>
<tr>
<th>City or County</th>
<th>Population (Census, 1951)</th>
<th>Total No. of Hospital Admissions</th>
<th>Schönlein Henoch Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>City of Edinburgh</td>
<td>466,761</td>
<td>468 (46.8%)</td>
<td>64 (55.2%)</td>
</tr>
<tr>
<td>Midlothian</td>
<td>98,974</td>
<td>177</td>
<td>11</td>
</tr>
<tr>
<td>West Lothian</td>
<td>83,577</td>
<td>86</td>
<td>8</td>
</tr>
<tr>
<td>East Lothian</td>
<td>52,258</td>
<td>62</td>
<td>3</td>
</tr>
<tr>
<td>Berwickshire</td>
<td>25,068</td>
<td>24</td>
<td>3</td>
</tr>
<tr>
<td>Peeblesshire</td>
<td>15,232</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Roxburghshire</td>
<td>45,557</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Selkirkshire</td>
<td>21,729</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Lanarkshire</td>
<td>524,596</td>
<td>33</td>
<td>3</td>
</tr>
<tr>
<td>Stirlingshire</td>
<td>167,537</td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>Clackmannan</td>
<td>37,532</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Fife</td>
<td>306,778</td>
<td>104</td>
<td>18</td>
</tr>
<tr>
<td>Inverness</td>
<td>84,930</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Moray</td>
<td>48,218</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Caithness</td>
<td>22,710</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Angus</td>
<td>97,536</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Isle of Lewis</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Cumberland</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Norfolk</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>COUNTY TOTAL</td>
<td></td>
<td>532 (53.2%)</td>
<td>52 (44.8%)</td>
</tr>
<tr>
<td>OVERALL TOTAL</td>
<td></td>
<td>1,000</td>
<td>116</td>
</tr>
</tbody>
</table>
Each number represents the cases of the Schönlein-Henoch syndrome occurring in the county whose name appears immediately above.
Aetiology of the Schönlein-Henoch Syndrome

Month of onset. In a review of over 140 cases of the Schönlein-Henoch syndrome admitted to Glasgow or Edinburgh hospitals, Lewis (1955) demonstrated a seasonal trend. Just over half of the Edinburgh cases of the present study were included in this previous report which revealed a peak incidence in the Spring and Autumn. In the 116 cases from Edinburgh and its surrounds, the trends were not so dramatic. However, in the warmer months there were far fewer admissions for the condition than at other times of the year (Table 8), (p. 40).

These findings suggest that either atmospheric conditions or upper respiratory tract infections play a part in the aetiology.

Preceding Infection. Infection of the upper respiratory tract was by no means an uncommon finding in the period preceding the onset of the Schönlein-Henoch syndrome. In the present series 73 (62.9%) of the cases gave this history. In the 93 cases in which throat swabs were taken 35 (37.6%)
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>10</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td>6</td>
<td>8</td>
<td>5</td>
<td>10</td>
<td>12</td>
<td>13</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>%</td>
<td>8.6</td>
<td>8.6</td>
<td>9.5</td>
<td>10.3</td>
<td>5.2</td>
<td>6.9</td>
<td>4.3</td>
<td>8.6</td>
<td>10.3</td>
<td>11.2</td>
<td>5.2</td>
<td>11.2</td>
</tr>
<tr>
<td>Season</td>
<td>33</td>
<td>29</td>
<td>23</td>
<td>23</td>
<td>31</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 8**

Month of Onset
grew haemolytic streptococci. These figures are much the same as the findings in acute rheumatism and acute nephritis (Lewis, 1955) and they would suggest a similar pathogenesis. Kreidberg et al. (1955) found a history of preceding infection in 15 of 16 cases reviewed by them.

**Streptococcal strains.** The association of a specific type of group A haemolytic streptococci with nephritis has been confirmed. The type 12 strain was noted commonly, but types 2, 4, 18 and 31 may also be cultured from the throats of patients with nephritis (Kelsey and Scholes, 1941; Hannelkamp, Weaver and Dingle, 1952; Wertheim et al., 1953; Wilmers, et al., 1954).

No serious attempt has been made to type the group A haemolytic streptococci isolated from cases of the Schönlein-Henoch syndrome.

Derham and Rogerson (1952) mentioned that haemolytic streptococci were isolated in 15 of 21 cases, but after typing 3 cases they dismissed further investigation on these lines because of lack of uniformity of their findings.
In the present series streptococcal typing was undertaken during 1955. The result of this investigation was as follows.

**TABLE 9**

**Haemolytic Streptococcal Typing**

<table>
<thead>
<tr>
<th>Type Identification</th>
<th>Precipitation</th>
<th>Agglutination</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
<td>3/13/B326</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5/11/27/44</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5/12</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>28</td>
<td>8/25/28</td>
</tr>
</tbody>
</table>

Denham and Rogerson (1952) reported types 6, 12 and 25 in the 3 cases they investigated. It is clear from Table 9 that a number of different strains of haemolytic streptococci may be found in association with the Schönlein-Henoch syndrome.
Both cases associated with the type 12 strain had nephritis but so had one of the cases in which type 5/11/27/44 and the case with type 28. No conclusions can be drawn from such small numbers and it will require years of typing before a series sufficient for statistical purposes has been obtained.

The Latent Period.

In 1955 Lewis drew attention to the similarity of the latent period between the upper respiratory tract infection and the subsequent attack of acute rheumatism, acute nephritis or the Schönlein-Henoch syndrome. In this series, including some of the cases in the 1955 review, the time interval was known in 44 cases and Table 10 shows the scatter.

### TABLE 10

<table>
<thead>
<tr>
<th>No. of days</th>
<th>0-3</th>
<th>4-7</th>
<th>8-11</th>
<th>12-14</th>
<th>15-21</th>
<th>22-28</th>
<th>29-35</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>6</td>
<td>15</td>
<td>4</td>
<td>5</td>
<td>8</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

The average number of days was 12 which compares favourable with the figures quoted for rheumatism and nephritis. A similar time interval was found by Kraidberg,
Dameshek and Latorraca (1955).

The Significance of the Preceding Upper Respiratory Tract Infection.

This is a question which cannot as yet be answered, but there are certain features which point to a bacterial hypersensitivity as a factor in the causation of the Schönlein-Henoch syndrome.

These may be enumerated as follows -

1. The increase in the number of cases during the cold months of the year.
2. The vast majority of cases occur in densely populated urban communities.
3. There is a high incidence of colds and sore throats in the histories obtained as in nephritis and rheumatism.
4. The haemolytic streptococcus is by far the commonest organism obtained from throat cultures.
5. The latent period between the infection and the onset of the Schönlein-Henoch syndrome.
6. The shortening of this latent period with subsequent upper respiratory tract infections (as mentioned in a later section) which again supports a theory based on a hypersensitivity reaction.

Food allergy. That an allergen in the diet may precipitate an attack of the Schönlein-Henoch syndrome is now well established. Cooke (1947) laid down conditions which must be fulfilled before an article of diet may be regarded as a
true allergen. He stated one must produce 3 exacerbations at the same period after the ingestion of the suspected food. Achroyd (1953) stated that a careful enquiry should be made into the dietetic habits of all chronic relapsing cases. He published a table summarising the patients in which food allergy was apparent although not all of them fulfilled Cooke's criteria. The table (Table 11.) is produced with additions as it shows the rarity of these cases. The only case in the present series which was undoubtedly due to food was No.99. This 11-year-old boy's case will be recorded shortly by Richmond and Davidson (1956), and it presents some interesting features. Firstly it was due to chocolate, the child having an exacerbation of the exanthem, intestinal colic and/or arthralgia within minutes of its ingestion. This was shown on 3 occasions and an intradermal scratch test produced not only evidence of a local sensitivity, but the child had generalised symptoms with rash and colic. It is the only recorded case of this type in which a skin biopsy has been taken, revealing the picture described by Gairdner
### TABLE 11

**FOOD ALLERGY CAUSING THE SCHÖNLEIN-HENOCHE SYNDROME**

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Author's Case No.</th>
<th>Sex</th>
<th>Age</th>
<th>Food Allergen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Galloway (1903)</td>
<td>1</td>
<td>F</td>
<td>?</td>
<td>Blackberries and nuts.</td>
</tr>
<tr>
<td>Burrows (1904)</td>
<td>1</td>
<td>M</td>
<td>11</td>
<td>Chocolate.</td>
</tr>
<tr>
<td>Sachs (1916)</td>
<td>1</td>
<td>M</td>
<td>11</td>
<td>Anchovy paste.</td>
</tr>
<tr>
<td>Duke (1921)</td>
<td>6</td>
<td>F</td>
<td>51</td>
<td>Rice, beef, milk, eggs.</td>
</tr>
<tr>
<td>Alexander and Eyermann (1927)</td>
<td>2</td>
<td>F</td>
<td>32</td>
<td>Milk.</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>M</td>
<td>4</td>
<td>Egg.</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>M</td>
<td>50</td>
<td>Milk.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>M</td>
<td>5</td>
<td>Egg, potato, wheat</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>M</td>
<td>14</td>
<td>Egg, chicken, beans.</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>F</td>
<td>32</td>
<td>Plums.</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>M</td>
<td>50</td>
<td>Wheat.</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>F</td>
<td>52</td>
<td>Pork, onions, strawberries.</td>
</tr>
<tr>
<td>Barthelme (1930)</td>
<td>1</td>
<td>F</td>
<td>22</td>
<td>Wheat, egg yolk.</td>
</tr>
<tr>
<td>Eyermann (1935)</td>
<td>1</td>
<td>F</td>
<td>30</td>
<td>Egg, chicken, beans, fish, lamb.</td>
</tr>
<tr>
<td>Diamond (1936)</td>
<td>1</td>
<td>F</td>
<td>5</td>
<td>Milk.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>F</td>
<td>4</td>
<td>Tomato and chocolate.</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>M</td>
<td>3</td>
<td>Popcorn.</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>F</td>
<td>8</td>
<td>Eggs.</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>F</td>
<td>11</td>
<td>Chocolate.</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>M</td>
<td>8</td>
<td>Chocolate.</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>F</td>
<td>5</td>
<td>Chocolate.</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>M</td>
<td>5</td>
<td>Rolled oats and chocolate.</td>
</tr>
<tr>
<td>Hampton (1941)</td>
<td>1</td>
<td>F</td>
<td>15</td>
<td>Milk, potato.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>F</td>
<td>20</td>
<td>Carrot, milk, wheat, pineapple, apple, orange, prune, string beans.</td>
</tr>
<tr>
<td>Brown (1946)</td>
<td>1</td>
<td>M</td>
<td>9</td>
<td>Tomato.</td>
</tr>
<tr>
<td>Jensen (1955)</td>
<td>1</td>
<td>M</td>
<td>6</td>
<td>Fish.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>M</td>
<td>4</td>
<td>Fish.</td>
</tr>
<tr>
<td>Present Series</td>
<td>93</td>
<td>M</td>
<td>11</td>
<td>Chocolate.</td>
</tr>
<tr>
<td>( Richmond and Davidson (1956)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Following tonsillectomy the child had no further trouble, and he is now eating chocolate without trouble and his intradermal chocolate test is negative. The reason why this boy should now be free of symptoms is obscure. It seems possible that chronic tonsillar infection with the streptococcus provided the antigen which required a trigger mechanism - in this case chocolate - to precipitate an exacerbation of the condition. It might be a variety of the Schwartzman-Sanarelli phenomenon which will be mentioned later.

**Family History of the Schönlein-Henoch Syndrome.** No case in the present series gave a history of the condition in other members of the family. Apparent examples, however, have been mentioned. Beimann and Angelides (1951) recorded 23 cases of a condition apparently identical with the Schönlein-Henoch syndrome occurring in 5 generations of the same family. Purpura simplex which is frequently a familial hereditary condition, is closely allied to the Schönlein-Henoch syndrome and reports dealing with the former condition
have mentioned cases of the latter disorder occurring in the families under review (Davis, 1941 & 1948; Ward and Kissin, 1955).

**Family History of Allergy.** Allergic disorders frequently arise in families whose allergic predispositions have already been recognised. If the Schönlein-Henoch syndrome is to be grouped among the allergic purpuras one would expect a higher incidence of allergic disorders in the families of the cases. Hartley and Bell (1936) found no such factor in the background to his cases, but Seidlmayer (1939) disagreed. Wedgwood and Klaus (1955) stated that there was an allergic diathesis in family background of 4 of his 26 cases.

This point was investigated in the present series and the relatives interviewed were questioned about allergy in members of the families. Twelve (10.3%) families gave a history of asthma, eczema, or hayfever. Five hundred parents of patients attending the Royal Hospital for Sick Children, Edinburgh, were questioned to obtain comparable figures to act as a control. Sixty three (12.6%) of the controls had
an allergic diaphysis which would suggest that in the Schönlein-Henoch syndrome there was no hereditary allergic predisposition as an aetiological feature.

**Family History of Rheumatic Fever.** Gairdner, (1948) mentioned that 3 of his 12 cases had a family history of rheumatic fever, but Wedgwood and Klaus (1955) remarked that there was "not any unusual incidence of any of the so-called 'collagen diseases'."

In the present series, 19 (16.4%) of the cases had a family history of acute rheumatism. The five hundred controls mentioned above gave a family history in only 37 (7.4%) instances. This difference might indicate an inherited susceptibility for the so-called collagen disorders.

**Relationship of the Onset with Drug Therapy.** Drugs have not been incriminated to any extent as an aetiological feature in previous series. In the present series many cases received antibiotics, sulphonamides, antihistamines and various analgesics, but only after the onset of the features of the Schönlein-Henoch syndrome. It was possible to obtain a
history of drugs taken prior to this disease in only 9 cases. These were given for throat infection and consisted of sulphonamides in 6 instances, and penicillin in the remaining cases. Drugs would, therefore, appear to have no bearing on the etiology of the Schönlein-Henoch syndrome in this series.

There have been occasional reports of cases of the syndrome caused by drugs. Quinine was implicated by Cregar and Houseworth (1954) in one of their cases, and Jensen (1955) published details of a 27-year-old man who had an attack of the Schönlein-Henoch syndrome after penicillin. He was shown to have a positive skin sensitivity test for this drug.

Summary of Aetiological Findings.

The present review revealed that more cases of the Schönlein-Henoch syndrome occurred in the cold months of the year, and of the 116 patients, 62.9% had a history of preceding upper respiratory tract infection. The haemolytic streptococcus was the usual pathogenic organism isolated from
the throat of these cases, but no particular strain of streptococcus was obtained. The average latent period between the upper respiratory tract infection and the development of the Schönlein-Henoch syndrome was 12 days.

Only one case due to food allergy was discovered in the series. A family history of the Schönlein-Henoch syndrome was not present, and there was no greater incidence of allergy among the relatives of cases than among the general hospital population. There was, however, a greater incidence of rheumatic fever in the family background. Drugs played no part in the aetiology.
Pathogenesis of the Schönlein-Henoch Syndrome.

Review of Hypersensitivity Mechanisms. It is clear that the features which characterise the Schönlein-Henoch syndrome are due to vascular damage. Skin changes have been studied histologically, and there have been pathological descriptions of the lesions in the bowel and kidney. Joint pathology has not received attention. Gairdner (1943) argued that the very close similarity between this feature and that of serum disease suggested a similar aetiological mechanism, i.e. a vascular reaction.

As will be described in the section on pathology, the characteristic lesion in the skin is an acute aseptic perivascular inflammation involving principally arterioles. In some cases the arterioles themselves show degenerative change, to which the term "necrotizing arteriolitis" has been applied. Similar changes have been found in the bowel, brain and kidney. Occasionally larger arteries have been affected, the changes being very similar to those found in polyarteritis nodosa. Balf's (1951) description of the
possible mechanism by which the bowel lesion may be produced is given in the section on bowel pathology.

In the previous section the aetiological features in favour of a bacterial sensitivity reaction were stressed, and it is now proposed to study the possible allergic mechanisms which may produce vascular damage.

The body tissues may become hypersensitive to a specific antigen as the result of exposure to this substance. Subsequent contact of tissues with the antigen invokes an intense inflammatory reaction which is due to an immunological reaction.

Hypersensitive reactions fall into two main categories and a further miscellaneous group.

1. An immediate or anaphylactic group.
2. A delayed or infectious group.
3. A miscellaneous group.

In the immediate reactions, hypersensitivity is induced by ordinary antigens and subsequent exposure precipitates a prompt reaction. Circulating or humoral antibodies against such an antigen may be demonstrated and hypersensitivity may
be induced temporarily in normal subjects by means of serum from a hypersensitive case. The manifestations of this type depend on changes occurring in blood vessels, smooth muscle and collagen.

In the delayed type no relationship between hypersensitivity and circulating antibodies has been shown, and reactions are delayed. The reactions are not restricted to certain tissues. In fact any tissue cell (if exposed to antigen) may be injured or destroyed.

The mechanisms concerned in the production of the immediate type of hypersensitivity have been widely studied. The reaction to the specific antigen follows within seconds or minutes of exposure. In some cases the reaction is not outwardly apparent, but it eventually becomes obvious after repeated antibody-antigen reactions which have a cumulative effect in producing the hypersensitive state.

It is probable that for the occurrence of the immediate type of hypersensitivity there must be a complete antigen capable of combining with tissue proteins which serve as
carriers. The period for sensitisation is about 10 days, and when it occurs the state is immunologically specific.

As a result of the reactions between antigen and antibody which may occur in the circulation or upon or within the cells, certain tissues such as smooth muscle, blood vessels and collagen are affected. Smooth muscle contraction may cause pulmonary difficulties, and vascular spasm may lead to leakage of fluid into tissue as well as tissue damage or necrosis due to occluded vessels. Collagen degeneration may interfere with the functions of vital structures such as heart muscle and heart valves.

There are two possible mechanisms involving an antibody-antigen reaction which could produce the changes in these tissues. The first is where there is a large amount of circulating antibody and the antigenic dose is large, the resulting precipitation seems to damage the walls of blood vessels, and probably this type of reaction explains the Arthus phenomenon which will be mentioned again later in this section.
The second mechanism is believed to be more usual. In this type an intermediate substance is released as the result of an antibody-antigen reaction, and only small amounts of antibody and antigen are required. Circulating antibody may not be directly detectable, but usually its presence may be demonstrated by passive transfer to normal recipients. Many hypersensitive reactions are thought to be due to this mechanism, including anaphylaxis, evanescent skin reactions and atopy. The intermediate substance sometimes known as H substance appears to be histamine or a closely allied substance.

Arthus (1903) described one type of immediate hypersensitivity which was produced by subcutaneous or intradermal injections of antigen at a few days' interval. After the second injection, reactions may develop which occur within half-an-hour of the injection, usually beginning with oedema lasting an hour or two, and with succeeding injections the reactions become more severe and prolonged until necrosis results. Rich (1947) found that one large dose of antigen
could sensitise an animal as well as these repeated small injections. Others have shown that reactions could be precipitated in any vascularised tissue (Seegal et al, 1932), and the Arthus phenomenon was also demonstrated in man.

This type of reaction appears to be due to a direct action of antigen with circulating antibody in the tissues.

The mechanism of the lesion produced by the Arthus phenomenon has been studied in animals microscopically by Abell and Schenck (1938). They showed that in the first stage there is contraction of smooth muscle of the arterioles. The endothelium of the spastic arterioles and also of the capillaries and venules becomes sticky, and the leukocytes adhere to this endothelium and also to each other forming thrombi. Injury to the vascular wall may result in necrosis and exudation of fluid and red blood vessels.

Severe vascular spasm may result in an area of tissue being deprived of its blood supply, and ischaemic necrosis may develop.

There are other types of immediate reaction related to
the Arthus phenomenon, but differing in that they appear within minutes and last for a brief period, never proceeding to necrosis (Zinsser, 1921; Chase, 1947). This type termed the evanescent form of reaction, is identical with the clinical lesion termed 'heat spot' or 'hives'.

A further variety in this group termed anaphylaxis represents an evanescent cutaneous reaction, but on a generalised or systemic scale, and results from the action of the so called H substance. If antigen is injected intravenously anaphylactic shock results. This type of hypersensitivity may be initiated by only small doses of antigen, and the reaction depends on smooth muscle and blood vessel response. The symptoms are elicited within seconds and death may result in only minutes. Some workers claim that anaphylaxis occurs only in animals and the symptoms produced are species specific, but others claim that certain hypersensitive states in man are due to this type of reaction. There is usually a fall in blood pressure and also in body temperature. Blood coagulation is decreased and frequently
an eosinophilia is produced.

Serum sickness is said to result in over 50% of normal individuals receiving animal antiserum or drugs, although less commonly from the latter. The symptoms listed in connection with this condition are as follows: angioneurotic oedema, hives, painful joints, fever and lymphadenopathy. They usually occur 8 - 10 days after the initial dose of antigen and may last for several days. The interval denotes antibody formation, and if antigen remains in the body an antigen-antibody reaction occurs possibly producing focal arteriolar lesions and collagen degeneration, as in polyarteritis nodosa and related conditions.

The sensitive state persists for a variable period during which further antigen elicits either serum sickness again or acute anaphylactic shock. Circulating antibodies may not be found either in vitro or on passive transfer. There may be a constitutional factor which explains why some people appear immune to serum sickness.

Atopic sensitivity is a type of immediate hyper-
sensitivity spontaneous in origin and it includes asthma, allergic rhinitis, urticaria and angioneurotic oedema. It may be produced by a number of inhalants or ingestants acting as antigens. There is frequently a constitutional factor present. It has been mentioned already that bacterial hypersensitivity is generally accepted as an important factor in the aetiology of acute rheumatism and acute nephritis. These diseases together with others reflect damage to vascular and collagen tissue. The fact that vascular damage takes place suggests that the hypersensitivity is of the immediate type. Once hypersensitivity has been established, in certain individuals repeated contact with antigen results in a widespread and progressive injury to vascular endothelium.

Polyarteritis nodosa is characterised by a generalised inflammatory change in small arteries in which the lesions progress from proliferation of the intima and a periarterial reaction to occlusion by proliferation or thrombosis. The nodules contain polymorphonuclear neutrophil and eosinophil
leukocytes and form on the adventitia. Rich (1942, 1943) demonstrated that it may be caused by hypersensitivity to serum or sulphonamide. It is certainly not an immediate response to antigen but rather does it represent the eventual pathological changes resulting from continuous or repeated immunological responses of an immediate type which produce permanent vascular alterations by a gradual build-up of the tissue reactions. It is probable that a constitutional factor is required and when present polyarteritis nodosa may result from different antigenic factors such as drugs or bacterial toxins.

The pathology found in the heart and in the lesions found in other tissues in cases of acute rheumatism allies this condition to polyarteritis. The Aschoff nodules occur in close proximity to vessels and in some cases arterial endothelial changes occur. The nodules are clustered about focal areas of degenerated myocardial collagen.

Clark and Kaplan (1937) and Gregory and Rich (1946) have demonstrated similar lesions in animals as well as in
sensitised humans. Murphy and Swift (1949) have produced pancarditis in rabbits by multiple reinjections of Group A streptococci into the skin. These lesions were similar to the changes found in the rheumatic heart.

There is strong evidence to support this theory based on tissue damage produced by a streptococcal antigen–antibody reaction following the establishment of a hypersensitive state. Cavelti and Cavelti (1945) discovered antibodies in rats and rabbits which react with heart tissue extract produced by injections of homologous heart tissue mixed with streptococci. Cavelti (1947) succeeded in demonstrating antibodies against heart muscle in patients with rheumatic fever.

Rheumatoid arthritis and disseminated lupus erythematosus are further examples of conditions in which immediate hypersensitivity reactions have been suggested.

It has been postulated that the vascular and collagen lesions represent a form of disseminated Arthus reaction depending on a high level of circulating antibody.
In the case of glomerulonephritis the evidence of direct
damage to glomeruli by an antibody-antigen reaction was
rather by analogy only until recently. Cavelti (1947) had
induced the development of antibodies to various homologous
tissues in rats by adding streptococci to tissue emulsions
and he found evidence of specific antibodies as well as
cross reacting ones. Lindemann (as long ago as 1900) first
observed the effect of antikidney serum. Kay (1940) did not
believe that direct damage took place but that the recipient
of antisera formed antibody against it termed by Kay anti-
antibody. When antirenal antibodies had been injected,
they became attached to kidney tissue but were not injurious
until a hypersensitive reaction developed in the production
of antibody. He submitted evidence in favour of this
theory. Cavelti and Cavelti (1945, 1951) experimenting in
rats, demonstrated glomerular lesions after repeated
injections of homologous kidney substance mixed with killed
haemolytic streptococci. Whereas one viewpoint had
considered the renal lesion to be a direct consequence of a
hypersensitive reaction involving streptococci, the findings of Cavelti and Cavelti (1945, 1951) suggested that streptococcal activity so altered renal tissue that it could act as an antigen. This theory stated that the characteristic pathological changes resulted from the immunological response of the body to its kidney tissues rather than to the streptococci. The work of the Cavelti's has not, however, been confirmed by all workers. The recent study of complement level and quantitative estimation of circulating auto renal antibody in man by Lange et al (1949) has given support to this theory. They demonstrated that after an attack of nephritis high complement and antibody levels existed, but that during the acute phase these factors were difficult to demonstrate. They suggested that renal tissue was acting as a vast antigenic surface which 'mopped up' antibody and complement producing the clinical picture of nephritis.

The delayed hypersensitivity reactions are irrelevant to this thesis. They differ from the direct group in
several respects. For instance the induction requires the presence of the organism or its derivative in the tissues in addition to the antigen and antibodies cannot be demonstrated by passive transfer to normal recipients. There are other differences but only one will be mentioned as it accounts for the irrelevancy of this group in an account of the Schönlein-Henoch syndrome. The cells of the body generally are subject to antigen and not just smooth muscle, blood vessel and collagen tissues.

The miscellaneous group contains certain reactions which have a resemblance to the hypertensive states. Two of these have some possible bearing on this thesis.

The term "anaphylactoid reaction" was used for a phenomenon in man which resembles the anaphylactic syndrome in animals. The injection of foreign substances into the body of an individual may result in acute shock. It is possible that in some cases histamine is liberated from the tissues as in anaphylaxis. In other cases a direct toxic reaction of the injected substance seems to occur producing
similar symptoms but a different pathology. A fairly constant feature of anaphylactoid reactions in man is bronchiolar spasm. Capillary thrombosis and embolism in the lungs are also common manifestations.

The Schwartzman-Sanarelli phenomenon is a term used to describe another hypersensitive-like reaction. Sanarelli (1924) noted necrosis of intestinal mucosa in rabbits which had been injected with a sublethal dose of cholera vibrios initially and then after an interval with a few colon bacilli. Sanarelli suggested that several acute abdominal conditions in man were caused by a similar mechanism. Schwartzman (1937) enlarged upon this theory and found that the intense haemorrhagic and necrotic skin reactions could be induced in the skins of rabbits if the filtrate from any of a number of organism cultures was injected intradermally initially and 24 hours later a small intravenous injection of the filtrate was given. The reaction occurred at the site of the first injection and occurred with 2 - 4 hours of the second injection. Histologically the lesions showed thrombosis
and blood vessel disruption. Schwartzman discovered that if there were local stasis and hyperaemia he could replace the intradermal injection by an intravenous one.

The essential requirements for this type of reaction which distinguish it from a true hypersensitive state are as follows.

(1) the provocative or second injection must be intravenous.

(2) the provocative or second injection usually has to be given within 8 to 32 hours of the initial injection.

(3) there is no antigenic specificity involved, as one filtrate may be used for the initial injection and an antigenically unrelated material employed as the provocative dose.

Apitz (1935) described vascular and degenerative changes in the kidneys, lungs, liver and heart following a series of intravenous injections of bacterial filtrate at 24-hour intervals, and later Schwartzman (1937) demonstrated that under certain circumstances only one intravenous injection was necessary to produce the characteristic haemorrhagic and necrotic lesions.

Thomas and Stetson (1949), Stetson and Good (1951) and
Stetson (1951) have demonstrated that the preparatory intradermal injection increased lactic acid production through polymorphonuclear infiltration. The lactic acid, it is suggested, damages the local blood vessels which are occluded by the adherence of platelets and granulocytes in these areas following the provocative injection leading to local tissue damage or necrosis.

Experimental Work. The above review of the hypersensitivity mechanisms reveals that if the type responsible for the Schonlein-Henoch syndrome conforms with one which has been described, it must fall either into the immediate reaction group or into the miscellaneous group.

The Arthus phenomenon, anaphylaxis and the Schwartzman phenomenon are all possible mechanisms. The vascular damage associated with the Arthus phenomenon is thought to be directly due to a severe antibody-antigen reaction with a high titre of circulating antibodies. Anaphylaxis is the result of an antibody-antigen reaction liberating an H substance (histamine) which causes the lesions. The
Schwartzman phenomenon is not fully understood but no-one has been able to demonstrate an antibody-antigen reaction.

The implications drawn from the aetiological findings in the Schönlein-Henoch syndrome led the author to contact Dr. B. Cruickshank of the Department of Pathology, University of Edinburgh in 1953. He was interested in immunological investigations in acute haemorrhagic glomerulonephritis, and was willing to include cases of the Schönlein-Henoch syndrome in his studies.

The following is a very brief summary of Cruickshank's work which will be published at a later date giving a full description of the methods used to determine the presence of antibodies.

Using serum from cases of the Schönlein-Henoch syndrome a series of precipitin reactions were attempted against different extracts of human mesenteric artery.

The first, a saline extract (Extract 1), was prepared by modifying a method described by Stefanini and Mednicoff (1954).
The second (Extract 2) is a potassium chloride extract which contains mucopolysaccharide.

The third (Extract 3) is a tryptic digest somewhat similar to the digest of glomeruli which contained the antigen of nephrotoxic nephritis. The extract probably contains substances insoluble in saline and potassium chloride (Cole et al., 1951).

The fourth (Extract 4) was a glomerular extract.

A fifth test (Staining test) was performed using patients' serum. This serum was 'labelled' (i.e. conjugated with fluorescin amine) and then applied to human skin (as this tissue is commonly affected in the Schönlein-Henoch syndrome). A positive reaction would be demonstrated by fluorescence in the skin section.

These tests were designed to demonstrate qualitatively circulating auto-antibodies to vascular, renal and skin tissues. They are considered to be sensitive for fairly low levels of circulating antibodies, but they will not demonstrate tissue fixed or sessile antibodies. Such
antibodies are difficult to demonstrate even in special tissue extracts.

The results of the above tests are recorded in Table 12, p. 72.

The cases of the Schönlein-Henoch syndrome (denoted by initials) have occurred this year and are not therefore included in the thesis. Polyarteritis nodosa and erythema multiforme are conditions closely allied to the Schönlein-Henoch syndrome and a case of each has been included in Table 12, p. 72. The photograph of the case of erythema multiforme appears on page 175.

It will be noted that these results are negative except for a doubtful positive reaction to renal tissue extract in Case 90. This child had had a severe attack of the Schönlein-Henoch syndrome followed by nephritis, and the specimen of serum was taken at the time of a flare-up of the nephritis without any sign of a relapse of the Schönlein-Henoch syndrome features.

Stefanini and Mednicoff (1954), using only a saline
TABLE 12
Tests for Antibodies

<table>
<thead>
<tr>
<th>Case No. or Initials</th>
<th>Precipitin Extracts</th>
<th>Staining Test</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>96</td>
<td>-</td>
<td>-</td>
<td>H.S. Synd. + Neph.</td>
</tr>
<tr>
<td>(111 (8.9.55)</td>
<td>-</td>
<td>-</td>
<td>H.S. Synd.</td>
</tr>
<tr>
<td>(111(14.11.55)</td>
<td>-</td>
<td>-</td>
<td>H.S. Synd. + Neph.</td>
</tr>
<tr>
<td>112</td>
<td>-</td>
<td>-</td>
<td>H.S. Synd.</td>
</tr>
<tr>
<td>H.A.</td>
<td>-</td>
<td>-</td>
<td>H.S. Synd.</td>
</tr>
<tr>
<td>G.P.</td>
<td>-</td>
<td>-</td>
<td>H.S. Synd.</td>
</tr>
<tr>
<td>M.C.</td>
<td>-</td>
<td>-</td>
<td>H.S. Synd.</td>
</tr>
<tr>
<td>(V.C. (10.1.56)</td>
<td>-</td>
<td>-</td>
<td>H.S. Synd.</td>
</tr>
<tr>
<td>(V.C. (8.2.56)</td>
<td>-</td>
<td>-</td>
<td>H.S. Synd.</td>
</tr>
<tr>
<td>T.S.</td>
<td>-</td>
<td>-</td>
<td>H.S. Synd.</td>
</tr>
<tr>
<td>E.M.</td>
<td>-</td>
<td>-</td>
<td>H.S. Synd.</td>
</tr>
<tr>
<td>R.F.</td>
<td>-</td>
<td>-</td>
<td>Polyarteritis Nodosa</td>
</tr>
<tr>
<td>I.N.</td>
<td>-</td>
<td>-</td>
<td>Erythema Multiforme Stevens-J. Synd.</td>
</tr>
</tbody>
</table>
extract, claimed to have demonstrated antibodies in 6 out of 8 cases of the Schönlein-Henoch syndrome and 3 out of 4 cases of polyarteritis nodosa. This work was not confirmed by Fabius (1955).

This failure to demonstrate antibodies might be due to faulty or incorrect techniques but this is thought to be unlikely. It may mean that antibodies were sessile or in very low concentration. However the tests should eliminate a reaction of the Arthus type with its high concentrations of circulating antibodies, and they may possibly weigh against an anaphylactic mechanism where the response may be produced in the presence of few circulating antibodies.

The Schwartzman phenomenon, however, would appear to be a possibility. No-one has demonstrated an antibody-antigen reaction. Moreover hyperaemia or stasis can be factors in siting the lesions produced by the subsequent intravenous injections of bacterial extract. In a hypothesis based on clinical observations Sheldon (1947) suggested the Schwartzman phenomenon as the mechanism in 3 cases of what
he termed purpura necrotica, probably a severe type of the Schönlein-Henoch syndrome.

In the Schönlein-Henoch syndrome the occurrence of skin lesions at the site of minimal pressure or trauma suggests that stasis or hyperaemia are important. Gairdner's (1948) observation on the influence of gravity in one of his cases would suggest hyperaemia, and in a case in this series the intense crop of the exanthem which occurred not only on the areas of skin in contact with the rim of the bedpan but also over the skin 'trapped' within the bedpan also implicates vascular stasis and congestion. The distribution of the skin lesions (dependent areas and pressure or trauma points) in the Schönlein-Henoch syndrome indicates as important factors hyperaemia and vascular stasis. These areas are the prepared sites for the bacterial toxins arising from an upper respiratory tract infection. Thus the conditions as laid down by Schwartzman could be fulfilled.

**Summary.** The immediate form of hypersensitivity reaction produces vascular lesions.
The Arthus phenomenon and anaphylaxis are two mechanisms depending on different forms of antibody-antigen reactions. The Schwartzman phenomenon is a reaction of unknown pathogenesis. All are possible explanations for the causation of the Schönlein-Henoch syndrome.

Experimental work failed to reveal the presence of circulating auto-antibodies.

The Schwartzman phenomenon would appear to be the most likely explanation for the hypersensitivity reaction producing the Schönlein-Henoch syndrome.
**Pathology of Schönlein-Henoch Syndrome.**

The diverse symptomatology of the Schönlein-Henoch syndrome affecting as it so frequently does more than one organ system makes the study of the pathological features difficult, particularly as so few cases die even within a year of the initial symptoms.

This account will be based on the findings of others as well as recording the reports on the findings in the present series. The features will be discussed in the following order:— skin, alimentary lesion, joint lesion, renal lesion and other findings.

**Skin.** Gairdner (1948) drew attention to the characteristic histology of the skin lesions in the Schönlein-Henoch syndrome. He performed biopsies in 7 cases, taking lesions at various stages, but he found the structural changes essentially the same, but varying in degree. He stated:

"The lesion common to all was an acute inflammatory exudate around the small vessels of the corium. The
cells were polymorphs and histiocytes in roughly equal numbers; eosinophils were prominent in some and predominant in one. Scattered red cells were generally seen in the neighbourhood of the perivascular inflammation though always less numerous than leucocytes. In the neighbourhood of the larger infiltrations the collagen was swollen and stained poorly, but fibrinoid degeneration of collagen was not present. Although the process was largely confined to the corium, here and there it had spread to involve the epidermis which was oedematous and infiltrated by polymorphs and eosinophils, while in one case collections of red cells formed minute bullae. The vessels of the corium were generally normal, but in one case showed endothelial swelling."

Gairdner reviewed the few previous reports and quoted details of a fatal case reported by Wassilieff (1937) in which the skin lesions ulcerated. The histiology showed the cellular infiltration mentioned above, but in addition some of the vessels showed endothelial proliferation.
sufficient to cause obstruction, and also medial necrosis of the arterioles.

Skin biopsies were performed on Cases 62, 83, 93, 98, 107, 108 and 109 of the present series (see illustrations 3 – 8, p. 79+), and these all showed the features described by Gairdner. In 3 cases a few eosinophils were seen, but in none was there any predominance of this type of cell. There were changes in the vessel walls described in 3 cases. The superficial dermis in Case 83 showed acute perivascular inflammatory reactions consisting of aggregations of polymorphs and lymphocytes and there was a precipitation of fibrin around small blood vessels. Several tiny vessels appear to contain fibrinous thrombi. The skin in Case 108 as well as perivascular inflammation showed fibrinoid necrosis of some of the walls in the small vessels of the cutis. The vessels in the corium of Case 109 revealed cuffing with neutrophil and a few eosinophil polymorphs and lymphocytes, but there was also fibrin deposition in and around them. The vessel walls were swollen and obscured
Skin Section X 100

From Case No. 98
The field shows early intradermal perivascular infiltration with lymphocytes, polymorph neutrophil and a few eosinophil leukocytes.

Skin Section X 100

From Case No. 107
There is a more pronounced degree of intradermal perivascular infiltration with lymphocytes and polymorph neutrophil leukocytes.
ILLUSTRATION NO. 5

From Case 91. This field shows considerable perivascular cellular infiltration.

ILLUSTRATION NO. 6

From Case 109 Pronounced perivascular cuffing with polymorphonuclear and occasional eosinophil leukocytes and lymphocytes.
ILLUSTRATION NO.7

Skin Section X 100
From Case 108
Pronounced perivascular cellular infiltration with spill-over into surrounding tissues.

ILLUSTRATION NO.8

Skin Section X 100
From Case 103
An even more severe reaction with early fibrinoid degenerative changes in arterioles present in some fields.
indicating an early stage of necrotizing arteriolitis.

While the biopsy was taken at a macular phase, the lesions developed large bullae the following day.

Thus, unlike Gairdner's cases, 3 out of 7 cases showed vascular degenerative changes in the skin. On of these cases had bullous lesions making it somewhat similar to Wassilieff's case with necrotizing arteriolitis.

Case 98 was severe, developing an ileal intussusception.

His skin biopsy report was as follows:

"There is a small area of inflammatory cell infiltration in the superficial part of the dermis. The cells are mostly lymphocytes with some degenerate neutrophil and a few eosinophil leucocytes. The infiltration is fairly dense in the centre of the affected area, and thine out at the periphery where it is clearly perivascular surrounding capillaries mostly and these capillaries have rather swollen endothelium. The capillaries under the epidermis are congested and a few red corpuscles have escaped, but haemorrhage is less conspicuous than might be expected. No necrosis of blood vessel walls is detectable. The epidermis is very slightly infiltrated by inflammatory cells over the central part of the lesion."

The epidermis was involved but not so severely as one of Gairdner's cases.

A biopsy from Case 62 was taken from an area of haemorrhage into the cutis. It showed, at this stage, effused and partly haemolysed blood only, and no congestion
or perivascular inflammatory changes.

A study of other clinically similar rashes conducted by Gairdner failed to reveal any with a similar histology to that of the Schönlein-Henoch syndrome, except for a case of erythema annulare. In this review he included erythema multiforme and dismissed it as dissimilar. A skin section from a severe case of erythema exudativum multiforme with the features of the Stevens-Johnson syndrome (illustration 9, p. 84) was reviewed and this revealed similar changes to those found in the Schönlein-Henoch syndrome as the following pathological report shows:

"There are small patches of inflammation in the dermis, where extravasated red blood corpuscles, polymorphs and lymphocytes form dense collections mostly in a perivascular distribution and in relation to skin glands. They penetrate to the deep edge of the section. No necrotizing vasculitis is present." (illustration 9, p. 84)

Dr. A.R. Macgregor stated that she would not be able to distinguish between the two conditions on a skin biopsy only.

Alimentary Lesion. Balf (1951) described the alimentary lesion and proffered a theory to account for its characteristic
Skin Section X 100

From a case of Erythema Exudativum Multiforme. The field shows well marked perivascular cellular reaction with more infiltration in the region of a hair follicle.
appearance. This theory has received little attention from subsequent writers, but certainly no attempt has been made at an alternative hypothesis. Balf gave the following explanation for the formation of the lesion described as acute regional enteritis which is so typical of the severe alimentary disorder in the Schönlein-Henoch syndrome.

"The bright red hyperaemic tissue indicates a fast blood-flow through dilated vessels whereas in paralytic distension following spasm it might be expected that the blood-flow would be sluggish and that there would be extravasation of blood into the tissues. The intestinal lesion could best be explained by a submucosal shunt with intense local spasm diverting the greater part of the blood-flow to the outer layers of the bowel. A mechanism of this type has recently been demonstrated by Barclay and Bentley (1949) in the gastric mucosa, and it is at least possible that similar shunts may occur throughout the bowel. Such a mechanism provides an acceptable explanation of the intensity and transience of the symptoms. Irreparable
damage would then depend on the degree of mucosal ischaemia and the consequent infection. Vascular disorders at the submucosal level may be expected to disturb the normal integration of the intrinsic nerve plexuses. It is probable that the abnormal peristalsis in Case 4 (present series, Case 22) and the development of true intussusception in Case 5 (present series, Case 13) are symptomatic of this disturbance."

Such an explanation will obviously be difficult to prove without sufficient pathological specimens and a great deal of experimentation. Case 98 of the present series, a 3-year-old boy, developed severe abdominal pain as well as the typical exanthem, and on admission a palpable abdominal mass was present which at operation was found to be an ileal intussusception. Viability of the intestine at this site seemed doubtful so the intussusception was resected and sent for pathological study. (Illustration No. 10, p. 87.) The child made an uninterrupted recovery and he had no evidence of any renal damage although he had only been out
Case No. 93 Child convalescing from resection of a gangrenous intussusception showing fading exanthem on forearms. He made an excellent recovery.
of hospital 9 months at the time of his last Addis count.

An extract of the report on the intussusception specimen was as follows:-

"............ A transverse section from the viable part near one end of the specimen shows fairly healthy wall at one side, but at the other is an area of necrosis penetrating right through the wall, and inflammatory cell infiltration spreads out on either side of this for a short distance. In this area, in and near the necrotic part, several small blood vessels show hyaline necrosis of the wall and perivascular inflammation - a picture very similar to polyarteritis nodosa. Some of these vessels are thrombosed. Some may be venules but some are certainly arterioles. Another section from the viable part shows one or two vessels affected in this way in places a little removed from necrotic areas. This suggests that the vascular change may not be entirely secondary to the necrosis. It is not usually found in this relation to strangulated bowel."

The vascular changes were found in the submucosa which is important in the light of the theory propounded by Balf (1951). He suggested a vascular shunt which bypassed the vascular damage found in the submucosa. Wassilieff (1937) found similar but far more extensive and severe lesions in one fatal case.

**Joint Lesion.** The joint involvement was not studied pathologically, but as Osler (1895-1914) pointed out there is a close similarity between the arthritis of the Schönlein-Henoch syndrome and serum sickness. The lesion is probably
due to vascular damage and the picture is presumably similar to that found in the skin tissues. Effusion into the joint space is probably minimal, if present at all.

**Renal Lesion.** Naturally, in view of the seriousness of the nephritis which frequently complicates the Schönlein-Henoch syndrome, the kidney has been examined with great care in those cases which have come to autopsy (Watson, 1903; Goldhart, 1928; Sturtevant and Graef, 1933; Rathery and Derot, 1934; Zothe, 1938; Johnson, 1942; Gairdner, 1948; Levitt and Burbank, 1951, 1953).

It is clear from these reports that two distinct types of pathology are being described, one a form of chronic nephritis identical with Bright's disease, and the other subacute nephritis with necrotizing arteritis and arteriolitis affecting the kidneys as well as tissues elsewhere. The first type represents a chronic but progressive process which on post-mortem examination reveals increase in interstitial fibrosis, changes of a degenerative nature in the tubules and fibroosed or hyalinized glomerular tufts.
The subacute nephritis cases reveal all stages of glomerular damage, but chiefly partial fibrosis and epithelial crescentic formation. There is also inflammatory cellular exudate pockets in the intertubular tissue with occasional haemorrhage. The vessels show to a greater or lesser extent fibrinoid necrosis.

Now most of the reports of fatal cases of the subacute type show that they occurred fairly rapidly after the initial illness (Gairdner, 1948; Levitt and Burbank, 1953). The chronic nephritis cases usually have a long history from the time of the attack of the Schonlein-Henoch syndrome.

Case 29, an 11-year-old girl, had an illness covering a period of some 5 months. The course of the disease was considered by paediatricians of considerable experience to be that of the Schonlein-Henoch syndrome. She died from congestive heart failure and a limited post-mortem examination was allowed by her father, who was a doctor. The kidneys, liver, spleen and pancreas were available for examination. The pathological details were as follows:

".... Kidneys were very large. Left kidney weighed 8\(\frac{1}{2}\) ozs. and right kidney weighed 7\(\frac{1}{2}\) ozs. Capsule was smooth and stripped easily. Underlying cortex was dull grey in colour and showed numerous small petechial haemorrhages, and some pale yellow streaking which suggested deposition of lipoid material. Pyramids were dark red in colour and showed no gross abnormality..."

The microscopy revealed widespread glomerular damage.
"..... All stages from early proliferation of the capsule to complete fibrosis can be seen. Many of the capillary tufts and afferent arterioles show fibrinoid necrosis. Many well-marked epithelial crescents are present and not a few glomeruli are represented by whorls of fibrous tissue. In an occasional glomerulus there are red cells in the capsular space. This haemorrhage has probably resulted from fibrinoid necrosis of the capillary tuft. The convoluted tubules are dilated and many contain acidophile fluid. The tubular cells are swollen and fatty degeneration has occurred. There is considerable infiltration of the interstitial tissue by chronic inflammatory cells. In the medulla many of the collecting tubules are packed with red cells. This haemorrhage is quite widespread although few glomeruli contain blood. ..... the presence of fibrinoid necrosis of afferent arterioles and capillary tufts suggests the presence of an allergic factor in the aetiology of the condition." (Illustration No.11, p.92.)

The liver showed arteritis (Illustration No.12, p.92) and the spleen arteriolitis (Illustration No.13, p.93).

This case represents the subacute nephritis type of kidney lesion similar to that described in detail by Wassilieff (1937) and Gairdner (1948).

The clinical history was in keeping with the diagnosis of the Schönlein-Henoch syndrome. The child had an upper respiratory tract infection, and a fortnight later she developed abdominal colic and following laparotomy a normal appendix was removed, but there were some enlarged ileo-caecal glands. A few days later she had painful swollen knee joints and an extensive rash involving the forearms,
This field shows extensive glomerular damage with swelling and/or early fibrosis of the glomerular tuft. There are adhesions between the tuft and the capsule. A preglomerular arteriole in the top right corner shows early fibrinoid necrosis.

The hepatic artery in this field reveals a thickened wall with infiltration with histiocytes, lymphocytes and polymorphonuclear leukocytes. There is pronounced perivascular cellular "cuffing".
Case No. 29 Section reveals gross thickening and considerable inflammatory cell infiltration of arteriolar wall.
elbows, buttocks and lower limbs. She was seen by a number
of distinguished paediatricians and the diagnosis of the
Schönlein-Henoch syndrome was made. She had had severe
headache, and was found to have a subarachnoid haemorrhage,
from which she made a good recovery. There was severe and
rapidly progressive nephritis with a marked haematuria.
The child was anaemic but at no time did she have an
eosinophilia or any respiratory features.

These clinical details are mentioned here to support
the diagnosis. It is obvious from reading this and other
reports on the pathology of the Schönlein-Henoch syndrome
that the dividing line between this condition and poly-
arteritis nodosa must be difficult (if not impossible) to
discern. Rose (1954) reviewed 66 cases of polyarteritis
nodosa and there was renal involvement at some stage in 52
of them. To quote from his report:

"A specific form of glomerulitis was present as the
only renal lesion at necropsy in 16 cases. This was
caracterised in its initial phase by capillary microthrombi,
focal fibrinoid necrosis, polymorph infiltration, and
capsular proliferation (often with crescent formation);
clinically such cases showed macroscopic or heavy haematuria
and early renal failure. Hypertension was not a feature of
this initial phase. The 3 patients who survived this stage
developed progressive hypertension and uraemia and died
within a year; at necropsy the microscopic appearances
resembled those of ordinary chronic glomerulonephritis. In
6 additional cases the typical glomerulitis was associated
with renal polyarteritis.

"...... The liver was involved in at least 29 out of 54
necropsy cases (54%)...... Splenic polyarteritis (usually
in arterioles or small trabecular arteries) was seen in 16
of the 39 cases from which sections were available......
Biopsy of the lesions (skin) was undertaken on 15 occasions,
on 10 of which it was possible to demonstrate local poly-
arteritis; in the negative sections the presence of
infarction or infection usually made interpretation
impossible."
These extracts from pathological reports emphasize the close connection between polyarteritis nodosa and the Schönlein-Henoch syndrome pointed out by Gairdner (1948) and others. Gairdner suggested that the conditions might only differ in the size of vessel affected and it is with this theory, subject to certain modifications, that the author agrees. It would appear that the pathological picture found in the severe or fatal cases of the Schönlein-Henoch syndrome is indistinguishable from polyarteritis nodosa.

The kidney lesion in the Schönlein-Henoch syndrome which has received attention in all fatal cases is probably a progressive disorder. The subacute cases with vasculitis represent a relatively early phase sometimes severe enough to cause death, and the chronic type is the terminal phase in which arteritis and arteriolitis have been replaced by fibrosis. It is this latter variety which is identical with chronic Bright's disease.

Summary. The skin, intestinal and renal vessels in the Schönlein-Henoch syndrome have been shown to be liable
to degenerative changes and to cause perivascular tissue reaction. These suggest a continued or intermittent reaction, possibly of the Schwartzman type.
THE CLINICAL PICTURE OF THE SCHONLEIN-HENOCH SYNDROME

The Schönlein-Henoch syndrome may present with a variety of signs and symptoms but its commonest features involve the skin, gastrointestinal tract, joints, limbs and kidney.

Onset

Mention has been made previously of the upper respiratory tract infection which so frequently precedes an attack of the Schönlein-Henoch syndrome but in this section the features which make up the disease will be considered.

The 116 cases in the series from Edinburgh and its environs presented with the exanthem, colic or arthralgia or by combinations of these. Not one of the cases suffered initially from renal symptoms such as haematuria. Table 13 (p. 99) demonstrates the opening symptoms and gives the frequency of each. The exanthem was the presenting symptom in 31 (26.7%) cases and when these are added to the group in which the rash had developed concurrently with one of the other main features, the total obtained accounts for 59 (50.9%) of the cases in the series. Twenty six (22.4%) presented with
This diagram shows the presenting symptom in the 116 cases of the Schönlein-Henoch syndrome.
alimentary symptoms and the same number with arthralgia. The onsets recorded as having two or more features refer to cases in which these symptoms appeared together or within a few hours of each other. The most common combination was exanthem and arthralgia which occurred in 21 (18.1%) of the cases. Exanthem and intestinal colic and arthralgia and arthralgia and colic combinations each claimed 5 (4.3%) of the cases while the presence of all three features initially occurred in only 2 (1.7%) of the patients.

It is cases presenting with arthralgia or intestinal colic, but with no skin involvement which may make an early diagnosis difficult, or even impossible. Fortunately the exanthem usually appeared within a few days of the first symptoms as is shown in Table 14. The average interval was 7 days.

In the subsequent pages of this section the symptoms and signs found in the Schönlein-Henoch syndrome will be dealt with under various headings and finally the influence of age and sex and the course of the condition will be discussed.
**TABLE 14**

**Time interval between onset of illness and appearance of exanthem**

<table>
<thead>
<tr>
<th>Initial symptom</th>
<th>1-3 days</th>
<th>4-7 days</th>
<th>8-14 days</th>
<th>15-21 days</th>
<th>21+ days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthralgia</td>
<td>13</td>
<td>8</td>
<td>5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Intestinal colic</td>
<td>9</td>
<td>9</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Both of these</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>
Exanthem

From the time of William (1808) onwards every record of the Schönlein-Henoch syndrome has contained a description of the exanthem. Those very features which make it characteristic have had a fascination for the observer and we, therefore, have had accurate day-by-day accounts of the stages undergone following an attack of the disorder. However, there was still some confusion as to what constituted the syndrome possibly caused, quite unintentionally, by Osler (1941, etc.) who described the visceral lesions in several unrelated types of purpura. The classical paper by Gairdner (1948) cleared the picture completely and his work must be considered the most important to medical literature on the Schönlein-Henoch syndrome. The following description could not improve on Gairdner's meticulous observations, but as it is based on a large series of cases it may be of some use as regards the less common features of the disease and also the relative incidence of the rash at the various sites.

The exanthem is the most important point in the diagnosis
of the Schönlein-Henoch. It will be dealt with in three stages: the first will deal with the appearance of the lesions; the second will describe the sites of the skin lesions, and lastly recurrences of the exanthem will be discussed.

**Type of Exanthem.** The initial lesion is urticarial in type in that it is white, raised, slightly itchy, discrete and frequently irregular in outline. (Illustrations 14 and 15 p. 104). This stage is short-lived; in fact it may not be noticed and within 2 to 3 hours the next stage is entered. It is during the next 24 to 48 hours when the typical skin lesions are seen and the diagnosis may be made with certainty.

The lesions become pink or rose-coloured (Illustrations 36 and 37 p. 124). They may be purely papular, particularly in exacerbations or more commonly they may be macular or a combination of the two. The lesion which at first will fade on pressure gradually becomes darker and in 12 to 24 hours has become a dull red hue which will not blanch.

(Illustrations 16-21 p. 105-107). It may be no longer
Illustration 14

Case No. 102
Showing 'urticarial' stage of the exanthem.

Illustration 15

Case No. 115
Showing fading haemorrhagic lesions on the knee and forearm but in addition there are numerous 'urticarial' type lesions which are difficult to discern but which may be seen on careful inspection on the dorsum of the hand towards the top of the photograph.
Illustration 16

Case No. 105
Forearm showing haemorrhagic areas over the elbow region and haemorrhages into the skin area at the wrist. Many petechiae may be seen.

Illustration 17

Case No. 115
The next 2 photographs together with No. 15 and this one were taken in sequence on the same patient and show the wide variety of skin lesions which may be found in any one case. The buttock lesions are papular.
The thigh shows coalescing erythematous patches (made brown in processing).

Case No. 115

The lower leg and foot show a mixture of papular and coalesced erythema on the skin and discreet and markedly haemorrhagic lesions on the dorsum of the feet.

Case No. 115
ILLUSTRATION 20

Case No. 107. Extensive maculopapular eruption in haemorrhagic face (photograph has browned the rose-red lesions).

ILLUSTRATION 21

Case No. 107. Knee area showed papular rash coalescing in par. The lesions were rose-red to purple in colour.
elevated and measures anything from 0.5 to 2 mm. in
diameter and there may be considerable variation in the size
and number of lesions not only at any one site of the rash,
but from one affected area to another. In a few cases the
rash is mildly itchy. In the present series, 15 (13.4%)
complained of irritation. In certain areas lesions may
coalesce (see Illustration No.18 p.106), particularly at
sites of trauma which may be comparatively slight. Common
examples of the effects of injury are the band of lesions
which may form at the margin of a sphygmomanometer cuff used
for the Hess Test. The lesions appear in 3 to 12 hours.
An intradermal injection (such as a Mantoux Test) may be
falsely positive if the disease is in an active phase, but
the reaction will go through the stages of any typical skin
lesion of the Schönlein-Henoch syndrome. This phenomenon
was observed several times in the present series. Case
No.60 was held firmly for a venipuncture, and by the follow¬
ing day she developed lesions at the sites of manual com¬
pression. A further example of this type of artificially
induced lesion occurred in a child who had an unexpectedly good response to an aperient having four bowel movements in one morning. He developed rings of typical lesions on the buttocks at the site of contact with the bedpan rim.

(Illustration No. 22 p. 110) shows the bedpan mark in another patient.

During the next 24 to 48 hours the lesions darken becoming purplish before fading gradually through brown and yellow hues taking a few days to almost a fortnight, depending on the initial size of the lesions, to disappear completely.


In a few cases more serious skin lesions arise which in the haemorrhagic phase go on to bullae formation or ulceration. In the present series, 9 (7.8%) developed this complication. In the bullous type of case the lesions develop as ordinary pink macules and then coalesce rapidly becoming haemorrhagic bullae in 12 to 24 hours. (Illustrations 26-31 p. 113-115).

In a few cases (illustration No. 32 p. 116) the macular
ILLUSTRATION 22

Case No. 110. Buttock lesions in the purplish red haemorrhagic stage showing a strip of rash occurring at the site of pressure from a bedpan rim.
Case No. 100. Showing less extensive and fading lesions. Many are already brown, others still have a dull red hue.
ILLUSTRATION No. 24

Case No. 100. Showing fading lesions around the elbow.

ILLUSTRATION No. 25

Case No. 110. Showing brown fading lesions of a discrete well defined type.
Illustration No. 26

Case No. 108. Showing markedly haemorrhagic skin lesions with some small discrete bullae over the left leg.

Illustration No. 27

Case No. 98. Showing extensive skin lesions in various phases, including an ulcer at the site of a bulla.
Case No. 109

Severe haemorrhagic bullous type of skin lesions in a case in which 'acute regional ileitis' was found on laparotomy.

Case No. 109

Close-up view of the feet of this child. The extensive nature of the bullae is clearly shown.
Case No. 109

The upper limbs of the same child as in the last two photographs. Note the typical distribution of the lesions.

Case No. 109

The feet of the same child some days later showing ulceration. The lesions healed leaving thin scar tissue.
Case No. 114. Small multiple ill-defined skin lesions over the legs which faded almost completely in 3 days.
phase consisted of small multiple but ill-defined lesions
which proceed to a haemorrhagic stage, fading completely
within two or three days.

True petechial haemorrhages may occur scattered between
the macules and there may be a great number or only an occas-
ional one. An inspection of the illustrations will show
petechiae between macular or papular lesions.

It only remains to stress the great variation not only
in the size of the lesions but also in the number. There may
be a few to a dense crop covering a wide area and patchy areas
of coalescing lesions at pressure points.

**Distribution of Exanthem.** So much for the type of lesions.
The next point to be discussed is the distribution of the
exanthem in 116 cases. Table 15 p.116 gives these details.
As the exanthem tends to appear in crops it must be remembered
that different sites are sometimes chosen in each attack.
Gravity or possibly compression may play some part in select-
ing the affected area as Gairdner (1948) suggested in one of
his patients who developed lesions over the arm on which he
<table>
<thead>
<tr>
<th>Site</th>
<th>No. of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Legs</td>
<td>110</td>
<td>94.8</td>
</tr>
<tr>
<td>Ankles and feet</td>
<td>57</td>
<td>49.1</td>
</tr>
<tr>
<td>Arms</td>
<td>88</td>
<td>75.9</td>
</tr>
<tr>
<td>Elbows</td>
<td>33</td>
<td>71.6</td>
</tr>
<tr>
<td>Buttocks</td>
<td>76</td>
<td>65.5</td>
</tr>
<tr>
<td>Pubis and genitalia</td>
<td>21</td>
<td>18.1</td>
</tr>
<tr>
<td>Trunk</td>
<td>14</td>
<td>12.1</td>
</tr>
<tr>
<td>Abdomen</td>
<td>8</td>
<td>6.9</td>
</tr>
<tr>
<td>Shoulders</td>
<td>8</td>
<td>6.9</td>
</tr>
<tr>
<td>Chest</td>
<td>4</td>
<td>3.4</td>
</tr>
<tr>
<td>Face</td>
<td>11</td>
<td>9.5</td>
</tr>
<tr>
<td>Buccal mucosa</td>
<td>7</td>
<td>6.0</td>
</tr>
</tbody>
</table>
invariably leaned while in bed. While there is a tendency to symmetry of the rash this is by no means always so. The number of lesions at any particular site frequently varied considerably between one limb and the other. In a few cases only one limb was affected. In the series under review the legs were by far the most common site for the skin lesions being involved in 110 (94.8%) of the cases. The exanthem may cover the whole foot including the plantar surface (Illustration No. 33a p. 120), but is usually restricted to the dorsal area. At the ankle and again at the knee the lesions may be denser and tending to coalesce. In these areas they may encircle the limb. In the lower leg the extensor surface is commonly involved but in a child who has been lying in bed the exanthem may appear over the calf muscles. The lesions are found most frequently over the lateral border of the thighs and proximally they extend on to the buttocks. A few may be found in the groin and on the genitalia. (Illustration No. 34 p. 121).

The buttocks may be the site of multiple large and
Case No. 116. This photograph shows exanthem involving the soles of the feet.

(The lesions have not photographed well.)
ILLUSTRATION No. 34

Case No. 107. Oedema of the penis with the exanthem on the thigh and genitalia.

ILLUSTRATION No. 35

Case No. 107. One or two lesions on the forehead and an extensive rash on forearms and elbows.
coalescing lesions or just a few papules. A few spots may occur in the lumbar region. In cases with a severe rash scattered lesions may be found on the trunk but in no case was it extensive or marked.

The scapular area which has been described as a relatively common site, was involved in only 8 (6.9%) cases. The upper arms usually escaped except towards the elbow region. Here over the olecranon process 83 (71.6%) cases had lesions. Like the knee and ankle joint the lesions tend to be more plentiful in this area and may coalesce. On the forearms the extensor surface is chosen most frequently. Sometimes severe lesions occur in the wrist area particularly on the dorsal aspect. Again just as in the foot region the whole of the hand may be involved including the palm (Illustration No. 33b p.120), but more often it is only the dorsal area.

A few spots may be found on the face (11 cases, 9.5%, see illustration No.35 p.121). In patients with facial involvement, particularly if the conjunctivae or oral cavity is affected one must consider erythema multiforme. These
ll cases seemed to be typical of the Schönlein-Henoch syndrome. One or two lesions rarely more were seen on the buccal mucosa usually on the hard palate in 7 (6.0%) patients. These never gave rise to frank haemorrhage.

**Recurrences of Exanthem.** It must be stressed that cases vary markedly in both symptoms and signs. The exanthem may appear in only one of the usual sites and recur there with each exacerbation. In some it is extensive initially, but it reappears in only one or two sites. In others it recurs in different places from the first affected area. In 20 (17.2%) cases the initial crop of lesions was the only skin manifestation and no recurrence took place. The importance of exanthem is obvious as the following case report shows.

Case 108 developed intestinal colic and intestinal colic and vomiting and he was referred to hospital remaining 7 days under observation before the exanthem appeared in a limited area over the elbows (Illustrations 36 & 37 p.124). This was the only rash the child developed, and of course gave a diagnosis to the child's otherwise non-specific symptoms.

It is difficult to get an accurate estimate of the number of exacerbations of the exanthem during the course of an attack of the Schönlein-Henoch syndrome. In many cases
The colour printing has made these early rose coloured lesions more brown than they actually were.

Case No. 106

A closer view of the above child. The elbows were the only region affected and the diagnosis was confirmed by studying the skin pathology.
a few new lesions appear daily on an area already involved.

The average number of crops in the 116 cases was four. This is undoubtedly on the low side, but it does give some idea of the difficulty in predicting the course of any one case.

Case 96 has had at least 24 attacks of the exanthem, and Davis (1948) has recorded an example of this syndrome with over 60 exacerbations.
The Alimentary Lesion.

Considerable attention has been given to the gastrointestinal symptoms and signs frequently associated with the Schönlein-Henoch syndrome. There is good reason for this interest for it may be difficult to distinguish the condition from the acute abdominal emergencies of childhood. In fact, intussusception, obstruction or perforation may be a complication of the Schönlein-Henoch syndrome.

Abdominal pain was present in 38 (75.9) cases in the present series. It was usually colicky in type and varied in its severity and periodicity. At its worst the pain was agonizing and the child presented the picture of an acute intestinal perforation. In the milder cases it may be little more than intermittent discomfort. In many cases an attack of colic is accompanied by fresh skin manifestations. The pain tends to recur intermittently for several days, but there may be only one or two attacks of colic in a few cases. The severe attacks of colic usually cause tachycardia, pallor and possibly sweating. Next to abdominal pain, vomiting was the
most frequent alimentary symptom and was nearly always associated with intestinal colic. In this series, 82 (70.7%) vomited during the course of the illness. The vomiting could be persistent or it may only occur occasionally. In the cases with severe colic the vomiting was frequently recurrent, and the vomitus was sometimes 'faecal' in character, particularly in the presence of intussusception or intestinal oedema. The vomitus was not infrequently bloodstained, the blood being present either as so-called 'coffee grounds' or in its fresh red form. Haematemesis occurred in 28 (24.1%) cases in this series. Naturally in the presence of these symptoms appetite is likely to suffer and 69 (59.5%) cases were said to be anorexic. These details are summarised in Table 16 p.13.

The more severe cases with intestinal colic may have changes in bowel rhythm and stool consistency. Constipation was present in 30 (25.9%) cases and diarrhoea was reported in another 19 (16.4%). Melaena occurred in 58 (50%) cases. It was more common than haematemesis and when present it was usually obvious to the naked eye.
It is not surprising that many cases of the Schönlein-Henoch syndrome with severe colic are admitted to surgical wards as abdominal emergencies, particularly if the exanthem has not appeared, has faded, is scanty, or has been overlooked. No less than 26 (22.4%) cases developed abdominal symptoms prior to the exanthem, but 8 (6%) of these had joint symptoms in addition. The time interval between the onset of symptoms and the development of the rash varied from 1 day to 7 weeks with an average of 7 days.

The alimentary symptoms if severe and prolonged may seriously interfere with nutrition. Illustrations No.38 a. and b. p.129 show case 90 after some 4 weeks of intermittent but severe attacks of colic and vomiting.

Fifteen (12.9%) cases were subjected to laparotomy. Sometimes this was due to a mistaken diagnosis, but in the majority the diagnosis was not in doubt and surgery was undertaken because of obstructive features or a palpable abdominal mass. Details of these cases are given in Table 17 p.130.

It will be noted that in only 3 were the findings irrelevant
Case No. 90 showing interference with nutrition caused by the Schönlein-Henoch syndrome in its severe recurrent form. The child was formerly a well nourished child.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Age</th>
<th>Laparotomy Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>M</td>
<td>6</td>
<td>ileocaecal intussusception</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>6</td>
<td>n.a.d.</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>8</td>
<td>colic intussusception</td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>4</td>
<td>&quot;acute regional ileitis&quot;</td>
</tr>
<tr>
<td>21</td>
<td>M</td>
<td>8</td>
<td>&quot;acute regional jejunitis&quot;</td>
</tr>
<tr>
<td>23</td>
<td>M</td>
<td>10</td>
<td>&quot;acute regional jejunitis&quot;</td>
</tr>
<tr>
<td>29</td>
<td>F</td>
<td>11</td>
<td>&quot;enlarged ileocaecal glands&quot;</td>
</tr>
<tr>
<td>50</td>
<td>M</td>
<td>8</td>
<td>n.a.d. other than a &quot;mildly inflamed appendix&quot;</td>
</tr>
<tr>
<td>55</td>
<td>F</td>
<td>5</td>
<td>perforated ileum</td>
</tr>
<tr>
<td>60</td>
<td>F</td>
<td>4</td>
<td>ileal intussusception</td>
</tr>
<tr>
<td>81</td>
<td>M</td>
<td>5</td>
<td>injected and oedematous ileum</td>
</tr>
<tr>
<td>85</td>
<td>F</td>
<td>7</td>
<td>patchy oedematous jejunum</td>
</tr>
<tr>
<td>98</td>
<td>M</td>
<td>3</td>
<td>ileal intussusception</td>
</tr>
<tr>
<td>104</td>
<td>F</td>
<td>5</td>
<td>oedematous terminal ileum</td>
</tr>
<tr>
<td>109</td>
<td>M</td>
<td>3</td>
<td>&quot;acute regional ileitis&quot;</td>
</tr>
</tbody>
</table>
or entirely negative. One case was found to have a perforation of the ileum, 4 had an intussusception and the remainder had either localised or patchy intestinal oedema. This, the type of lesion described by Balf (1951), is usually called acute regional ileitis or acute regional jejunitis.

Bailey (1930) in his review entitled "Purpura as an Acute Abdominal Emergency" made the rather rash statement that purpura was itself a definite entity and that there was no need for subdivisions into thrombocytopenic, nonthrombocytopenic, allergic, Henoch Schönlein and other varieties of purpura. The alimentary lesion, he claimed, was due to haemorrhage into the wall of the small intestine, subserosal haemorrhage in particular causing interference with the normal peristaltic action and producing symptoms of intestinal obstruction. These and other points expounded by an eminent surgeon are such an over-simplification of a wide subject as to be positively dangerous if accepted by the inexperienced, but since 1930 further papers have appeared, and the management of the thrombocytopenic patient undergoing surgery is well
understood and the dangers of the Schönlein-Henoch syndrome are recognised by the paediatric physician and surgeon. Bailey (1930) after a review of the literature, published two tables of considerable interest. The first gave details of 16 cases in which laparotomy had revealed haemorrhage into the bowel wall. Six of these cases were under 12 years of age. The other table contained details of 14 patients in which intussusception was found, of these 11 were in the under 12-year-old group. Details of these and other more recent cases have been recorded in Tables 18 and 19, pages 133 and 134), and Balf's cases, as mentioned previously, have been recorded in the present series as they were all from the Royal Hospital for Sick Children, Edinburgh. A study of these two tables reveals that males outnumber females 3 to 1, compared with the overall sex ratio of 3 to 2, and the greater tendency for intussusception to occur in the younger child, whereas the other types of bowel lesion occur more commonly in an older patient. The average age of the intussusception cases was
### TABLE 18

Laparotomy Findings - petechiae, acute regional lesions, etc.

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Sex</th>
<th>Age</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Murray (Sutherland, 1904)</td>
<td>M</td>
<td>5</td>
<td>haemorrhages into wall near lower end of ileum</td>
</tr>
<tr>
<td>Burrows (1904)</td>
<td>M</td>
<td>11</td>
<td>haemorrhages into ileal wall</td>
</tr>
<tr>
<td>Greig (1908)</td>
<td>M</td>
<td>9</td>
<td>haemorrhage into wall of small intestine</td>
</tr>
<tr>
<td>Pybus (1909)</td>
<td>F</td>
<td>9</td>
<td>haemorrhage into lower ileum</td>
</tr>
<tr>
<td>Kennedy (1928)</td>
<td>M</td>
<td>9</td>
<td>haemorrhages into small and large intestine</td>
</tr>
<tr>
<td>Bailey (1930)</td>
<td>M</td>
<td>8</td>
<td>haemorrhages into wall of jejunum</td>
</tr>
<tr>
<td>Fraser (1930)</td>
<td>M</td>
<td>8-9</td>
<td>petechial haemorrhages diffusely in gut and mesentery</td>
</tr>
<tr>
<td>Balf (1951) No.23</td>
<td>M</td>
<td>10</td>
<td>acute regional 'jejunitis'</td>
</tr>
<tr>
<td>&quot; No.16</td>
<td>M</td>
<td>4</td>
<td>'ileitis'</td>
</tr>
<tr>
<td>&quot; No.21</td>
<td>M</td>
<td>8</td>
<td>'jejunitis'</td>
</tr>
<tr>
<td>Present series Case No.81</td>
<td>M</td>
<td>5</td>
<td>injected and oedematous ileum</td>
</tr>
<tr>
<td>&quot; No.85</td>
<td>F</td>
<td>7</td>
<td>patchy oedematous jejunum</td>
</tr>
<tr>
<td>&quot; No.104</td>
<td>F</td>
<td>5</td>
<td>oedematous terminal ileum</td>
</tr>
<tr>
<td>&quot; No.109</td>
<td>M</td>
<td>3</td>
<td>acute regional ileitis</td>
</tr>
<tr>
<td>Author(s)</td>
<td>Sex</td>
<td>Age</td>
<td>Findings</td>
</tr>
<tr>
<td>---------------------------</td>
<td>-----</td>
<td>-----</td>
<td>----------------</td>
</tr>
<tr>
<td>Sutherland (1896)</td>
<td>F</td>
<td>7</td>
<td>ileocaecal</td>
</tr>
<tr>
<td>Lett (1908)</td>
<td>M</td>
<td>3</td>
<td>ileocaecal</td>
</tr>
<tr>
<td>Hall (1908)</td>
<td>M</td>
<td>5</td>
<td>ileoileal</td>
</tr>
<tr>
<td>Morse and Stone (1909)</td>
<td>F</td>
<td>7</td>
<td>ileocolic</td>
</tr>
<tr>
<td>Sutherland (1909)</td>
<td>F</td>
<td>7</td>
<td>ileocaecal</td>
</tr>
<tr>
<td>Collinson (1910)</td>
<td>M</td>
<td>4</td>
<td>ileoileal</td>
</tr>
<tr>
<td>Tonking (1910)</td>
<td>M</td>
<td>5</td>
<td>ileoileal</td>
</tr>
<tr>
<td>Robinson (1910)</td>
<td>M</td>
<td>5</td>
<td>ileoileal</td>
</tr>
<tr>
<td>McKechnie (1911)</td>
<td>?</td>
<td>2</td>
<td>ileoileal</td>
</tr>
<tr>
<td>Gara (1912)</td>
<td>M</td>
<td>5</td>
<td>ileocaecal</td>
</tr>
<tr>
<td>Barling (1913)</td>
<td>M</td>
<td>4</td>
<td>ileocaecal</td>
</tr>
<tr>
<td>Lederer (1913)</td>
<td>M</td>
<td>2</td>
<td>? site - passed rectally</td>
</tr>
<tr>
<td>Caizergues (1929)</td>
<td>F</td>
<td>3</td>
<td>ileoileal</td>
</tr>
<tr>
<td>Gamstedt (1933)</td>
<td>F</td>
<td>7</td>
<td>ileoileal</td>
</tr>
<tr>
<td>Schwartzman (1933)</td>
<td>M</td>
<td>3</td>
<td>ileocaecal</td>
</tr>
<tr>
<td>Wolfsohn (1947)</td>
<td>M</td>
<td>4</td>
<td>ileoileal</td>
</tr>
<tr>
<td>Balf (1951) Case No.13</td>
<td>M</td>
<td>8</td>
<td>colic</td>
</tr>
<tr>
<td>Present Series No.5</td>
<td>M</td>
<td>6</td>
<td>ileocaecal</td>
</tr>
<tr>
<td>&quot; &quot; No.60</td>
<td>F</td>
<td>4</td>
<td>ileoileal</td>
</tr>
<tr>
<td>&quot; &quot; No.98</td>
<td>M</td>
<td>3</td>
<td>ileoileal</td>
</tr>
</tbody>
</table>
4.7 years as opposed to 7.2 years for intestinal oedema or haemorrhage into the gut wall.

Two other cases in this series are worthy of special mention. Case 3, a 7-year-old girl had severe colic over a period of 8 months. Initially the pain was agonizing and after 5 days she passed shreds of bowel mucosa which continued intermittently together with melaena for 10 days. She finally settled but has a persistent albuminura 8 years after this illness. It is possible that this child had an intussusception which reduced itself, but the mucosal membrane was damaged and sloughed away. Case 22, a 9-year-old girl had the classical features of the Schönlein-Henoch syndrome with an extensive exanthem, gastrointestinal symptoms, arthralgia and nephritis. She had severe colic over a period of 4 weeks and she vomited frequently. An abdominal x-ray taken 3 weeks after admission showed the distended loops and fluid levels associated with intestinal obstruction (Illustration No. 39 p. 136). She was having loose offensive stools and after 3 days, during which time she continued to
Case 22. Print taken from abdominal X-ray, showing fluid levels in distended bowel loops (the signs of obstruction). The condition settled without laparotomy and she has made a full recovery.
have colic and frequent motions, she gradually settled and was able to go home after treatment for the concomitant nephritis. This child has presumably had a localised oedematous lesion in the lower ileum which has produced a partial obstruction.

**TABLE 16**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colic</td>
<td>88</td>
</tr>
<tr>
<td>Vomiting</td>
<td>82</td>
</tr>
<tr>
<td>Anorexia</td>
<td>69</td>
</tr>
<tr>
<td>Melaena</td>
<td>58</td>
</tr>
<tr>
<td>Constipation</td>
<td>30</td>
</tr>
<tr>
<td>Haematemesis</td>
<td>28</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>19</td>
</tr>
</tbody>
</table>
The Joint Lesion and Oedema.

The majority of cases of the Schönlein-Henoch syndrome develop arthralgia or limb pains at some stage. In the series of 116 cases under review, 82 (70.7%) were so affected. The joints affected were frequently asymmetrical or one side might be much worse than the other. The symptoms might recur over several days and the pains might be described as 'flitting' and involve several joints, but in many cases only one or two joints were affected. The severity of the arthralgia varied considerably. In some cases oedema surrounding a joint brought no complaint but in others mild discomfort was present and in yet others frequently with considerable periarticular swelling the pain was severe enough to prevent the use of the involved joint. Table 20 p.138 shows the joints affected and the relative frequency. This Table shows that lower limbs were more frequently affected than upper limbs. Oedema associated with arthralgia or limb pains was a not infrequent finding and Table 21 p.140 shows the sites where these associated symptoms were found. It may be seen that once again it is the lower
<table>
<thead>
<tr>
<th>Limb or Joint</th>
<th>Bilateral</th>
<th>Rt. only</th>
<th>Lt. only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foot</td>
<td>7 (6.0%)</td>
<td>3 (2.6%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Ankle</td>
<td>25 (21.6%)</td>
<td>11 (9.5%)</td>
<td>3 (2.6%)</td>
</tr>
<tr>
<td>Knee</td>
<td>32 (27.6%)</td>
<td>15 (12.9%)</td>
<td>6 (5.2%)</td>
</tr>
<tr>
<td>Leg</td>
<td>8 (6.9%)</td>
<td>4 (3.4%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Hip joint</td>
<td>1 (0.9%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Spine (lower)</td>
<td>4 (3.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand joints</td>
<td>7 (6.0%)</td>
<td>2 (1.7%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Wrist</td>
<td>8 (6.9%)</td>
<td>4 (3.4%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Elbow</td>
<td>17 (14.7%)</td>
<td>5 (4.3%)</td>
<td>6 (5.2%)</td>
</tr>
<tr>
<td>Arm</td>
<td>1 (0.9%)</td>
<td>0</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Shoulder</td>
<td>1 (0.9%)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
### TABLE 21

**Arthralgia or Limb Pain associated with Oedema**

#### Incidence

<table>
<thead>
<tr>
<th>Site</th>
<th>Bilateral</th>
<th>Rt. only</th>
<th>Lt. only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foot</td>
<td>4 (3.4%)</td>
<td>0 0</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Ankle</td>
<td>17 (14.7%)</td>
<td>6 (5.2%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Knee</td>
<td>22 (18.9%)</td>
<td>9 (7.8%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Leg</td>
<td>2 (1.7%)</td>
<td>1 (0.9%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Handjoints</td>
<td>3 (2.6%)</td>
<td>3 (2.6%)</td>
<td>0 0</td>
</tr>
<tr>
<td>Wrist</td>
<td>7 (6.0%)</td>
<td>2 (1.7%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Elbow</td>
<td>8 (6.9%)</td>
<td>3 (2.6%)</td>
<td>3 (2.6%)</td>
</tr>
<tr>
<td>Shoulder</td>
<td>0 0</td>
<td>1 (0.9%)</td>
<td>0 0</td>
</tr>
</tbody>
</table>
limbs which have the greater incidence of oedema combined with
pain. There remains a group of cases few in number in which
pain was absent but in which oedema was associated with a
joint. Tables 20 and 21 demonstrate the asymmetrical nature
of the symptoms in many cases.

It was Schönlein who focussed attention on arthralgia
associated with the Schönlein-Henoch syndrome and he thought
in terms of a rheumatic condition, hence his term 'peliosis
rheumatica'. Writers have since disagreed with Schönlein.

Gairdner (1948) for instance wrote as follows:—

"The pain is rarely as severe as in the arthritis
of rheumatic fever, nor is the joint so tender to touch
or movement. Pain in a joint may be present without
objective signs, while if any swelling is apparent it
is generally due to a periarticular oedema. The
impression was gained that these joint pains are not
relieved by salicylates, though opportunities to
observe this have been few. Fever, if present, is
low grade and rarely above 100°F. In all these ways
the joint symptoms of Schönlein's 'peliosis rheumatica'
differ from true rheumatic arthritis, a fact which has
been pointed out frequently ever since Schönlein's
use of the word 'rheumatic' to describe these cases".

While one must agree that the acute case of juvenile
rheumatism with high fever, swollen, inflamed and acutely
painful joints which is now almost a rarity, bears little
resemblance to the case of the Schönlein-Henoch syndrome
with arthralgia. Today the child with rheumatism has all too often vague limb pains and a low grade fever, tachycardia and an elevated erythrocyte sedimentation rate. It is suggested that with this type of rheumatic disease the differentiation from the Schönlein-Henoch syndrome may be superficially difficult although there is usually no tachycardia and fever is not persistent in the latter condition.

Oedema in relation to an area other than a joint is by no means uncommon. It occurred in 54 (46.6%) cases. It may occur at various sites which have been listed in Table 22 p.143. As will be shown later haematuria was no more common in cases with facial oedema than with other cases of the Schönlein-Henoch syndrome. Once again the most frequent site for oedema was the lower limbs but the genitalia were also commonly affected.

The Renal Lesion.

While the signs and symptoms of the Schönlein-Henoch syndrome associated with skin, bowel, or joint may lead to great discomfort they seldom give rise to permanent disability
TABLE 22

Odema only

In Relation to Joints or Other Areas

<table>
<thead>
<tr>
<th>Site</th>
<th>No. &amp; %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankles</td>
<td>6 (5.2%)</td>
</tr>
<tr>
<td>Knees</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Wrist</td>
<td>3 (2.6%)</td>
</tr>
<tr>
<td>Elbows</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Face</td>
<td>16 (13.8%)</td>
</tr>
<tr>
<td>Sacrum</td>
<td>5 (4.3%)</td>
</tr>
<tr>
<td>Legs</td>
<td>21 (18.1%)</td>
</tr>
<tr>
<td>Feet</td>
<td>16 (13.8%)</td>
</tr>
<tr>
<td>Arms</td>
<td>7 (6.0%)</td>
</tr>
<tr>
<td>Hands</td>
<td>10 (8.6%)</td>
</tr>
<tr>
<td>Genitalia</td>
<td>12 (10.3%)</td>
</tr>
</tbody>
</table>
or lead to a reduced life expectancy. The same, however, cannot be said of the renal lesion. It is not only common, but the prognosis must be guarded. As was mentioned in the section on that subject, the pathology of those cases coming to autopsy may be identical with that found in Bright's disease or nephritis.

In the acute stage of the syndrome haematuria must be regarded as the sign of renal involvement. It is possible, however, that in some cases haematuria is caused by purpura of the bladder mucosa. Mucous membranes elsewhere are commonly affected and so there appears to be no reason why the urinary tract should be exempt. Of the 116 cases reviewed, no less than 54 (46.6%) had haematuria and in 31 (26.7%) it was present in macroscopic amounts. In 38 (32.5%) cases albumen was also significantly present. The long term follow-up of these cases is reported in the section on prognosis.

These figures compare favourably with those published by Philpott (1952). In his series of 40 cases, 19 had
haematuria although in only 4 was blood visible macroscopically. Simpkiss (1953) found evidence of nephritis in 15 of his 51 cases and Oliver & Barnett (1955) stated 11 of their 26 cases aged 2½ to 10 years had haematuria and/or albuminuria. Nine of 26 childhood cases of Wedgwood and Klaus (1955) revealed haematuria. There are other series with somewhat similar findings and, therefore, the results published by Davis (1948) were rather surprising. In a series of 44 patients aged 4 to 71 years he reported haematuria in only 3 cases.

The influence of age and presence or absence of haematuria is shown in Table 24p.154 and is discussed in the section dealing with the effect of age on the clinical picture. Similarly the sex ratio in those developing haematuria is mentioned in the section dealing with this factor and its effect on the clinical picture.

Of the 16 cases of the Schönlein-Henoch syndrome with facial oedema, 8 had haematuria or albuminuria which is much the same ratio as that for the whole series. Oedema without
arthralgia was not associated with a higher incidence of nephritic features.

Simpkiss (1953) stressed that when haematuria occurred it did so in the first week or so of the onset of features of the Schönlein-Henoch syndrome. In many cases haematuria was discovered on admission and it may have been present for an unknown period microscopically. These patients have, therefore, been discarded. The period between the initial symptoms and the onset of haematuria could be calculated in 37 cases. The details are shown in Table 23.

**TABLE 23**

<table>
<thead>
<tr>
<th>Days</th>
<th>1-7</th>
<th>8-14</th>
<th>15-21</th>
<th>21+</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>21</td>
<td>7</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

The average period was 14 days, but one case did not develop nephritic symptoms for 120 days after the first attack of intestinal colic (case No.18). Most cases
developed haematuria in the first 14 days, but one should not lose sight of the fact that nephritic symptoms may develop in a few cases even at a late stage.

Neurological Features.

Previous reports concerning the Schönlein-Henoch syndrome have paid little attention to symptoms referable to the central nervous system and yet they are by no means uncommon.

Headache was not mentioned by Gairdner (1948), Davis (1948), Philpott (1952) and others in their descriptions. It was a relatively frequent complaint amongst the 116 patients reviewed here. No less than 30 (25.8%) had this symptom in the acute phase. These cases were not febrile to any extent and the incidence of haematuria, albuminuria or hypertension was not excessively high. There were, in fact, 18 cases of haematuria in this group which represents 60% compared with 48.3% for the whole series.

Convulsions did not occur in any of the cases in the Edinburgh series but Philpott (1956) reported a child with the Schönlein-Henoch syndrome who developed fits associated
with hypertension. There was no evidence of haematuria or albuminuria. Philpott considered that the features were due to "cerebral arteriolitis similar to the changes found elsewhere".

A most unusual complication of the syndrome was recorded by Green (1946) where he described a case with subarachnoid haemorrhage. Philpott (1955) reported the case of a 7-year-old boy, a typical case of the Schönlein-Henoch syndrome, who developed subarachnoid haemorrhage and later had a residual hemiplegia. Case 29 of the present series, an 11-year-old girl, had also a subarachnoid haemorrhage and made a good recovery only to die 4 months later of renal failure.

Other findings.

Frank haemorrhage is not a feature of the Schönlein-Henoch syndrome but in 3 cases epistaxis was reported. This symptom is usually associated with thrombocytopenic states, but there was no evidence of a lowered platelet count in these 3 cases which were all typical of the Schönlein-Henoch syndrome.
Body Temperature. Of the 116 cases, 48 (41.4%) had some febrile response and in the vast majority it was low-grade (100°F or under) and then only a few spikes. A few who had upper respiratory tract infections on admission or during their time in hospital had temperatures of up to 103°F. These findings confirm the observations of Davis (1948), Wedgwood and Klaus (1955) and Ackroyd (1953).

Haematology. The blood findings in those cases in which full examinations were performed were quite unspectacular. The haemoglobin estimations were all within normal limits except in cases where surgical interference had been required and in Case 29 (the girl who had had subarachnoid haemorrhage and who died of renal failure).

A total white blood cell count was performed in the majority of the cases, but was within normal limits in many. Of 78 cases in which counts were performed, 18 were between 12,000 to 15,000 cells/mm³, 9 were between 15,000 to 20,000 cells/mm³ and one case had a count over this figure. As these figures were taken from cases in the acute phase when concurr-
ent upper respiratory infections existed or had but recently been present, it is probably true to say that there is nothing characteristic about the total white blood cell count, nor indeed in differential white cell count. Only 5 of the cases presented with an eosinophilia of 10% or over. These findings are in general agreement with the conclusions of Bartley and Bell (1936), Gairdner (1948), Davis (1948) and Ackroyd (1953).

The bleeding and clotting times were always normal in those cases where these tests were performed which again is in agreement with the authors mentioned in the last paragraph. The platelet count was recorded in 54 cases and was within normal limits in each case.

Capillary fragility tests were performed in 50 cases by the positive pressure method (Hess test) in the majority of cases or by the negative pressure method used by Walker (1952). Forty-three cases were within normal limits and the remaining 7 showed increased capillary fragility. These figures roughly conform with those given by Davis (1948) and Wedgwood and Klaus (1955). On several occasions the author had the
opportunity of confirming the observation of Balf (1951) who stated that petechiae could be readily produced in areas of skin still stained by the fading exanthem.

The blood sedimentation rate was performed in 83 (71.6%) cases. The upper limit of normal was taken as 10 mm/hour using the so-called 'micro' method. Fifty-eight cases had raised blood sedimentation rates and the proportion of these patients with haematuria was no greater than the overall ratio for the series.

The blood pressure was recorded in some 41 (35.4%) cases. The findings were said to be high if the diastolic pressure was 85 mm. Hg or above and/or the systolic pressure was 130 mm. Hg or above. Thirty-two readings were within normal limits but 9 were abnormal. Among the 41 cases, 24 had symptoms possibly nephritic in origin and 8 of these were associated with raised blood pressure. Therefore, 8 of the 9 hypertensive cases had a possible renal pathology which could account for the blood pressure reading. It is, however, not always as the hypertensive case mentioned by Philpott (1956).
demonstrates. This case is noted later under the heading of neurological symptoms of the Schönlein-Henoch syndrome.

In no case was hypertension sustained and at the time of leaving hospital the blood pressure was normal in all 9 cases.

**Biochemistry**

In a small series of 6 cases plasma protein estimations were made and all the total figures as well as the albumen globulin ratios fell within the accepted normal boundaries. In one case No. 90, a 7-year-old girl, three electrophoretic examinations of serums at weekly intervals failed to reveal any changes in the distribution of the protein fractions. There was no increase in urinary amino acid content as shown by paper chromatography. This case developed a severe nephritis from which she has not fully recovered.

**Splenomegaly.**

Splenomegaly was not a common finding in this series of the Schönlein-Henoch syndrome. In only 4 cases was this feature present and even in these the spleen was only tipped
on deep inspiration. The low incidence is in agreement with the findings of Davis (1946) and Ackroyd (1953).

The Effect of Age on the Clinical Picture.

Before one is able to assess the effect of the age of the patient on the severity and course of the disease the cases must be graded according to their symptoms. The 116 cases of the series were divided into four groups. The first was comprised of patients who arthritic and/or intestinal symptoms lasted less than 3 weeks without any great physical discomfort. The second group were patients with less than 3 weeks' symptomatology, but with severe pain, sometimes requiring analgesics, or where laparotomy had been performed. The 3rd. and 4th. group corresponded to groups 1 and 2 respectively, but the symptoms in these patients lasted longer than 3 weeks.

The results of this division of the series and age of the patients are shown in Tables 24 and 25 p.154 and 155. The figures in parenthesis represent the numbers with haematuria and/or albuminuria. The average ages were:— group 1, 4.7 years; group 2, 5.7 years; group 4, 6.4 years. Group 3
<table>
<thead>
<tr>
<th>Age</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 (1)</td>
</tr>
<tr>
<td>1 - 2</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>2 - 3</td>
<td>12 (4)</td>
<td>3 (3)</td>
<td>2 (2)</td>
<td>17 (9)</td>
<td></td>
</tr>
<tr>
<td>3 - 4</td>
<td>8</td>
<td>4 (3)</td>
<td>1 (1)</td>
<td>13 (4)</td>
<td></td>
</tr>
<tr>
<td>4 - 5</td>
<td>5 (2)</td>
<td>6 (2)</td>
<td>2 (2)</td>
<td>13 (6)</td>
<td></td>
</tr>
<tr>
<td>5 - 6</td>
<td>7 (2)</td>
<td>5 (2)</td>
<td>2 (1)</td>
<td>14 (5)</td>
<td></td>
</tr>
<tr>
<td>6 - 7</td>
<td>6 (4)</td>
<td>4 (1)</td>
<td>3 (2)</td>
<td>13 (7)</td>
<td></td>
</tr>
<tr>
<td>7 - 8</td>
<td>4 (1)</td>
<td>3 (2)</td>
<td>1</td>
<td>14 (8)</td>
<td></td>
</tr>
<tr>
<td>8 - 9</td>
<td>1</td>
<td>4 (1)</td>
<td>6 (5)</td>
<td>11 (7)</td>
<td></td>
</tr>
<tr>
<td>9 - 10</td>
<td>3 (1)</td>
<td>2</td>
<td>1 (1)</td>
<td>2 (2)</td>
<td>8 (4)</td>
</tr>
<tr>
<td>10 - 11</td>
<td>2 (1)</td>
<td></td>
<td>1 (1)</td>
<td>1</td>
<td>4 (2)</td>
</tr>
<tr>
<td>11 - 12</td>
<td>2</td>
<td>3 (2)</td>
<td>1 (1)</td>
<td>6 (3)</td>
<td></td>
</tr>
<tr>
<td>TOTALS</td>
<td>52 (15)</td>
<td>34 (16)</td>
<td>3 (2)</td>
<td>27 (23)</td>
<td>116 (56)</td>
</tr>
</tbody>
</table>
This table shows the effect of age on the severity of the Schönlein-Henoch syndrome.

**Group 1.** Symptoms mild and of less than 3 weeks' duration.
**Group 2.** Symptoms severe and of less than 3 weeks' duration.
**Group 3.** Symptoms mild and of more than 3 weeks' duration.
   (only 3 cases so not plotted)
**Group 4.** Symptoms severe and of more than 3 weeks' duration.

**TABLE 25**
had too few cases in it to be significant. In other words it would appear that the older the child the more severe and more prolonged are the symptoms. When analysed statistically this trend was suggestive but not significant.

The Table is also of interest as it not only shows that the 2 – 3 age group tended to have short mild attacks of the Schönlein-Henoch syndrome but that acute nephritis or features suggestive of acute nephritis were not related to the age of onset but rather to the severity of the symptoms.

In group 1 containing 52 cases, 15 (29.8%) had haematuria; in group 2 of 34 cases, 16 (47.1%) had haematuria; (group 3 had too few cases for any comment) and group 4 of 27 cases no less than 22 (51.5%) had haematuria. If the final column containing the yearly totals is examined the incidence of haematuria does not alter much with the increase in age.

The average age of the 31 patients whose first symptom was the exanthem was 5.3 years, of the 26 who presented with intestinal colic, 5.8 years, and of the 26 who had arthralgia
initially, 5.8 years. Age, therefore, did not seem to influence the presentation of the disease.

Reference has already been made to the average ages of surgical cases of the Schönlein-Henoch syndrome. Intussusception was found to occur in children whose average age was 4.7 years compared with the average of 5.5 years of the 116 cases of this series. Other surgical cases which were found to have bowel oedema or gut wall haemorrhage on laparotomy had an average of 7.2 years.

Before leaving the effects of age, the average age of 23 cases which had exanthem arthralgia and intestinal colic while in hospital was 5.3 years. There were 37 cases which had haematuria in addition to the features of these cases and their average age was 6 years. In other words the more severe illness again tended to affect the older child.

The conclusion to be drawn from the effects of age on the Schönlein-Henoch syndrome appears to be that in the acute stages the older child tends to have severer symptoms which last longer and they are more liable to have haematuria.
The Effect of Sex on the Clinical Picture.

Gairdner (1943), noting a predominance of males affected by the Schönlein-Henoch syndrome, was particularly struck by the heavier male incidence amongst the cases which had developed some acute abdominal complication, and this is one of the few references to a possible sex factor in the clinical severity of the disease.

In the present series the sex ratio was 3:2 (73:43), and that for the cases associated with haematuria 34:21 which is a very similar ratio.

Sex ratio in cases graded as short and mild (group 1) was 29:23; in those regarded as short and severe (group 2) 24:10, and those with prolonged and severe symptoms (group 4) 17:10. If anything these figures suggest that the female is more liable to have a short mild illness than the male.

With regard to Gairdner's observation mentioned above, the 15 patients on whom laparotomies were performed, had a ratio of 10:5, which is obviously not statistically different from the overall sex ratio and if one excludes two cases in which
no abnormality was discovered the ratio would be 8:5, giving a very similar figure.

It may be of interest to note that the sex ratio of the admissions to the medical wards for the year 1955 was not different statistically from that for the Schönlein-Henoch syndrome.

**Clinical Course**

The Schönlein-Henoch syndrome runs an unpredictable course characterised by sudden (and often unexplainable) exacerbations which may be followed by equally unexpected remissions. The duration of the disease is very variable. Ackroyd (1953) reported that the average duration of symptoms in cases of the Schönlein-Henoch syndrome was one month during which time there were four to five recurrences. The extremes of the condition have been recorded by Davis (1948) one of whose patients had relapses over 50 years and Pratt (1908) who reported a case with 60 exacerbations in 5 years.

An attempt will be made here to give some generalisations derived from the 116 cases studied.
In many cases, for instance, the exanthem occurred in crops, and Table 26 shows some details of these.

<table>
<thead>
<tr>
<th>No. of crops of exanthem</th>
<th>1</th>
<th>2 - 5</th>
<th>6 - 10</th>
<th>11+</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>20</td>
<td>68</td>
<td>23</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 26 refers to the number of crops of the exanthem occurring in each case. The majority of the patients (58.6%) had two to five attacks. Table 27 refers to the time in days between the first and last crop of the exanthem. More than half the cases had no fresh skin lesions after the first 2 weeks but some cases have exacerbations for much longer, one
for instance having had fresh spots occurring over a period of 10 months.

The intestinal colic and arthralgia may cause considerable discomfort and repeated attacks of pain may last for many days. Tables 28 and 29 show statistical details of the cases in this series.

TABLE 28

<table>
<thead>
<tr>
<th>No. of exacerbations</th>
<th>1</th>
<th>2-5</th>
<th>6-10</th>
<th>11+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal colic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>24</td>
<td>19</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>Arthralgia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>22</td>
<td>50</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

TABLE 29

<table>
<thead>
<tr>
<th>No. of days</th>
<th>1-5</th>
<th>6-10</th>
<th>11-15</th>
<th>16-20</th>
<th>21-30</th>
<th>31-60</th>
<th>61-180</th>
<th>181+</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>49</td>
<td>12</td>
<td>7</td>
<td>9</td>
<td>17</td>
<td>14</td>
<td>7</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 28 shows that the arthralgia tended to have few recurrences e.g. 90% of the cases had 5 or fewer attacks,
but abdominal discomfort had many more, e.g. over half had 6 or more exacerbations and 35.2% had 11 or more. Table 29 p.161 reveals that the period of time during which attacks of pain occurred varied considerably, but in 52.6% of the cases it was 10 or less days. The average duration was 23.5 days.

The features of the acute stage of the Schönlein-Henoch syndrome varied from case to case but the preceding pages of this section have shown that a large number of patients have a multiplicity of symptoms. Table 30 p.162 shows the main complaints diagrammatically.

Twenty three (19.8%) had exanthem, intestinal colic and arthralgia and a further 37 (31.9%) had haematuria or albuminuria as an additional complication. Thus, 60 (51.7%) had at least three of the characteristic features.

Fourteen (12.1%) required hospitalisation on more than one occasion. One case (No. 57) was admitted five times over a period of 2 years. The longest interval between relapses was almost 7 years (case 8). This 6-year-old boy had severe symptoms of the Schönlein-Henoch syndrome in September 1946,
TABLE 30

Distribution of Main Symptoms.
but remained well until June 1953 when he was admitted to
another hospital with a history of a rash on his legs and
lower trunk and abdominal pain associated with melena.
Although the diagnosis was not suggested during his second
admission, it seems more than likely that he had suffered
during his second admission a recurrence of his original
illness.

Naturally with such variations in the clinical course,
the spent in hospital showed considerable differences.
Table 31 gives the distribution.

<table>
<thead>
<tr>
<th>Time in hospital (in weeks)</th>
<th>0-1</th>
<th>1-2</th>
<th>2-3</th>
<th>3-4</th>
<th>4-8</th>
<th>8-16</th>
<th>16-26</th>
<th>26+</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>8</td>
<td>25</td>
<td>15</td>
<td>14</td>
<td>20</td>
<td>16</td>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>

More than half the patients spent under 4 weeks in
hospital. The average time in hospital was 36 days. These
findings are in agreement with those of Wedgwood and Klaus (1955).

**Other Diseases and the Schönlein-Henoch Syndrome.**

**Upper Respiratory Tract Infection.** The effect of upper respiratory tract infections may be studied on occasion in patients who have been in hospital for a long period. Seven cases in the present series while convalescing complained of sore throats and in 2 of them haemolytic streptococci were isolated. These patients developed fresh skin lesions at the time of this infection or shortly after, and in addition abdominal discomfort recurred in 2 patients within a few hours.

**Nephritis and Rheumatic Fever.** The possible association of these diseases with the Schönlein-Henoch syndrome was discussed very fully by Gairdner (1948).

Nephritis, of course, is the main and most serious complication of the Schönlein-Henoch syndrome and this will be discussed at length under the section on prognosis, but reference is to 2 cases No.27 and 90. The first, a 10-year-old male was first admitted to hospital on 8.4.49. Following a
sore throat he had developed intestinal colic, arthralgia and exanthem. He remained in hospital for 3 weeks, during which time he had a transient microscopical haematuria. He then remained well until the 28th September of the same year when a further sore throat was followed within 2 days by a frank haematuria and albuminuria with granular casts. He had a transient hypertension, but no skin, bowel, or joint lesions. Again after a 2 months stay in hospital his urine was apparently normal. On December 15th, he developed typical exanthem and a painful swollen right ankle joint.

The second case, a 7-year-old girl, was admitted on 9.9.54 with all the features of a severe case of the Schönlein-Henoch syndrome. A week later she developed haematuria and albuminuria while she continued to have severe intestinal colic and persistent vomiting. Renal damage was evidently severe and she was kept in hospital for 10 months. She was discharged on 4.7.55 with a persistent albuminuria. She remained well until October 1955 when she had frank haematuria and an increase in albuminuria with some facial oedema.
hypertension and was discharged in December with albuminuria but no haematuria on routine testing.

There were no features of the Schönlein-Henoch syndrome associated with either of these attacks of nephritis, the one acute and the other an exacerbation of the chronic type. These two cases reveal that acute episodes of nephritis may occur in close relationship with the Schönlein-Henoch syndrome but yet distinctly separated from it in features and acute course.

Gairdner (1948) drew attention to the association of the Schönlein-Henoch syndrome with rheumatic fever. One of his own cases a 15-year-old boy developed rheumatism 9 days after the onset of the disease. Another, a 40-year-old man had had rheumatism at the age of 24, and again at 32, and 8 months after an attack of the Schönlein-Henoch syndrome he had a further episode. Only one child in this series had a somewhat similar history. She was a 6-year-old girl (No. 48) who suffered from the Schönlein-Henoch syndrome in March 1952, acute rheumatism in December 1952 and again in September 1954.
Endocarditis was not discovered in any other case during the acute phase and when 71 cases were reviewed for renal damage the opportunity was used to undertake a cardiological examination. No evidence of cardiac damage was discovered.

**Tuberculosis.** No case in this series had tuberculosis, but the association has been recorded by Bauch (1916), Dalgliesh and Pinsell (1950) and Levitt and Burbank (1953).

**SUMMARY.**

The initial symptoms varied, almost equal numbers presenting with exanthem, arthralgia or colic. In cases in which the exanthem was not the initial feature subsequent symptoms appeared after an interval varying from one day to over 3 months, but in the vast majority within a week.

The most common site for the exanthem was over the lower limbs and the average number of crops was four.

Abdominal colic was present in three-fourths of the cases and was frequently accompanied by vomiting. One half of the patients had melena and haematemesis occurred in one fourth.
Fifteen cases were subjected to laparotomy while 4 cases had an intussusception and 8 patchy or localised oedema of the bowel.

Arthralgia or limb pains occurred in 70.7% of the cases and was frequently accompanied by oedema.

46.6% of the cases had haematuria and in addition 2 (1.7%) had albuminuria without haematuria.

Oedema of the face had no greater incidence of renal features.

Most cases developed haematuria within 7 days.

Headache was present in 28% of the cases and low grade fever in 41%.

The blood picture was of no help in the diagnosis. A raised blood sedimentation rate was present in two-thirds of the cases in which this test was performed. Where hypertension was present (9 cases) it was associated with haematuria in all but one patient.

Serum electrophoretic studies were normal.
Splenomegaly was recorded in only 4 cases.

There was a suggestive tendency for the older children to have a more severe attack of the Schönlein-Henoch syndrome lasting for a longer period.

Haematuria appeared to be more common in the severe long-standing case.

Sex did not seem to have much bearing on the clinical features.

The disease tends to relapse particularly within a month of the first attack.

12% of cases required further periods in hospital, 1 case having been admitted 5 times in 2 years. One case had a relapse after an interval of 7 years. More than half the cases spent less than 4 weeks in hospital.

Other diseases, acute rheumatism, acute nephritis and tuberculosis may be associated with the Schönlein-Henoch syndrome.
The Differential Diagnosis of the Schönlein-Henoch Syndrome.

It is surprising how many times the Schönlein-Henoch syndrome is misdiagnosed as there are few conditions with which it can be confused if the case is typical. The milder and atypical forms particularly if the exanthem is delayed in its appearance may cause considerable diagnostic difficulties. The subsequent pages deal briefly with some of the diseases with which the Schönlein-Henoch syndrome might conceivably be confused.

Polyarteritis Nodosa. The clinical picture of a case of the Schönlein-Henoch syndrome presenting with the exanthem, intestinal colic and arthralgia is not difficult to diagnose, and the only condition which may cause confusion is polyarteritis nodosa. By quoting from the report on the latter condition produced by Rose (1954) some of the similarities will be demonstrated.

"Data are presented from 66 cases of polyarteritis nodosa (41 males and 25 females). There was a maximum age incidence of the onset of the disease in the 7th. decade of life. The
highest incidence of the onset of the disease fell in the
winter months. At the time of onset of the
disease, 27% of patients had chronic respiratory infections,
and another 18% had had recent acute upper respiratory infec-
tions (attributable in 12% to haemolytic streptococcal).

Renal involvement occurred at some stage in 52 patients
(79%). Clinically this was associated in nearly all
cases with proteinuria and microscopic haematuria.

A specified form of glomerulitis was present as the only
renal lesion at necropsy in 16 cases; clinically such
cases showed macroscopic or heavy microscopic haematuria and
early renal failure. Hypertension was not a feature of this
initial phase.

There was evidence of gastro-intestinal polyarteritis in
46 patients (70%). The commonest symptom was poorly localised
pain; haemorrhage was common and sometimes severe.
Muscle pain and tenderness were a frequent (often an initial)
manifestation of the disease, but the presence of nodules was
recorded only once.

Arthritis arose during the course of the disease in 18
patients (27%). In 6 of these the changes were acute and
transient (sometimes migratory as in rheumatic fever) .......

Focal indurated skin lesions, probably all due to local
polyarteritis, occurred in 18 patients (27%). These ranged
from subcutaneous nodules to superficial papules, often with
haemorrhage and ulceration. .... Other types of lesion
observed included purpuric rashes, painful subcutaneous oedema,
and (in one case) scleroderma."

There were differences from the usual picture of the
Schönlein-Henoch syndrome. "A constitutional illness (with
loss of weight, fever and tachycardia) was a prominent feature
at some stage of the disease in nearly all patients. Erythro-
cyte sedimentation rate was nearly always high and anaemia and
leukocytosis were common; slight or moderate eosinophilia was
noted at some stage in 30% of patients .... There was evidence
of coronary polyarteritis in 32 patients (42%). The common-
est clinical manifestations were cardiac failure and enlarge-
ment. .... Valid records of arterial blood pressure were
available in 55 cases. In 24 cases the pressure was normal
on all occasions. ....The spleen became palpable in 8 patients. ......There was clinical evidence of peripheral nerve lesions in 24 patients (36%). Combined sensory and motor loss was usually present."

Thus there were many features which were absent or uncommon in the Schönlein-Henoch syndrome, but as has been discussed in the pathological section, the diseases have much in common. So much so that one wonders whether the Schönlein-Henoch syndrome represents a mild type of polyarteritis, and it might be that in the near future these two conditions will be grouped together under the heading of some term such as the diffuse vasculitis syndrome. Capillaries show primary degenerative processes in the renal glomeruli, and arterioles and arteries are affected in both conditions.

**Erythema Exudativum Multiforme.** One other condition may possibly cause some diagnostic difficulty. Erythema exudativum multiforme which has a similar skin pathology may have features suggestive of the Schönlein-Henoch syndrome (Neale, 1948). The exanthem may be preceded by a period of
up to 2 weeks by upper respiratory tract infection. The subsequent disease varies in severity, and the milder types may have few mucosal lesions. The exanthem may vary from macules to papules or bullae and target lesions may be found. The lesions are rose to red in colour initially, but later tend to become haemorrhagic. Distribution may be generalised but is more frequently found on the extremities. Mild intestinal symptoms occasionally occur and joint swellings have been described.

Once again skin histology shows that these two conditions are related, and even the clinical picture may show similarities between erythema exudativum multiforme and the Schönlein-Henoch syndrome. The more severe cases of the former condition, however, usually have typical mucous membrane involvement, particularly of the eyes and the mouth. (Illustration 40 p.175).

Infectious Diseases. Infectious diseases such as varicella, rubella, measles and variola should cause no difficulty in differentiation from the Schönlein-Henoch
Case of Erythema Exudativum Multiforme which showed features of the Stevens–Johnson syndrome. The skin biopsy from this child is described in the section on pathology.

Case of Erythema Nodosa. The colour print shows the irregular outline of the lesions but does not reveal their slightly elevated nature.
syndrome. In rare instances scarlet fever may be complicated by purpura fulminans or post-scarlatinal gangrene. Both of these conditions are regarded by Gairdner (1948) as closely allied to the Schönlein-Henoch syndrome, and he offered evidence to support this contention.

**Erythema Nodosum.** Another condition which may simulate features of the Schönlein-Henoch syndrome is erythema nodosum. This condition may be accompanied by mild constitutional disturbances or there may be no symptoms at all. Some children complain of aching discomfort in the lower limbs. Lesions occur on the anterior surfaces of the shins and less commonly on the antero-lateral aspects of the thighs and the extensor surfaces of the forearms. Very rarely lesions have appeared on the face. They are rose-red in colour at first, before becoming dusky and fading gradually to a yellowish brown, the whole process taking a week to a fortnight. The lesions are slightly indurated and elevated and are irregular in outline measuring between 1 - 3 cm. in diameter and are tender on palpation in most cases. The Schönlein-Henoch
syndrome may present with a few red irregular macules on the shins. These macules may be slightly elevated and until arthralgia, intestinal colic and/or nephritis develop, the condition may be misdiagnosed. Lesions of the Schönlein-Henoch syndrome are seldom, if ever, tender although they may be mildly itchy. In erythema nodosa there may be features of the underlying disorder which has produced this allergic manifestation. In this part of Scotland erythema nodosa is a manifestation of primary tuberculosis in 85% of cases.

**Intestinal Colic.** Intestinal colic and the associated symptoms may simulate many acute abdominal conditions. The common disorders such as appendicitis, intussusception and acute obstructions may be suspected. The main point that should be remembered is that intestinal perforation and intussusception do occur and the lesson to be learned from the reports on the surgical complications of the Schönlein-Henoch syndrome is that laparotomy should not be delayed in any case where a palpable tumour or severe obstructive
features develop. Even in recent reports the phrase
"unnecessary laparotomies" is used, and while by no means
every case with severe colic needs surgery, great care must
be taken to avoid unnecessary tragedies.

**Melaena.** Melaena is a common feature of the Schönlein-
Henoch syndrome but in the young child it may be sign of
several unrelated conditions.

The infective group is most frequently represented by
the dysenteries. The stool is usually very loose or watery,
foul smelling and contains red blood and slime. The child
has frequent motions, colicky abdominal pain, anorexia and
vomiting. In addition, fever and headache are common findings.

A Meckel's diverticulum may produce a serious haemorrhage
with the passage per rectum of large amounts of red blood.
Abdominal pain is usually absent or mild at the most. An
intussusception per se is usually characterised by severe
spasmodic pain in an otherwise healthy child and in many cases
'red currant jelly stools' are found. A volvulus or duplica-
tion of the bowel, blood dyscrasias and scurvy may all produce
mealaena, but each condition has features which make differentiation from the Schönlein-Henoch syndrome a comparatively easy matter.

In the Schönlein-Henoch syndrome the presence of the exanthem should eliminate all the above conditions.

Arthralgia. Arthralgia or limb pains are a feature of many disorders of childhood. The common ones such as discomfort due to postural defect and psychological upset are usually quite easily distinguished from the Schönlein-Henoch syndrome. In the former the very chronicity and the genu valgum or pes planus deformity are characteristic. In the latter group a carefully taken history may reveal an upset in the parent-child relationship and there may be other features of a disturbed or maladjusted child such as behaviour disturbances or 'tics'. Rheumatism may present a greater diagnostic problem. The acute case so well described in older textbooks with a high fever, acutely tender swollen and inflamed joints, a marked tachycardia and other signs of carditis, and a high blood sedimentation rate does not cause
any difficulty, though this type of illness is now relatively uncommon. The rheumatic child now usually presents either with an established carditis or with arthritis giving moderate or vague discomfort. Fever is frequently low-grade or moderate and while cardiac features may be prominent the overall picture may be very similar to the Schönlein-Henoch syndrome. As shown in the present series the blood sedimentation rate may be elevated in this condition, but it is not usually as high as in cases of acute juvenile rheumatism.

**Purpura.** Purpuric conditions have not been mentioned before as these are usually quite easily distinguishable from the Schönlein-Henoch syndrome. Thrombocytopenic disorders are frequently associated with haemorrhage from some site such as the nose or mouth. The skin lesion is truly haemorrhagic and while the development of lesions may be influenced by gravity they commonly develop at sites of trauma or compression. Arthralgia and intestinal colic are rare, but occasionally a case may give a history which may lead to difficulties in
diagnosis without haematological investigations as did the
following case admitted to a ward in the Royal Infirmary,
Edinburgh.

CASE REPORT.

O.C., a 14-year-old schoolgirl, developed a rash over
the shins and forearms following a sore throat some
months before admission on 21/5/54. She had had an
epistaxis and menorrhagia admittedly, but the latter
symptom is not uncommon at or about puberty. Her
urine was thought to be darker. About 2 months
before admission to the Royal Infirmary she had been
admitted to a district hospital because of colicky
abdominal pain and vomiting which recurred for 2
weeks. She was queried as a case of appendicitis.
She was admitted to the Royal Infirmary and investi¬
gations revealed a platelet deficiency and an increased
capillary fragility. Following a diagnosis of primary
thrombocytopenia, she was treated with cortisone with
a good response preoperatively. Splenectomy resulted
in recovery.

When it is not possible to obtain a good description of
the skin lesion, as in this case, confusion may arise. Simple
tests such as a bleeding time and a platelet count readily
distinguish the thrombocytopenic states from the Schönlein-
Henoch syndrome. Secondary thrombocytopenias should cause
even less trouble as they usually have a very acute onset or
progressively more severe course. Non-thrombocytopenic
purpuras affecting children other than the allergic group
should cause little confusion. Scurvy causes acutely painful
limbs, haemorrhages from mucosal surfaces and anaemia as well as purpura, but it should not be mistaken for the Schönlein-Henoch syndrome. Toxic states such as uraemia may produce alimentary discomfort and vomiting as well as petechial skin haemorrhages, but again the picture is most unlike the condition under review.

**Serum Disease and Angioneurotic Oedema.** Oaler (1914) drew attention to the similarities between the Schönlein-Henoch syndrome and serum disease. In this condition urticarial rashes, oedema of joints, limbs, face or elsewhere may arise together with arthralgia. The history of injection should be a guide to the correct diagnosis, and the course of the illness will differ from the Schönlein-Henoch syndrome. Angioneurotic oedema may cause limb pains and it is of course similar to serum disease in many ways. Nephritis occasionally complicates the picture of these two conditions (Hiström, 1941).

**Haematuria.** Haematuria is quite a common symptom in childhood and may be a feature of numerous diseases, some
metabolic or generalised, others related to the kidney or renal tract. Most of these have no place in the differential diagnosis of the Schönlein-Henoch syndrome, particularly as haematuria seldom, if ever occurs as a presenting symptom, but is always preceded by intestinal colic or arthralgia and the exanthem. If, however, the skin lesions etc. should be overlooked or their significance not realised, conditions such as acute nephritis, renal calculus and certain haemorrhagic disorders and blood dyscrasias, e.g. leukaemia, might come into the differential picture.

Acute nephritis is the commonest cause of haematuria in childhood and as Lewis (1955) demonstrated its age of onset and sex ratio were very similar to the corresponding features of the Schönlein-Henoch syndrome, but purpura did not occur in some 300 cases of nephritis reviewed at that time. Vague abdominal pain or lumbar discomfort was quite a common complaint, but in view of the usual course of the two conditions no difficulties should be encountered in the uncomplicated cases. However, it should be remembered that nephritis,
apparently identical to Bright's disease, is the commonest complication of the Schönlein-Henoch syndrome.
Treatment.

No treatment has been proved to influence the course of the Schönlein-Henoch syndrome. There are numerous difficulties in assessing the value of any line of therapy. The condition may run a short course with one or two relapses or a protracted one punctuated by irregularly spaced exacerbations. The progress of any one case is quite unpredictable and, therefore, it is only by assessing the effect of a drug in a large number of patients and by comparing the results obtained in other patients who have received no therapy that conclusions can be drawn.

Vitamins, Antihistamines, Antibiotics and Hormonal Drugs.

The lines of treatment which have received attention in the past have involved vitamins, antihistamines, antibiotics and hormonal preparations such as corticotrophin and cortisone. None of these drugs has proved an unqualified success, and the majority have been found to have no effect on the disease.

Avitaminosis in the light of modern knowledge, and in the absence of suggestive features in the histories is a most
unlikely aetiological factor, but claims have been made usually on the basis of experience in one or two cases that deficiencies of Vitamin C existed (Böger and Schröder, 1934), Vitamin K (Schaad, 1941), and Vitamin P (Jersild, 1938).

Others have failed to substantiate these views, and it seems far more likely that the administration of the vitamin was associated with a coincidental remission.

Davis (1948) found antihistamines of no value as did also Derham and Rogerson (1953), Ackroyd (1953) and Wedgwood and Klaus (1955). Gairdner (1948), and later authors stated that penicillin had no effect on the course of the disease.

Cortisone and corticotrophin were acclaimed as effective therapeutic agents (Stefanini et al., 1950; Kugelmass, 1951; Levinson et al., 1951; Adamson et al., 1953; and Leese, 1955). These reports were based on a total of 8 cases. In 4 of these complicated by nephritis, the renal lesion was uninfluenced by hormonal therapy, and in Leese's case the patient (the only adult in this group) had a fresh skin eruption while still on therapy. Woolley (1952), Philpott and Biggs
(1953), Simpkiss (1953) and Wedgwood and Klaus (1955) obtained no clinical response using these drugs in 19 cases. These authors stated that exacerbations of exanthem, nephritis and other symptoms developed while the patients were on the drugs.

In the cases under review various drugs were used and these fall into the above groups. Vitamin C and hesperidin were each used in one case without effect, while antihistamines were used in 17 cases. In all but 4 patients symptoms continued after the institution of therapy and these 4 probably had spontaneous remissions.

Fourteen cases had sulphonamide, 26 had penicillin and 6 had other antibiotics. These were given because haemolytic streptococci were present in the throat, or because their presence was suspected. Penicillin therapy is justified if the presence of haemolytic streptococci in the throat is diagnosed clinically or after culture. Corticotrophin was used in cases 74 and 81. The former received 60 mgm daily, but fresh exanthem and intestinal colic developed during the
administration of the drug. The latter received 40 mgm daily and while there was no further colic or arthralgia, nephritis, (which had been present before the drug was commenced), was not influenced by the therapy.

Cortisone was given orally 100 mg. daily to cases 46, 76, 88, 89, 90 and 95. Vomiting, colic or rash or combinations of these features continued in an attenuated form in all but one case (No. 89). This patient and 4 of the others had nephritic symptoms which were uninfluenced by the therapy.

These drugs certainly did not completely suppress the signs and symptoms of the Schönlein-Henoch syndrome and they did not prevent the development of nephritis, nor did they influence the cause of this complication. Case 90 had severe and frequent attacks of intestinal colic and vomiting. They ceased while she was on cortisone 100 mgm daily, but recurred when the dose was halved and ceased again when the former dose was resumed. It would appear that this drug may partially relieve intestinal symptoms when the patient is receiving full amounts, but reduction of the dose may allow the disease
to breakthrough.

The important fact, however, is not what effect these drugs have on skin, alimentary or arthritic features, but whether they prevent either the onset of nephritis or rapidly terminate nephritis which has already developed. Nephritis is the chief danger that threatens every child with the Schönlein-Henoch syndrome.

It may be stated, therefore, that no therapeutic measure yet available is the complete answer to this disorder.

**Analgesics.** In the absence of curative measures, symptomatic treatment is important, but it has received very little, if any, mention in the previous papers on the Schönlein-Henoch syndrome. Arthralgia is usually not severe enough to need powerful analgesics. Salicylate was adequate for the majority of these cases, but it did not have the dramatic effect experienced with its use in acute rheumatism. Intestinal colic and vomiting constitute distressing symptoms in some patients and pethidine in 25 to 50 mgm doses given
4-hourly may be necessary and this drug seems to be of considerable benefit in such cases. Occasionally stronger analgesics are required and then heroin in doses from 1/48th. gr. (1.25 mgm) to 1/12th. gr. (5 mgm) depending on age usually suffices. Several modern autonomic blocking agents were tried without success. In particular, Propantheline Bromide ("Probanthine") in 30 mgm oral doses was completely ineffective.

Once again it should be emphasised that close observation should be kept on any case of the Schönlein-Henoch syndrome experiencing severe abdominal colic and vomiting. Physician and surgeon should meet frequently over such an abdomen in order that intussusception or perforation may be early recognised and thus avoid the all too frequent tragedies reported in the world's literature.

Care of the Skin. The skin lesions when severe may require particular attention over such pressure points as the elbows and buttocks. Sponge rubber rings or pads should be used at these sites if there is any tendency for the
exanthem to coalesce. Bullous eruptions should be protected with dry sterile gauze if they are large, but smaller blisters on areas not liable to trauma are best left alone.

**Haematuria and Tonsilllectomy.** If haematuria is present the case should be regarded as one of nephritis and bed rest must be observed. The throat should be repeatedly swabbed if the symptoms persist and if group A haemolytic streptococci are cultured, penicillin therapy is indicated. The duration of bed rest depends on the progress, but it should be continued until the nephritic features and blood sedimentation rate have been stationary for at least a month. The place of tonsilllectomy in the treatment of the Schönlein-Henoch syndrome is difficult to determine and unfortunately there are no case reports in other series to add to the small number of patients who underwent this operation in the present review. However, some use may be served by giving details of the 11 cases in this group.

**Case 22,** a 9-year-old female had severe recurrent symptoms with obstructive features. The child had no
symptoms for 3 months prior to the operation, but as she had
had recurrent tonsillitis, tonsillectomy was performed under
penicillin cover. A recurrence of the Schönlein-Henoch
syndrome occurred 9 months later but there was no residual
nephritis.

Case 25, a 6-year-old boy, had severe colicky pain,
arthralgia and nephritis. He had an attack of tonsillitis
in the course of the illness. After 3 months tonsillectomy
was performed and the nephritic signs cleared in a further
6 weeks and the blood sedimentation rate returned to normal.

Case 60, a 4-year-old girl, with very severe features
had fresh attacks of haematuria over a period of 7 months,
one exacerbation being associated with an acute throat
infection. Following tonsillectomy the urine rapidly
cleared, the blood sedimentation rate returned to normal
and the patient has remained well to date.

Case 65, a 2-year-old boy had a prolonged illness with
exacerbations over a period of 7 months. Nephritis was
present but there had been no symptoms for 2 weeks prior to
operation and thereafter the child had no further trouble and the urine rapidly returned to normal.

Case 74, a 7-year-old boy appeared to have recovered from a severe attack of the Schönlein-Henoch syndrome lasting nearly 4 months. Tonsillectomy was performed after a period of 4 further months and the child remains well.

Case 87, a 6-year-old boy, had haemolytic streptococci in his throat and moderately severe colic and arthralgia. After a symptom-free interval of 2 weeks tonsillectomy was performed and the patient has remained well.

Case 89, a 3-year-old boy, was symptom-free at the time of the operation and nephritic features were improving. Following tonsillectomy he had no colic and his urine continued to improve, but 2 months later he had a fresh and extensive crop of the typical exanthem though his urine remained normal.

Case 90, a 7-year-old girl, had a severe and prolonged attack of the Schönlein-Henoch syndrome and was left with a latent nephritis. Following an exacerbation of nephritis,
tonsillectomy was performed, but her nephritic condition remained unchanged.

Case 93, an 11-year-old boy, had an attack of the condition due to chocolate hypersensitivity but following tonsillectomy he has been able to consume this sweetmeat without disability.

Case 96, an 8-year-old girl, (a severe relapsing case extending over a period of 14 months) was uninfluenced by tonsillectomy.

Case 99, a 7-year-old boy, with a previous history of frequent sore throats had a mild but recurring attack which was uninfluenced by tonsillectomy.

It would seem from these case summaries that tonsillectomy is of doubtful value except possibly in an occasional case like No. 60, or where there are indications for tonsillectomy independent of the Schönlein–Henoch syndrome as in cases 22 and 99.

**Summary of Treatment.**

The conclusions to be drawn from this section may be
summarised as follows. There is no 'wonder' drug for use in the Schönlein-Henoch syndrome. If group A haemolytic streptococci are present in the throat, penicillin therapy is indicated. Severe intestinal colic should be treated with analgesics, pethidine being recommended. Severe alimentary features may indicate the necessity for surgical intervention. Pressure points which are the site of the exanthem may need protection. Nephritis should be treated by recognised measures such as bed rest. Tonsillectomy may be of benefit in an occasional case, but it would not appear to be indicated in all patients with chronic relapsing symptoms.
Prognosis.

The discussion of this very important and controversial aspect of the Schönlein-Henoch syndrome will be divided into two parts; the first dealing with the acute phase and its prognosis, and the second with the long-term picture obtained from a follow-up of cases occurring in this series.

The Immediate Prognosis. It is accepted that the patient nearly always survives the acute stage of the Schönlein-Henoch syndrome, and it is proposed to deal in turn very briefly with the main features of the condition.

The exanthem in the majority of cases clears within a few days to about a fortnight, but when large bullae form, skin destruction occurs and thin pliable scars may develop. These scars cause little trouble except when (as in case No. 76) keloid formation occurs, but this particular case will be mentioned in the long-term follow-up.

The joint symptoms and the oedema of the various areas mentioned previously have never caused any serious disability. In the present series one boy had difficulty in micturition
because of marked oedema of the penis. The alimentary lesions, when they occur, may endanger life, and reference has been made to the diagnostic difficulties. The literature contains several reports of fatalities following perforation of the intestine or a gangrenous intussusception (Bailey, 1930; Schwartman, 1940). In case No. 55 of the present series, a 5 year old boy was gravely ill, having a perforation of the ileum which did not receive immediate surgical treatment, and death might easily have resulted. Four (3.4%) cases developed an intussusception, 7 (6%) were found to have acute regional enteritis on laparotomy and 1 case had a perforation as previously mentioned.

Other symptoms likely to cause trouble are rare. Possible nephritis in the acute stage might cause hypertensive encephalopathy, anuria or heart failure, but no examples of such complications have appeared in the literature. Convulsions associated with hypertension, but without evidence of nephritis, occurred in a case mentioned by Philpott (1956) and although this child recovered, such
features are potentially dangerous to life. Another of Philpott's cases developed a subarachnoid haemorrhage and has been left with a hemiplegia. This is the only reported case with such a complication and it must be extremely rare.

It should be stressed, however, that in the acute stage serious complications are rare with the exception of acute abdominal emergencies, which should always be borne in mind whenever a case of the Schönlein-Henoch syndrome develops severe, recurrent intestinal colic. Ackroyd (1953) implied that surgery and laparotomy are resorted to far too readily, but a review of the literature with its many tragedies suggests that all too frequently the physician has delayed surgical intervention until too late.

The Long-Term Follow-up. This, the most important question to be answered with regard to the prognosis, is controversial.

Macalister (1906) regarded the outlook as serious when nephritis was present, and others like Gairdner (1948), Philpott (1952), Simpkiss (1953) and Wedgewood & Klaus (1955)
were in agreement. Davis (1948), however, painted a rosy future based on his follow-up of 44 cases, only 4 of which had had haematuria. Recently Oliver & Barnett (1955) reviewed their findings in 26 children, 11 of whom had haematuria and/or proteinuria. Three of these patients were still having symptoms but they regarded the prognosis as good in children.

These follow-up reports deal entirely with renal function, and in the present series an assessment of renal damage was made, but before discussing this aspect it should be mentioned that no other long-term disabilities arising from the disease, with one exception, were discovered. Case No. 76 developed painful keloid tissue in the scars arising from bullae over the olecranon processes, and this patient is awaiting excision of these with possibly subsequent skin grafting.

Fifty-four patients in the series had haematuria, and 2 further cases albuminuria without haematuria, and these will be mentioned in particular in order to estimate the
seriousness of these features of the acute stage in relation to subsequent developments.

The urines of patients reviewed for follow-up purposes were tested for the presence of albumin and an Addis count was performed on a 12-hour specimen. The method and criteria of normality for Addis counting in children proposed by Giles (1947) were used.

In this way the vast majority of the 116 patients were examined. Of those not traced, 3 had gone to Canada, and 2 had moved from the district leaving no clue as to their present whereabouts. Table 32 shows the length of time between the illness and follow-up, and the number of cases tested in each group. About two-thirds of the series had been examined by the writer in 1953, and therefore many urines were examined twice.

The results of this study are as follows:--

One case (No. 29) had died of renal failure after an illness lasting 5 months. The others all appeared to be in good health, but on urinalysis 8 patients had albuminuria,
### No. of cases examined

<table>
<thead>
<tr>
<th></th>
<th>2/12 - 6/12</th>
<th>6/12 - 1</th>
<th>1 - 2</th>
<th>2 - 5</th>
<th>5+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. of cases in each group</td>
<td>6</td>
<td>22</td>
<td>18</td>
<td>33</td>
<td>37</td>
</tr>
<tr>
<td>No. of cases tested in each group</td>
<td>6</td>
<td>22</td>
<td>18</td>
<td>32</td>
<td>33</td>
</tr>
</tbody>
</table>

### TABLE 33

**Urinary findings on follow-up**

<table>
<thead>
<tr>
<th>Time in Years</th>
<th>2/12 - 6/12</th>
<th>6/12 - 1</th>
<th>1 - 2</th>
<th>2 - 5</th>
<th>5+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary findings on follow-up</td>
<td>Normal</td>
<td>Abnormal</td>
<td>Normal</td>
<td>Abnormal</td>
<td>Normal</td>
</tr>
<tr>
<td>No. of cases (No urinary features initially)</td>
<td>4</td>
<td>1</td>
<td>6</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>No. of cases (Urinary features present initially)</td>
<td>1</td>
<td>0</td>
<td>11</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
<td>1</td>
<td>17</td>
<td>5</td>
<td>16</td>
</tr>
</tbody>
</table>
and 17 (16.2%) had abnormal Addis counts, including the 8 cases with albuminuria (Table 33). If one excluded the cases of less than one year's duration at the time of follow-up, 13 had evidence of renal damage, or nearly 15% of this series of cases of the Schönlein-Henoch syndrome. The risk of a latent nephritis in those who have had haematuria associated with active phase of the Schönlein-Henoch syndrome was much greater. Of the 53 such cases tested 15 (28.3%) had evidence of renal damage in the form of an abnormal Addis count, with albuminuria as an additional factor in 6 of these.

Effect of Age and Subsequent Renal Prognosis. Wedgwood & Klaus (1955) stated that "there was a distinct correlation between the age of the child at the onset of the disease and the later finding of urinary abnormality. While 9 of the 13 (69%) over the age of 6 years at the time of onset of the disease had abnormal urine on follow-up examination, only 1 of 13 (8%) under the age of 6 years when the disease began its acute phase was found in this abnormal group."
This difference is statistically significant .......

Their numbers were small and by grading the present series of cases similarly a completely different and "statistically significant" picture is obtained, showing no difference between the 2 groups (Table 34, p.203). Thus it may be said that the conclusion of Wedgwood & Klaus is not borne out in a much larger series of cases than employed in their study.

The sex ratio of those who had 'abnormal' urine at the time of follow-up was 1:1, but the apparently poorer female prognosis is not statistically significant as the numbers are small.

**TABLE 34**

<table>
<thead>
<tr>
<th>Age at Onset</th>
<th>Urine on Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td>Under 6 yrs.</td>
<td>48</td>
</tr>
<tr>
<td>Over 6 yrs.</td>
<td>45</td>
</tr>
</tbody>
</table>
Summary of Prognosis. The findings in this series show that the immediate prognosis is good, but care should be taken to avoid scarring if bullae are present. Abdominal emergencies such as intussusception and perforation occur in about 5% of the cases, and localised acute ileitis or jejunitis in another 6%. Rarely is central nervous system involvement disabling.

The long-term prognosis deals entirely with renal function. Those cases with haematuria and/or albuminuria in the acute phase have about an almost 30% chance of being left with evidence of renal damage.

In this series of 116 patients the mortality has so far amounted to one case which died of renal disfunction.
SUMMARY

The Schönlein-Henoch syndrome has been defined and the terminology discussed briefly.

The history of the condition has been recorded with extracts from some of the more notable contributions.

The incidence in hospital and general population has been reviewed and age of onset, sex ratio and social background have been investigated.

The month of onset and the occurrence of preceding upper respiratory tract infections after a latent period have been recorded together with some bacteriological investigations on haemolytic streptococci cultured from the throats of patients. The rarity of food allergy is noted. The family history as regards other cases of the Schönlein-Henoch syndrome, nephritis acute rheumatism and allergy has been reviewed. The possibility of a drug induced condition was investigated.

The mechanism of hypersensitivity reactions has been discussed and some experimental work performed in an attempt to clarify the picture. The reasons why the Schwartsman
phenomenon is preferred are given.

The pathology of skin, bowel and kidney is described and the findings of others noted.

The clinical picture of 116 cases has been studied in detail. The main features have been discussed individually and the effect of age and sex are discussed together with the clinical course.

A brief differential diagnosis of the condition has been given.

Treatment is discussed and mention made of cure by certain drugs which has been claimed from time to time. The symptomatic management of patients has been recorded.

Prognosis, both immediate and long term, has been discussed and the seriousness of the renal lesion indicated.

A bibliography is included along with very brief case summaries.
Conclusions.

1. The account of the Schönlein-Henoch syndrome given by Ollivier in 1827 deserves wider recognition.

2. The Schönlein-Henoch syndrome is not an uncommon disorder of childhood. It occurs more frequently in the hospital population than acute rheumatism, and it has a similar admission rate to acute nephritis.

3. The common ages of onset lie between 2 and 8 with a slight peak around 3 years. Three males are affected for every 2 females. The disease is less likely to occur in the professional classes. Cases arise in closely populated urban communities.

4. The clinical indications that the vast majority of cases are due to a form of bacterial hypersensitivity are:

   (a) the increased incidence of the condition in the colder months of the year;

   (b) the high incidence of preceding upper respiratory tract infection often associated with the haemolytic streptococcus;

   (c) the characteristic latent period between the sensitising infection and the onset of the disease;
(d) the tendency of cases to occur in towns and cities; (suggesting bacterial infection as a factor)

(e) a possibility that collagen disorders are more prone to develop in the families of the Schönlein-Henoch syndrome.

5. The type of reaction has not been proved, but it must be of the direct type as this variety affects blood vessels. The most likely would appear to be the Schwartzman phenomenon, since no circulating antibodies could be demonstrated in the serum of patients with the Schönlein-Henoch syndrome. In addition the tendency for lesions to occur in areas of hyperaemia pressure or trauma would support this theory.

6. The pathology of the condition is produced by vascular inflammation and damage which could be caused by recurrent reactions of the Schwartzman type.

7. There is wide variation in the clinical picture, but certain facts emerge:

(a) the exanthem is remarkably pleomorphic and tends to occur in dependent areas;

(b) intestinal colic may be very severe and protracted;

(c) about 4% of cases develop intussusception;
(d) about 6% develop 'acute regional jejunitis' or ileitis;

(e) 48% had urinary features suggestive of nephritis. Oedema of the face or elsewhere did not indicate an increased risk of nephritis;

(f) headache not previously mentioned in connection with the Schönlein-Henoch syndrome was present in 25% of the cases;

(g) low-grade fever and an elevated blood sedimentation rate are not unusual features;

(h) no change was found in serial electrophoresis of the serum;

(i) the older child tends to have a more prolonged and severe illness (statistically suggestive). The long-standing case with severe symptoms tends to have haematuria;

(j) the disease tends to relapse particularly within the first month. It is impossible to say when the child can be regarded as fully recovered. One case relapsed after 7 years. Over 10% require further hospital care.

8. The differential diagnosis reveals that polyarteritis nodosa may be almost indistinguishable from the Schönlein-Henoch syndrome.

9. There is no specific therapy of proven value. Tonsillectomy in chronic relapsing cases is of doubtful value.

10. The immediate prognosis is good if surgical complications are treated promptly. The long-term view reveals
that when haematuria and/or albuminuria were present initially over 30% subsequently had evidence of renal damage. One case died.
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<td>M.D.</td>
<td>2</td>
<td>F</td>
<td>W.G.H.</td>
<td>4.2.55</td>
<td>Abdominal pain, vomiting, arthralgia, haematuria.</td>
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<td>02</td>
<td>L.McV.</td>
<td>4</td>
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<td>R.H.S.C.E.</td>
<td>26.2.55</td>
<td>Abdominal pain, arthralgia, haematuria.</td>
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<td>03</td>
<td>P.B.</td>
<td>7</td>
<td>F</td>
<td>R.H.S.C.E.</td>
<td>26.2.55</td>
<td>Abdominal pain, vomiting, arthralgia, haematuria.</td>
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<td>04</td>
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<td>F</td>
<td>W.G.H.</td>
<td>8.3.55</td>
<td>Abdominal pain, vomiting - operation oedematous ileum - haematuria.</td>
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<td>R.H.S.C.E.</td>
<td>12.4.55</td>
<td>Abdominal pain, vomiting, melena, arthralgia, haematuria.</td>
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<td>J.R.</td>
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<td>M</td>
<td>Leith</td>
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<td>M</td>
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<td>Abdominal pain, vomiting, haematuria.</td>
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<td>Initials</td>
<td>Age</td>
<td>Sex</td>
<td>Hospital</td>
<td>Date of Admission or when seen</td>
<td>Main symptoms and signs (other than exanthem)</td>
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<td>I.C.</td>
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<td>Arthralgia.</td>
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