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AN INVESTIGATION INTO AN UNUSUAL DISEASE
SEEN IN EPIDEMIC AND SPORADIC FORM IN A
GENERAL PRACTICE IN CUMBERLAND IN 1955 &
SUBSEQUENT YEARS.

By

A. L. WALLIS.
Plan of Study:

It is proposed that the disease under study should be considered under the following headings:

**INTRODUCTION.**

Epidemiological aspects of the disease considered under the subheadings:

1. **Time relationship**, including season and weather during the period of epidemic prevalence.
2. **Place**: A description is given of the locality in which the epidemic took place.
3. Lines of communication.
5. Host reactions.
6. Incubation Period.
7. **Course of the Outbreak**.
8. Communicability.
9. Susceptibility of the population.
10. Attack rate.
11. Mode of spread.

**Aetiology**

**Clinical Features**:

1. Symptoms and Signs.
2. Complications.

Diagnosis and Differential Diagnosis.

Treatment.

Prognosis.

Preventive Measures.
2.

General discussion, including the problem of investigation of an unusual infective disease in general practice.

Conclusion.

Appendix.
INTRODUCTION:

In the first half of 1955 an unusual infective disease appeared in my practice, which is centred on Dalston, a village which lies 4½ miles south-west of Carlisle, in the valley of the River Caldew. The condition became prevalent in February and March and affected a considerable number of my patients; there were no fatalities but the disease was the cause of much disability and loss of working time.

The disease appeared to be infectious, and the illness was characterised by acute myalgia, disturbances of the reticuloendothelial system and central nervous system, and psychogenic sequelae which, in some instances, persisted for many months.

Relapses, with recrudescences of symptoms, occurred in a proportion of those infected; in some cases, several relapses occurred over a period of months, symptoms being minimal or absent between the recurrences.

The clinical picture that emerged was one with which I was not familiar. At an early stage in the epidemic I considered the condition to be most like glandular fever, and therefore sent serum samples and blood films to the Pathological Laboratory of the Cumberland Infirmary for Paul Bunnell screening and examination of the films for the picture seen in glandular fever.

The Paul Bunnell test was consistently negative and the blood films were not characteristic of glandular fever. As the disease reached epidemic proportions and the laboratory findings
remained negative I was forced to abandon the diagnosis of glandular fever and seek aid in establishing the cause of the disease.

I called in the Director of the Public Health Laboratory, Carlisle, and the Medical Officer of Health for the Border District, to further this aim. I would like to pay tribute to their consistently helpful attitude, and also to the interest and helpfulness of the consultant psychiatrist called in, when psychogenic sequelae appeared.

Cases of the disease were seen by all three and it was agreed that the clinical picture was unfamiliar and that the disease warranted further investigation. My part in the subsequent laboratory investigation was limited to the taking of throat and eye swabs, samples of faecal material and urine, paired samples of blood and blood films; obtaining the samples and getting them to the laboratory as quickly as possible - in the case of samples for attempted virus isolation in less than one hour - did, however, involve me in a considerable amount of extra effort over and above the usual day's work, particularly so as the practice is widely spread.

During the early stages of the investigation, at the request of the Director of the Public Health Laboratory, Carlisle, an epidemiologist from the staff of the Central Public Health Laboratory, Colindale, London, came to Dalston to study the outbreak. His conclusion was that a large number of people had been affected by a disease which gave a distinct clinical with which he was unfamiliar, but which showed some similarities to the disease described by Neva, Feemster and

The results of the laboratory investigations, which are given in detail in another section, have been negative to date.

A description of various aspects of the disease, as it was seen by me, is given in the subsequent pages of this thesis.

Reference:
Neva, Franklin A., Feemster, Roy F., Gorbatch, Isle J.
Bell, J.A., Rowe, W.P., Engler, J.T., Parott, R.H., Huebner, R.J.
Epidemiological Aspects:

Time:

The disease was first recognised by me in January, 1955 when several obviously similar cases occurred, presenting a clinical picture unfamiliar to me.

A large number of cases occurred during February, the maximum incidence being reached in the latter part of March and the first three weeks of April. Thereafter, the number of fresh cases appearing declined, although with lesser peaks of incidence during the period of decline, until, by August, sporadic cases only were appearing.

From August 1955 to the present date fresh cases have appeared sporadically and there have also been recurrences of symptoms in some of those previously infected. It is perhaps noteworthy that persons from other localities, coming to live in the district, during this intervening period following the epidemic, have in a number of cases developed a disease with a clinical picture similar to that seen in the epidemic.

There is a possibility that sporadic cases were present in the district from the late autumn of 1954, as several cases seen by me in 1955 gave a history of having similar but milder symptoms during the autumn of 1954. Those giving such a history were farmers and farmworkers, who, following the harvest and during the process of stack building found themselves suffering from vertigo, when up on the stack receiving materials for the completion of the upper part. Other symptoms experienced conformed to the general picture seen later, but, as they were
in the midst of a busy time, and found they could go on, they did not seek medical attention in case they were sent to bed.  


The weather during the winter months showed no great variation from the norm of the Solway plain. Following a mild, wet autumn, January and February had wind and rain which intermittently gave place to clear days and nights with hard frost. As is commonly the experience here, there was little snow. March and April gave some periods of good weather, spring being early as a result of the generally mild weather. May and June had broken weather with some gales and late frosts, but July and August were sunny, dry and hot, the unusually good weather being prolonged well into September - a most uncommon prolongation of good weather for these parts.  

Place:  

The general practice from which this epidemic was observed is centred on the village of Dalston, $\frac{1}{2}$ miles south-west of Carlisle. The patients in the practice are drawn largely from the parishes of Dalston, Orton and Thursby in the County of Cumberland. The main villages in this area are those of Dalston, Great Orton and Thursby, and there are also the hamlets of Raughton Head, Gatesgill, Durdar, Curthwaite and Little Orton. Dalston, itself, is an ancient centre of population, situated in the valley of the River Caldew. The parish of Dalston contains the traditional seat of the Bishops of Carlisle, Rose Castle. The parish church, successively restored and rebuilt, is on the site of an early Norman church, part of whose walls are embodied in the present building.
In previous times the village was of considerably greater importance than it is at present. Then it was the local town for the people of the adjacent dales, with numerous small industries. It also had two breweries and many taverns and ale houses for the thirsty populace. The thirsty nature of much of the land, which overlies glacial debris and sandstone, in conjunction with the habits of Dalstonians of a previous generation, gave rise to a familiar local saying of last century—"Dalston land and Dalston men need a drink every day."

As late as the turn of the last century Dalston was still a focal point for a large district, and, on a Saturday, the Square at Dalston would be thronged by four hundred or more, coming from outlying districts to do their shopping or frequent the public houses.

The valley, up to this time, was largely self-contained, with patterns of movement of the population that were still well defined within it.

With the advent of modern transport the old order has changed to a very marked extent. The small local industries have died out in the face of modern competition, with the exception of a cotton wool factory which has kept its head above water and expanded to meet present day competitive needs.

The village is not now the focal point it was for adjacent districts. This is due to the proximity of Dalston to Carlisle, a relatively large centre of population, with which Dalston, as an industrial, a shopping and an amusement centre, cannot compete.

Prior to the building of the railway line between Carlisle and the Cumberland Coast, which passes through Dalston, those
9.

wishing to go to Carlisle had to make their way on foot or by means of horse-drawn vehicles. The advent of the railway station at Dalston made communication between Dalston and Carlisle much easier, but the coming of the bus services and private motor transport was the end for the relative isolation of the Caldew Valley, with its own independent pattern of life.

In effect, the villages have been urbanised, becoming outlying suburbs of the town.

Lines of Communication:

The means by which infection can reach Dalston are now many.

Long-range introduction of infection.

Farms:

Most farmers possess cars in this district, and attend auction marts not only in Carlisle but further afield. Double-decked cattle trucks of their own, or a local contractor, bring back the animals bought at the auction from possibly a hundred miles away or more, and the farmers or contractors may bring, in addition, unwanted infection contracted at the crowded auctions.

Railways:

Carlisle is a railway centre, and a number of men living in the Caldew Valley district are employed on the railways. Some of these are drivers and firemen. Those employed on the long distance runs have to spend their off duty hours at the other end of the run, in railway hostels, where they eat and sleep, with perhaps an excursion outside to shop, or to go for a drink at a neighbouring public house. They are thus exposed to the risk of contracting some "foreign" infective disease, and
10.

bring it back with them on their return journey.

Dalston Hall:

This property, one of the oldest in the parish, was bought by the Co-operative movement, and, since the last war, has been run as a holiday and instructional centre. A resident staff caters for an influx each week of up to 60 or 70 people, who replace the previous week's occupants. The age groups of these people vary from 12 to 70 years for different intakes, and consist of diverse elements from this country and abroad. A recent group included Pakistanis, Africans from Ghana and several Chinese. Lecturers may come from Great Britain, European America.

These people come into contact with the local population when shopping in the village, at social functions at Dalston Hall, and where the hospitality of local homes is extended to them.

Gypsies or Potters:

Downstream from Dalston Square and perhaps half a mile away lies the Old Village, now represented by two antiquated cottages and some rusted boilers and iron work on the crumbling concrete foundations of a derelict factory.

Across a now disused and dry water race, near the factory site, there is a field abutting on the Caldew, which was bought and used as a gravel bed. The land was bought, it is said, by a man, now wealthy, who was once a "potter" himself and who sympathises with the difficulty they have in getting camping sites.

Whatever the truth of this, once the gravel bed operations
were completed, a potter encampment appeared in the field, and
the field has acted as a transit camp for potters ever since.
The potters, while in Dalston, hawk from door to door for scrap
and old clothes, and to sell such goods as they have to offer.
Further contact with the local people by this transient
population is made at the village shops and public houses.

**Visitors:**

Apart from the visits to families from relatives living
elsewhere in the country, the villages of the Caldew Valley
have in summer a quota of families on holiday in the district
by virtue of one of the routes to the Lake District which passes
through Dalston and then mounts the fells to descend to
Bassenthwaite and Keswick - a matter of forty minutes or so by
car from Dalston - there is a fair amount of holiday traffic
through Dalston with human contacts at places of refreshment.

**Short range lines of infection:**

**Occupational and other channels:**

Every working day there is a considerable influx of workers
into Carlisle from the surrounding districts, which are now
serving as a dormitory area and labour reservoir for Carlisle.
Other workpeople come into Dalston from Carlisle, Wigton and
celsewhere, to supplement the number of local workers at the
cotton wool factory in Dalston.

There is also the daily movement of people into and out of
Carlisle, in the interests of shopping and social activities,
and also the movement of children from the district to secondary
schools at Carlisle and Wigton.

If an infective disease was introduced into Carlisle, there
would thus be many possible pathways for it to be carried out into the surrounding districts.

Within the Caldew Valley district local pathways of infection exist in the aggregations of the youthful members of the population at the primary schools, and of their elders at whist drives, other social functions, and the public houses.

Further dispersal of an infective disease would be ensured by the habit of dropping in for the evening to see one's relations - in this district there is an intricate network of relationships occasioned by much intermarriage.
Population and Practice Population:

My practice is drawn largely from the parishes of Dalston, Orton and Thursby, with scattered elements in other parishes and Carlisle.

The practice gives a fair section of the community only in the three parishes mentioned above, and although I encountered the disease under study in these other parishes and Carlisle also, I shall confine the study to the three main parishes from which the practice draws patients.

The total number of persons in the parishes of Dalston, Orton and Thursby was 2,174 at the Census of 1951. This figure included 1,579 males and 1,595 females.

Since the Census of 1951 both Thursby and Dalston have had small housing estates built in their midst, but these have, in the main, been occupied by local inhabitants, where married couples were living with their parents in conditions of overcrowding.

Table I.

<table>
<thead>
<tr>
<th></th>
<th>Population 1951</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Persons</td>
</tr>
<tr>
<td>Dalston</td>
<td>1834</td>
</tr>
<tr>
<td>Orton</td>
<td>423</td>
</tr>
<tr>
<td>Thursby</td>
<td>917</td>
</tr>
<tr>
<td>Total</td>
<td>2174</td>
</tr>
</tbody>
</table>
The Census of 1951 shows that the population was housed as shown in Table 2:-

<table>
<thead>
<tr>
<th>Private Households</th>
<th>Population in private Households</th>
<th>Structurally separate dwellings occupied</th>
<th>Rooms Occupied</th>
<th>Density of Population Persons per room</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalston</td>
<td>543</td>
<td>1818</td>
<td>534</td>
<td>2584</td>
</tr>
<tr>
<td>Orton</td>
<td>98</td>
<td>385</td>
<td>98</td>
<td>483</td>
</tr>
<tr>
<td>Thursby</td>
<td>227</td>
<td>891</td>
<td>224</td>
<td>1068</td>
</tr>
</tbody>
</table>

The number of persons included in my practice in 1955 from the parishes of Dalston, Orton and Thursby was 1,675. This total included 825 males and 850 females.

Table 3 shows the total derived from each parish and the sub-division into the totals for each sex.

| Number of Patients derived from the Parishes of Dalston, Orton and Thursby. |
|-------------------------------------------------|-----------------|----------------|
| Dalston                                        | 1264            | 621            | 643            |
| Orton                                          | 171             | 85             | 86             |
| Thursby                                        | 240             | 119            | 121            |
| Total                                          | 1675            | 825            | 850            |
Table 4 shows the patients from Dalston, Orton and Thursby classified into groups by age and sex:

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>Dalston Male</th>
<th>Dalston Female</th>
<th>Orton Male</th>
<th>Orton Female</th>
<th>Thursby Male</th>
<th>Thursby Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 5 years</td>
<td>47</td>
<td>51</td>
<td>7</td>
<td>6</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>5 - 11 years</td>
<td>97</td>
<td>60</td>
<td>9</td>
<td>12</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>12 - 19 years</td>
<td>69</td>
<td>53</td>
<td>12</td>
<td>7</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>20 - 29 years</td>
<td>57</td>
<td>74</td>
<td>15</td>
<td>11</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>30 - 39 years</td>
<td>112</td>
<td>106</td>
<td>14</td>
<td>10</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>40 - 49 years</td>
<td>82</td>
<td>70</td>
<td>7</td>
<td>10</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>50 - 59 years</td>
<td>73</td>
<td>92</td>
<td>9</td>
<td>14</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Over 60 years</td>
<td>84</td>
<td>137</td>
<td>12</td>
<td>16</td>
<td>20</td>
<td>28</td>
</tr>
</tbody>
</table>
Host Reactions:

Reticulo Endothelial System.

Irritability of the reticulo endothelial system was displayed in varying degree in all cases.

Marked enlargement of the lymphatic glands was most common in children of primary school age.

In this age group the glands of the cervical chain were frequently visibly enlarged, and in a number of cases early in the epidemic the mother would send in her request for the child to be visited with the ready made diagnosis that the child had mumps.

In no case, however, was the parotid gland involved and serological tests later showed no evidence, in any of the cases checked, of infection with the virus of mumps.

While the cervical glands were the most commonly enlarged, enlargement also occurred of the inguinal and less frequently the axillary group.

In children, the enlarged glands were usually tender to palpation, but not particularly painful in themselves; in the adolescent and the adult, the glands, although much less enlarged, sometimes minimally so, were however, usually actively painful and exquisitely on palpation.

Involvement of the liver and spleen was a typical finding. In 5 cases, frank jaundice occurred during the course of otherwise typical illnesses.

The costal margins were the site of considerable complaint of pain, and the liver and spleen were tender to palpation. In several cases actual enlargement of the spleen was noted.
Morphological abnormalities in the lymphocytes associated with an eosinophilia were present in 30% of the cases, but no abnormalities or increase in numbers were noted in the case of the monocytes.

An indication that the production of this abnormal blood picture was essentially a display of individual host reaction to the infection was given by the reaction of two sisters, aged 15 and 17 years respectively, both attending the same school in Carlisle. The onset of the disease in the older girl preceded that in her younger sister by 24 hours. The clinical features were similar in both with the exception that the degree of glandular involvement, with splenic and hepatic tenderness, was much more marked in the case of the older girl. In her case, also, changes occurred in the blood, with the appearance of morphological abnormalities in the lymphocytes and an eosinophilia, as shown by a number of other hosts in this series; in the case of the younger girl, however, no change in the blood picture occurred throughout the course of the illness.

This varying degree of reticulo endothelial reaction to an apparently similar infection in hosts infected about the same time was shown in several other instances by hosts, who were members of a family, as well as more commonly in the series as a whole.

Neurological Involvement.

Objective neurological involvement was seen in about 20% of hosts; in the greater number of these cases the involvement was fortunately of a mild degree. Subjective phenomena were frequent concomitants, being complained of by more than 60% of hosts.
Recurrences.

Hosts, showing more severe involvement of the reticuloendothelial system and neurological involvement, had a more prolonged illness, with a greater liability to recurrences of symptoms. In some hosts, however, the original response to infection was minimal, to be followed at a later date by a recurrence when the reaction was much more severe.

Tissue affinity.

The causal agent was pan-tropic in the sense that systems derived from each of the three embryonic layers of the host showed clinical evidence of involvement in the disease process.

The Incubation Period.

This proved difficult to establish as, in the early cases, there was little evidence of contact between succeeding cases seen in the practice, and, in the later cases, too many possible contacts existed to fix an absolute time for the infection to have entered the host.

In several instances, however, it was possible to establish the probability of infection from exposure to one established case of the disease, and here the evidence suggested the incubation period was 5 - 7 days. This agreed reasonably well with the periods elapsing between the onset of symptoms in one member of a family and the onset of symptoms in the secondary attack in families were multiple cases occurred, even though the members might have been exposed to infection through extra-familial sources.

Further evidence of a possible maximum incubation period was given by three cases, where the persons concerned had
arrived in the district to stay with relations. They had arrived in the district apparently fit and free from infection, and had developed the symptoms of the onset of the disease within 12 - 14 days of their arrival. Assuming that these persons had not, in fact, been incubating a disease with a clinical picture similar to that seen in cases in this district, prior to their arrival in this district, it is reasonable to conclude that they had been infected subsequent to their arrival in this district, giving the maxima for their incubation period of 12 - 14 days.

Some examples of the more reliable instances of case to case infection are given in Table 5.
<table>
<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of onset</td>
<td>14.4.55</td>
<td>7.5.55</td>
<td>14.4.55</td>
</tr>
<tr>
<td>Date of exposure</td>
<td>11.4.55</td>
<td>12.4.55</td>
<td>12.4.55</td>
</tr>
<tr>
<td>Contact</td>
<td>Host of case</td>
<td>Host of case</td>
<td>Host of case</td>
</tr>
<tr>
<td>Date of infection</td>
<td>16.4.55</td>
<td>16.4.55</td>
<td>16.4.55</td>
</tr>
<tr>
<td>Incubation period</td>
<td>6 days</td>
<td>7 days</td>
<td>7 days</td>
</tr>
<tr>
<td>Case</td>
<td>Host's children</td>
<td>Host's children</td>
<td>Host's children</td>
</tr>
<tr>
<td>Hosted by</td>
<td>Host's children</td>
<td>Host's children</td>
<td>Host's children</td>
</tr>
</tbody>
</table>

Table 5: Instances of apparent case to case infection
Abortive Infections.

When called in to new cases, during the course of the epidemic, I commonly found that one or more members of the family, other than the one whom I was called in to see, had been visited by a transient malaise during the week preceding the onset of symptoms in the more severe case.

The malaise, associated with some of the prodromal symptoms of the disease, had lasted for not more than two or three days and usually had not been severe enough to cause those affected to stay away from work or school.

The fact that other members of the family might have been affected in this way was often only elicited by direct questioning, and as often was dismissed by some such phrasing as "Oh, Dad was poorly for a day or two last week, but it was nothing, and it didn't stop him from going to work."
Course of the Outbreak:

The course of the outbreak, as seen in my practice, during the months of January to July, 1955, is illustrated by the figure below.

Figure illustrating the course of the epidemic of an unusual infective disease, seen in general practice in Dalston, and adjacent districts, in Cumberland, during 1955, cases being shown by dates of onset.
The first cases seen in the practice occurred in Dalston parish, when a workman on an estate was taken ill on 16.1.55, followed six days later by a neighbour in an adjoining cottage on the estate with whom he had been in contact prior to the onset of symptoms.

During January 1955, eight cases in all were seen, four in the parish of Dalston, and two each in the parishes of Orton and Thursby.

There was no evidence of contact between the cases, apart from the first two cases already mentioned.

Of the eight cases, two were primary school children, two were young adults, two were middle-aged and the remaining two elderly.

During February, 27 cases occurred. 26 of these were seen in the parish of Dalston and one in the Parish of Orton. The emphasis in age distribution had shifted to the youngest age groups, six cases occurring in children under school age, and seventeen cases occurring in children of primary school age, with only four adults affected.

March produced a large increase in the number of cases, most notably in the second half, and the epidemic tendency continued into April.

In March, 54 new cases were seen, 38 of these occurring in the parish of Dalston, seven in the parish of Orton and nine in the parish of Thursby. Four cases occurred in children under 5 years, 10 cases occurred in primary school children, six in secondary school children and others in the 12 - 19 age group, and 34 adults were affected.

In April, 84 new cases were seen, all age groups being
attacked; 54 cases were seen in the parish of Dalston, 19 in Orton and 11 in Thursby. There were 10 cases in the under 5 age group, 21 cases in primary school children, 15 cases in the 12 - 19 age group, and 38 cases in the adult age groups.

In May, June and July, the number of new cases appearing diminished, the figures for each month being respectively 28, 16 and 16.

Of these new cases having their onset in May, 24 were resident in the parish of Dalston, and 2 in each of the parishes of Orton and Thursby. In June, 12 new cases were seen in Dalston, 1 in Orton and 3 in Thursby, while in July, 10 cases were seen in Dalston, 2 in Orton and 4 in Thursby.

The largest number of cases occurred in the parish of Dalston, followed by Orton and Thursby in that order. Proportionately to total numbers at risk, however, Orton had the highest incidence of cases.

During the initial period of the outbreak the few cases seen were scattered in various age groups, but as the outbreak continued by the end of February 85% of new cases seen had occurred in children of school age or below. From March onwards, however, new cases were seen in children of school age and under, and the adult age groups, in roughly equal proportions.
Communicability

The level of infectiousness of the causal agent of the disease appeared to be fairly high as shown by the numbers of families where secondary attacks had occurred subsequent to the primary introduction of the disease into their midst. Another instance of this high level of infectivity can be shown in the instance of a children's residential home in Dalston, where Carlisle Corporation lodge 20 children, mainly boys, aged from 5 to 15 years.

Three boys developed attacks of the disease, which left them debilitated for more than two months, while the remainder developed attacks of varying degrees of severity down to the minimal. All cases showed signs of glandular enlargement, and blood films showed abnormal lymphocytes even in several of the cases with minimal attacks.

Dispersal of the infection was ensured by the insidious onset of many of the attacks. The patients, in a number of cases, did not come for medical advice until symptoms had been present for a week or more, and in one case symptoms had been present for four weeks before the patient sought attention, and then only because she had become alarmed at the loss of muscular power in the lower limbs.

The time of maximum infectivity appeared to be at or about the time of the onset of symptoms, as judged by the secondary attacks in families.

Recurrences of symptoms of the disease became a well marked feature of the epidemic, and it was noted that in some instances a contact of the primary host, who was having a recurrent
attack, would develop the typical disease, suggesting, therefore, that, at the time of the recurrent attack, the host was again infectious.

As some hosts had as many as five recurrences of symptoms over a period of months, I feel it is improbable that these recurrences were, in fact, re-infections.
Susceptibility.

Table 6 shows the number of cases that occurred in the practice during the months of January to July, 1955, classified into their age and sex groups and the percentage of the total of each group affected during that period.

**Table 6.**

<table>
<thead>
<tr>
<th>Total Practice population at risk.</th>
<th>Age Group.</th>
<th>Number of cases in each age group.</th>
<th>Number of cases in each age group.</th>
<th>Percentage of cases affected in each age group.</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>-----</td>
<td>----</td>
<td>-----</td>
<td>----</td>
<td>-----</td>
</tr>
<tr>
<td>66</td>
<td>62</td>
<td>11</td>
<td>16</td>
<td>16.66</td>
</tr>
<tr>
<td>122</td>
<td>84</td>
<td>40</td>
<td>19</td>
<td>32.79</td>
</tr>
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Totals for combined age groups:

From the percentage of cases attacked in the differing age and sex groups, shown in Table 6, it is seen that primary schoolboys were the most severely affected in the percentage of their group contracting the disease, followed by girls under 5 years and then by primary schoolgirls. It is interesting to note that in the
20 - 29 age group the percentage of males affected by the disease outnumber females by almost 2 to 1, while in the 30 - 39 age group the reverse is the case.

The lowest level of susceptibility, as shown by the percentage of their age group attacked, was seen in males in the 40 - 49 age group, and in females in the 20 - 29 age group.

In general, age groups up to 19 years appeared most susceptible to the disease, although susceptibility of these age groups to the infection did not necessarily indicate greater severity of the individual attack, and, in fact, the more severe attacks in general occurred in the adult age groups.
Attack Rate.

Table 7 shows the numbers of cases occurring in the months of January to July, 1955, classified into age and sex groups, by month of onset, and by the parish in which they occurred.

The attack rate amongst patients in the three parishes for the months of January to July, 1955, and the total attack rate for the practice as a whole is given in Table 8.
### Table 7:
Cases classified into Age & Sex Groups and by month of onset:

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The proportions of the total population, as shown by the Census of 1951, of the parishes of Dalston, Orton and Thursby that belonged to my practice, were respectively 68%, 40% and 26%. Of the numbers from each parish, male and female representation was almost equal, and further breakdown of the total number of patients from each parish into groups differentiated by age and sex revealed adequate representation for each group.

The practice population was, therefore, apparently representative of the population of the parishes as a whole, and attack rates for the practice population could be extended to include the total population of the parishes.

Indirect evidence that infection of a similar nature had, in fact, affected persons in these parishes, who were not patients of mine, was volunteered by district nurses and by relatives of those affected, who were patients of mine and who were interested in the disease through personal experience of it.

The attack rates for the practice population in the three parishes show that Orton had the highest number of cases proportionate to the population at risk. This increased attack rate in the parish of Orton may be explained by the probability of a greater degree of exposure experienced by the inhabitants.

The parish of Orton contains one larger and one smaller village, and several small closely knit communities or hamlets clustered about several farm houses. The villages are on minor roads and public transport facilities are poor. The inhabitants of the parish are, therefore, relatively more isolated than the other parishes, from Carlisle, and more
dependent on their local social activities. Infection disseminated from the school would thus tend to resemble, in a lesser degree, the attack upon a closed community, consequent upon the greater degree of exposure to the disease of its individual members.

The proportionately higher incidence of cases in children of school age, than in the other age groups, may also be due to their greater degree of exposure in classrooms, over a period of hours, each school day, to the risk of contracting infection from other school children, already in an infectious state of the disease, rather than from a greater degree of immunity to the disease in the older age groups.

As shown in Table 6 there was no evidence of a steadily rising level of immunity in the older age groups.
Mode of Spread.

During the early months of the epidemic the weather was seasonal for the Colway plain during the months of January, February and March.

Possible Vectors.

During the first quarter of the year insect vectors of the disease could be dismissed, with some confidence, as disseminators of the disease in the epidemic under study. There was a curious coincidence, however, of an epizootic disease amongst budgerigars during the period of the epidemic.

In a large number of households where members had contracted the disease, budgerigars were present as pets, in cages in the living room, and morbidity amongst these birds prior or subsequent to the human infection was common, with a considerable fatality rate amongst them.

An indication that the disease was infectious for budgerigars was provided by two instances. In one case two budgerigars were housed in separate cages in different rooms in a house. One bird developed the illness which was characterised by lethargy, and lack of attention, even to food, and difficulty in holding on to the perch, and subsequently died.

The cage in which the diseased bird had been was the better cage, and the second budgerigar, which up until then had, to all appearances, shown normal health was removed from the inferior cage and placed in the better cage, which had not been sterilized or had the foodstuffs removed from their containers. Four days later the second budgerigar became ill and was dead within a fortnight.
In the second case a man bred a small number of budgerigars as a hobby and had been attending to the birds for a week after the onset of symptoms of the disease under study in himself.

He remained ambulant, the symptoms not being severe enough to send for medical attention, until one week later he developed an intercurrent infection - an acute tonsillitis caused by haemolytic streptococci, Group A - and was pleased to be sent to bed. He remained in bed for several days and during this period, six of his budgerigars, which were being looked after adequately by his wife, became ill, five dying and one subsequently recovering.

Recovery from this disease in budgerigars was slow, and several months would elapse before the bird regained its pre-infective condition and lost its apathetic behaviour.

Psittacosis as a cause of this disease amongst budgerigars was excluded by laboratory means.

A connection between this infective process in budgerigars, and the disease concurrently epidemic amongst humans, could not be established either by complement fixation testing, using the spleen of diseased birds, or by the production of avian disease, by the intranasal introduction of suitably treated and presumably infective material, obtained from throat swabs and faeces of human cases of the epidemic disease, into healthy birds.

The disease in budgerigars was, therefore, regarded as a coincidental finding during the investigation into the causation of the human disease - a red herring that involved a
good deal of laboratory work before its disposal was reasonably accomplished.

Water, Milk and Food.

There was no evidence on which any of these three possible sources of infection could be incriminated. The water supplies were from differing sources for the three parishes, and it appears improbable that each source could be accidentally contaminated by the same contaminant at the same time. Previous testing had always shown the water to be of a high standard of purity.

The milk, as in the case of the water, was supplied from differing sources for the three parishes, and cases of the disease also occurred on farms where only their own milk was consumed, and amongst non-milk drinkers.

The possibility that infection had been conveyed through foodstuffs, such as pastries and cakes made up from contaminated constituents and sold from the bakers' vans that ply from door to door throughout the district, was considered, in view of the transient diarrhoea that occurred at the onset in some cases, but was thought implausible. There was no laboratory evidence to suggest such an infection, and, furthermore, cases of the disease occurred in households old-fashioned enough to believe that home cooking was best, and which, therefore, had no truck with any made up foods, whether products of the baker, or potted meats or pies from the butcher.

Host to host spread.

At the onset of the disease, the throat was commonly irritable and a slight degree of laryngitis was often present, as was an inflammatory reaction in the trachea, which gave rise
in some cases to an irritating, spasmodic cough, worst on going to bed and on getting up. In children, vomiting was induced in a few cases and the cough was severe enough to mimic whooping cough — a diagnosis second only to mumps, as a diagnosis made by the mothers at the onset of the disease in their children. There was no clinical or laboratory evidence to suggest this diagnosis, and there were no cases of true whooping cough seen in my practice during the period of the epidemic, although there may have been some cases in the district, as, during the course of the epidemic, I heard of one family consisting of two middle-aged adults and two adolescent children, who were attended by another physician, where the whole family was considered to have contracted whooping cough.

In addition to the irritated throat, the nose usually felt dry, with a prickling feeling in the post-nasal region. During this early phase, spasmodic sneezing was experienced in a proportion of cases, three or four spasms of sneezing occurring in the day, when up to a dozen severe sneezes might take place in rapid succession, followed by a profuse rhinorrhea which lasted several minutes.

This tendency to coughing and sneezing in a proportion of cases, at the onset, suggested that droplet infection was one mode of exit of the causal organism from the body, and, conversely, the reaction in the upper respiratory passages suggested these as one portal of entry of the infecting organism.

Transient diarrhoea, lasting for a period of not more than 12 to 24 hours usually associated with nausea, if not vomiting, was the presenting symptom in some cases, and in
these cases involvement of the upper air passages was minimal, and no coughing or sneezing was experienced.

Nevertheless a dry mouth and throat were complained of to some degree, in these cases, and a patchy injection of the fauces was often present; it appears probable that the portal of entry was the nasopharynx in these cases also, the gastroenteric reaction being their individual reaction to the infection.

Instances of presumable case to case infection were given in the section on the incubation period, and secondary attacks in families also support the concept that the disease was spread by host to host contact.

The probability of dissemination of the causal agent of the disease by droplet infection and case to case spread of the disease is emphasised by the age distribution of the cases against the time sequence in the epidemic under study.

To quote Pickles (1939) "Having reached the district it is easy to understand the method of spread of these infections. There are now cinemas and there are, of course, concerts, whist drives and dances, which are available to the inhabitants over a large area owing to the increase in transport facilities, of which a recent development is an excellent 'bus service. All these channels have provided opportunities for infection to my knowledge during the last few years, but the school remains and will remain the largest factor in disseminating the infective agent of an epidemic."

The sequence of events in the Dalston epidemic is in agreement with this dictum. There was, in the first stages of the epidemic, the introduction of infection into the district and the appearance of a few scattered cases in various age
groups. The following month school children were predominantly affected, and thereafter the infection was widely disseminated through all age groups.

A similar situation has arisen this autumn - autumn 1957 - when an invasive strain of Influenza A appeared in the district. In the early stages of this epidemic, a few scattered cases occurred in adults, followed in a similar manner but to a very much greater degree than in the 1955 epidemic, by widespread illness in primary school children. In the present influenza outbreak children have been affected wholesale, numbers of them having to be taken home ill having arrived well in the morning. In some classes only one or two children were left unaffected, and a high proportion of teachers also have been affected.

In 1955 the numbers affected were less and spread over a longer period and there was none of the present dramatic picture of infection in the schools affecting virtually the whole school population.

The state of affairs still existing, of widespread dissemination through all age groups, followed the dispersal of infected school children to their homes.

Comparing the epidemic of influenza to date, in 1957, to the epidemic of 1955 as it has been seen in my practice, the attack rate of influenza 1957 is already considerably higher than it was for the whole epidemic period of 1955, and the secondary attack rate in families, in the case of influenza, has been from 50 to 100% in a considerable number of families so far seen. It was not possible to obtain a secondary attack in families, in 1955, with any real accuracy, as there were,
doubts about the periods of infectivity in these cases and secondary attacks in families seemed fairly frequently to follow a period of recurrence of symptoms in the primary case. Exclusion of infection from sources other than the primary case could not be made in these instances.

Nevertheless, cases of secondary infection in families, where the onset coincided reasonably well with the lapse of the incubation period from the exposure of the secondary contact to the primary host having an initial attack, were not as frequently observed as in the present influenza epidemic, the clinical impression being that the causal agent of the 1955 epidemic was infectious to a degree very much less than the 1957 influenza strain.

In the instances both of the 1955 epidemic and the 1957 influenza epidemic, once the infection had entered the district, dissemination locally was ensured through the schools and other local lines of communication mentioned in an earlier section of this thesis.

Tracing the origin of the infection entering the district was easy in the case of influenza 1957, the first cases giving a history of contact with cases in Carlisle or, in several instances, with cases occurring in boarding houses, at resorts in which they were holidaying, where the disease had already appeared in epidemic form.

No such history was available in the instance of the 1955 epidemic, and the early cases were able to provide no clue on the original source of infection to which they must have been exposed. A number of cases, however, were mild, or abortive, and it appears probable that the infection was brought to the
district along one of the longer lines of communication mentioned earlier, through mild or abortive cases in whom the temporary indisposition might well be attributed to a cold or "chill" of some sort, insufficient to put them to bed or seek medical advice, thus remaining in circulation, locally, as a source of infection to others.

Reference:
**Aetiology**

Investigations into the nature of the disease were both pathological and electroencephalographic.

Facilities for electromyographical studies of the muscular dysfunction seen in this disease were unfortunately lacking in Carlisle, and investigation by this means had to be foregone.

**Pathological Investigations.**

I collected material for bacterial and virus isolation, at various stages of the disease, from patients exhibiting the more severe clinical picture, whether presenting during the epidemic period or as later sporadic cases.

The material included throat and conjunctival swabs, gargles, rectal swabs and faeces; this was collected and taken to the Public Health Laboratory in Carlisle within the hour of collection, where samples were stored in a low temperature refrigerator pending virological investigations and the remainder examined bacteriologically.

No significant bacterial pathogens were encountered in the bacterial flora apart from the occasional finding of the haemolytic streptococcus in cultures from throat swabs.

Virological investigations included the inoculation of suckling mice, and the intranasal inoculation of budgerigars for the reasons given regarding the possible role of these birds as vectors of the disease.

Tissue cultures of HeLa cells were inoculated from specimens sent to the Central Public Health Laboratory at Colindale, London, and later repeated, with other specimens, at the Public Health Laboratory, Carlisle, when virological
research facilities became available there, during the past year. No virus was isolated from tissue culture, and the suckling mice and the budgerigars remained unaffected by their inoculation. Further attempts to isolate a virus from the material supplied, using tissue cultures other than those of HeLa cells are being considered.

**SEROLOGICAL TESTS.**

I obtained paired serum samples, from the acute and the convalescent phases, from almost 100 cases, which occurred during the epidemic period or appeared subsequently as sporadic cases.

Complement fixation tests on these specimens were negative against influenza viruses A, B and C, Q Fever, Psittacosis, the lympho-granuloma venereum group of viruses, mumps, V & S antigens and toxoplasmosis.

The adenovirus group was excluded in serological tests made on more than 50 paired samples of serum sent to Colindale.

**Paul Bunnell Test.**

This test was performed on all paired serum samples, and on an additional number of single acute phase specimens obtained earlier in the epidemic, with uniformly negative results.

**Blood Picture.**

I made blood films in 140 cases, and also took blood for a total white blood corpuscle count in the earlier cases.

The total count was not outside normal limits, although the tendency was for the counts to be on the low side of normal except in two cases where urticarial lesions were a prominent part of the clinical picture, and the total count reached 20,000.
Approximately 30% of the blood films showed morphological changes in the lymphocytes, with a relative lymphocytosis and eosinophilia. The number of large lymphocytes was increased and immature forms present; changes consistent with a diagnosis of glandular fever were seen in only two cases.

Dr. A. Inglis, the haematologist examining the films for me, considered the picture recurring in the films he examined from patients in my practice formed a recognisable entity, which he labelled "Dalston Disease." He informed me that he was finding a similar picture sporadically in films sent from the Cumberland Infirmary from other parts of the county, and from several boys at Sedbergh School, where obscure illnesses, associated with adenitis, had occurred.

These alterations in the blood picture could be persistent in some cases. For instance, in the case of a boy of 6 years of age the above picture was present in the blood 20 months from the original onset, and in the case of a family of 6, 5 members showed typical changes 18 months from the first onset of the illness.

This persistence of the altered blood picture in some cases may have been due to intermittent stimulation from the recrudescences, which have proved a marked picture of the disease.

Cerebro-Spinal Fluid.

The cerebro-spinal fluid was fully examined in 6 cases and no abnormality was found. The cerebro-spinal fluid examined was from the later sporadic cases, except in two instances, where lumbar puncture was done in patients having recurrences, but whose original time of onset had been in the epidemic period.

No cerebro-spinal fluid was obtained from acute cases in
the epidemic period, as I felt it was subjecting the patient to an unjustifiable risk in domiciliary practice, and such patients as were sent into hospital, with the added request that their C.S.F. be examined while they were in-patients, did not, in fact, have this procedure carried out, no doubt for excellent reasons.

The upshot was, however, that no specimens were obtained during the epidemic phase, and those that were obtained were done so through the individual kindness of a member of a hospital staff. The patients having the samples taken, had the lumbar puncture performed under hospital conditions. They were fully informed as to the lack of benefit that they could expect to derive from the procedure, which was for information only, and the possible, although remote, risks entailed. Nevertheless, they volunteered to undergo lumbar puncture and gave written consent to that effect, for which I was most grateful to them.

**Morbid Anatomy.**

There were no deaths attributable to the disease, in its epidemic or sporadic form. Three patients, however, who had been infected during the epidemic phase, later died from other causes. In two of the cases, where death occurred at home, I obtained permission to have a post-mortem examination carried out, and in the third case death occurred in hospital, where permission for examination was also obtained.

One of the two cases dying at home was that of Kinnier Wilson disease in a female in her middle thirties; the first symptoms of this disease appeared 9 years before her death, and thereafter the disease steadily advanced until the woman was unable to make co-ordinated movements and presented the typical
features of the syndrome. She remained static in this phase, until a fortnight before her death, when she developed symptoms of the epidemic disease, which had been brought into the house and had affected two other members.

Following the onset of symptoms of the epidemic disease, further general physical deterioration developed rapidly, in association with extreme lethargy, death finally occurring in coma.

Post-mortem examination, including microscopic examination of the brain, showed no changes that were not consistent with changes described as occurring in cases of Kinnier Wilson Disease.

The second fatal case, dying at home, a male in his late fifties, developed the symptoms of the onset of the epidemic disease one week after the onset in his niece, who lived in the same house and had developed a typical attack. Several days from the onset he became very lethargic and was sent into hospital, semi-comatose. Some superficial abscesses appeared while he was in hospital, from which a little pus containing staphylococci was obtained, and although staphylococci were not recovered from blood cultures a staphylococcal septicaemia was postulated as the cause of the illness. Recovery was protracted, and he did not, in fact, regain normality before his death 11 months later, which followed a coronary thrombosis.

Post-mortem examination again was negative other than for signs of the immediate cause of death, which was shown to be due to extensive infarctions of the myocardium.

The third case in which a post-mortem examination was carried out was a woman in her early fifties. She had a febrile
illness at the height of the epidemic, for which she had not consulted me at the time; the history of that illness, as described to me 3 months later by the patient, was consistent with an attack of the epidemic disease, which had left her debilitated, depressed and emotional.

During the 15 months from the onset of the febrile illness until her death, psychiatric disturbances first appeared with no physical signs of organic disease of the central nervous system. Electroencephalography, however, was abnormal, the findings being compatible with those seen in pre-senile dementia.

Slow deterioration occurred until three weeks before her death, when she suddenly became stuporous, with a decerebrate type of rigidity; she remained in this state, in the meantime running a low grade pyrexia, until her death at the end of 3 weeks.

Post-mortem examination revealed nothing of note except in the brain.

The brain was examined by Dr. R. Klein of the Crichton Royal, Dumfries, who reported:

"In macroscopical examination of the brain there was slight atrophy of both frontal poles; meninges and vessels did not show any pathological changes. On cross-section of the brain no lesion could be found. Section in various levels of the brain stem, below the mid-brain, did not show any histological lesion, but the cells of some of the cranial nerve nuclei show some degenerative signs. There are no conspicuous changes in the cortex, and only one senile plaque was found in the number of slides I examined. There are in the entire diencephalon, particularly round the third ventricle numerous small
haemorrhages, which extend into the adjacent parts of the mid-brain. Similar haemorrhages can be seen in the corpora mamillare. The haemorrhages are mostly around small vessels, but some are also to be seen in the free tissue. This is a significant finding and is probably the cause of death in this patient. These haemorrhages are a characteristic finding in Korsakoff's and Wernicke's diseases – most frequently in chronic alcoholics, but may also have some other aetiology.

A microphotograph of a typical haemorrhage seen, in this instance, in the supra-mammillary nucleus, is mounted below.

Microphotograph of a typical haemorrhage in the supra-mammillary nucleus.
I am indebted to Dr. Klein for the report quoted above and for the microphotograph illustrating his report.

The three cases described above comprised the total of histopathological material available to me, and of this material, the first two cases, dying at home, showed no evidence of any lesion that could be attributed to the epidemic disease, and the third case dying in hospital, gave a picture characteristic of Korsakoff's or Wernicke's Disease. In this third case, alcohol as an aetiological factor in the production of the disease could be ruled out with complete confidence. Whether the febrile illness, presumably of the same nature as those seen in the epidemic, was an aetiological factor in the subsequent course of the illness and the organic changes found in the brain at post-mortem examination, must at present remain open to doubt.

Other Material.

Other material that might have been obtained for histopathological examination included the appendix from two cases and material from biopsy of one of the enlarged glands so commonly seen.

In two cases appendicitis occurred during the early course of the illness in two males, and I requested that the appendix be saved for histological examination, but unfortunately, while this was agreed to prior to the operation, the appendix in each case was destroyed in common with the rest of the expendable matter, following the operation.

I considered the possibility of gland biopsy - and material could readily have been obtained from one of the enlarged,
superficial glands commonly seen - but decided that it was not practical politics to do so in general practice, at the present time, and reluctantly gave up the idea.

**Electroencephalographic investigations.**

As psychogenic sequelae were a feature of the disease and its subsequent course, it was considered that electroencephalographic investigation might yield some information. Unfortunately it did not prove possible to arrange this investigation until 1956; prior to this time there was no electroencephalographic machine in Carlisle, the nearest apparatus then being in Newcastle.

The same lack of instrumentation was present in the case of electromyography and still remains so, which has proved unfortunate in that electromyograms in cases of disturbed muscle function were not able to be obtained at all.

In the case of the electroencephalographic investigation, however, it was a case of better late than never; while the acquisition of the electroencephalographic apparatus was too late for making recordings of cases in the epidemic period, nevertheless recordings were made, through the courtesy of the Superintendent and staff of Garlands Hospital, Carlisle, in a total of 23 sporadic or recurrent cases.

Of the 23 cases, 15 showed a fairly constant, but non-specific type of abnormality, most evident in the occipital leads, and on eye opening. 8 cases showed no abnormality in the record.

A photostat copy of a typical recording showing the type of abnormality seen in 15 of the 23 cases is mounted below.

The first section shows the normal recording when the eyes
were closed, followed in the second section by the abnormalities seen in the occipital leads of the recording with the eyes open.
Clinical Features.

The clinical picture seen in cases of this disease varied from that of a mild disease, in which the patient was not indisposed for more than three or four days, to one of considerable severity, with sequelae, which, in several instances, persisted for a year or more.

Onset.

A sudden onset was common, but it could be either insidious or abrupt; the insidious mode of onset was more commonly seen in adults than in children.

Cases of Abrupt Onset.

Symptoms and Signs:

The onset was marked in the majority of these cases by:-

(1) General bodily prostration and somnolence.
(2) Severe headache.
(3) Aching pains, affecting the back of the neck, the lower limbs, the back, the shoulders and the upper limbs in that order of frequency of occurrence.
(4) Subcoastal pain.
(5) Dizziness.
(6) A dry irritable throat.
(7) Enlarged tender lymph glands - the cervical chain being most affected.
(8) Sore eyes.
(9) Blurred vision.

In a minority of cases the symptoms of the onset were referable to the gastro-intestinal tract, and consisted of the precipitate appearance of diarrhoea, with associated nausea,
which sometimes proceeded to actual vomiting, the episode
lasting 12 - 24 hours, and giving way to the emergence of the
depicting of the onset as seen in the majority of cases.
The initial stage of the onset:

This was ushered in by the development of a feeling of
lethargy, weariness, headache and dizziness, which usually
increased rapidly in degree. It was common to find this stage
had developed in the evening, which was fortunate for the
victims, who longed for nothing so much as to get to bed. Many
patients told me that, while they longed to get off to bed, they
found it needed a considerable effort of will to summon up the
energy to do so. If stairs had to be climbed to get to the
bedroom, the effort of doing this left them feeling exhausted,
with the legs aching and feeling leaden.

These patients, having got to bed, sank into a deep sleep
from which they awakened, two or three hours later, spending the
rest of the night in a restless fashion with intermittent dosing
and dreaming, a pattern of sleep with which some of them were to
become familiar during the ensuing weeks or months.

Within 48 hours of the initial symptoms of the onset the
headache had become severe, and aching pains had developed in
the back of the neck and the other sites mentioned above. The
headache was usually frontal, but not infrequently was temporal
or occipital in location, and was often described as being of
a dull "grinding" character.

Aching in the back of the neck was always present, and
varied in intensity from a dull ache to acute pain; true neck
rigidity was not seen.

Myalgic pain most frequently affected the muscles of the
thigh and calf, the right lower limb being more severely affected than the left, in the cases seen by me. The affected muscles were acutely tender and hyperaesthesia was present in the overlying skin.

Similar acute myalgic pain also frequently affected the para-spinous muscles, especially in the lumbar region, and also the muscles of the shoulder girdle and upper arm. In several cases acute pain and spasm developed in the sternomastoid muscles. Occasionally in adults the pain that developed in the back was sufficient for them to consider they had developed lumbago.

At this stage, the mouth felt parched, the throat dry and irritable, abnormalities of taste and smell had developed, and thirst was a prominent feature. A dry, irritating cough began to appear in many cases, but in some instances laryngitis developed, and subsequent cough was usually absent in these cases.

Tender enlarged lymph nodes appeared first in the posterior triangle of the neck, and later were found along the anterior border of the sternomastoid, in the inguinal and saphenous group, and less commonly in the axilla.

Pain was complained of along the costal margins, and fairly frequently in the right iliac fossa, from whence it extended into the groin and down the right thigh for one or two inches distal to the saphenous opening.

The eyes felt sore and retroorbital pain was present; sudden movements of the eyes at this stage often caused sharp stabs of pain. Photophobia was a short lived phenomenon in many of these cases. A slight degree of conjunctivitis, blepharitis, and watering of the eyes was common.
The vision became blurred and patients complained that it needed a conscious effort to bring objects into focus.

**During the first week from the time of onset:**

The headache and myalgic pains persisted in the severe cases, and intermittent waves of vertigo were usually present, in some cases associated with the development of a lateral nystagmus which was usually short lived, being intermittently present over a period of two days or so. Diplopia on upward and lateral gaze was also present in all severe cases and in some that were clinically mild.

**Hyperaesthesia** of the skin overlying the affected muscles was present from the onset of the myalgic pains, while **paraesthesiae** made their appearance any time from the onset.

These consisted of feelings of numbness of variable distribution and "pins and needles" which commonly affected the extremities; sometimes the little finger and ulnar border of the hand would alone be affected, and in this case pain was usually felt in the interosseal muscles of the hand, particularly the 4th interosseus muscle.

Other abnormal cutaneous sensations experienced included a feeling as of trickles of cold water running over various parts of the skin, and a feeling of insects crawling under the skin. The latter type of sensation was experienced in a few cases only and was limited to the arms and legs.

Four cases complained of a feeling as if a worm was crawling in their legs, under the skin. In one case where I was present at the time of the complaint, a slow wave of contraction was seen to travel along a bunch of muscle fibres in the gastrocnemius muscle at the site of the complaint.
Attacks of sweating were usual, drenching sweats often occurring at night.
On physical examination, the patient was apathetic and did not want to be bothered. The colour was pale and the skin clammy.

The temperature was usually raised to between 99°F. and 100°F., but in some instances was subnormal and remained so throughout the illness. In a few cases the temperature rose to 103°F., but in these cases the throat was much more inflamed than was usual and streptococci were recovered in some instances from the throat swabs. The pulse was raised to 100/min. in the usual case, but tachycardia of up to 150/min. in association with a low grade fever was also observed.

The tongue was always found to be dry, and heavily coated with a yellowish fur, in the early stages of the acute attack. The nasopharynx was also dry and was mildly injected, in the absence of secondary infection, the injection being of a dull purplish-red colour; a few clusters of petechiae on the palate appeared in some instances, and occasionally surrounded two or three shallow ulcers, which were only discovered on examination, as they seemed to cause remarkably little pain.

The abdomen showed some degree of flatulent distension. Palpation of the abdominal wall revealed occasional tender nodes especially in the recti. Tenderness without muscular guarding was always present on palpation at the subcostal margins, and was also frequently present over the right iliac fossa, the zone of tenderness extending down, over the inguinal ligament, to a point an inch or so distal to the saphenous opening.

The liver and spleen were very tender in the more severe cases, and in a few instances the spleen was enlarged. No enlargement was noted in the case of the liver.
Obstinate constipation was a fairly regular concomitant of the disease and this was noted also as a later manifestation in those in whom diarrhoea and vomiting had occurred at the onset.

Involvement of the respiratory system was usually slight and confined to the upper respiratory passages. The mild inflammatory reaction in the nasopharynx fairly commonly descended to the larynx and trachea, producing a few cases of laryngitis and in others a common tendency to the development of a dry paroxysmal cough, which in some children was severe enough to mimic whooping cough. The lung fields were ordinarily clear.

Changes that occurred in the blood picture in a proportion of cases have already been described, and further evidence of disturbance of the reticulo-endothelial system was shown by the regularity with which tender enlargement of lymph glands occurred, by the tenderness of the liver and spleen and by the occasional splenic enlargement. Marked enlargement of the lymph glands was found mainly in children and adolescents.

The urinary system was unaffected and no cases of retention of urine were seen. The urine occasionally showed a trace of albumin.

The skin was affected by rashes, in a few instances, and these will be described later.

The eyelids appeared a little puffy and the upper lid tended to droop. A minor degree of blepharitis and conjunctivitis was usually present, the conjunctival reaction mainly affecting the palpebral conjunctiva. Watering of the eyes was seen in most cases but to a slight degree.
Blurred vision, which was commonly complained of, was not due to refractive errors, as refraction was done on a number of these cases without any objective evidence of refractive error.

The joints were not affected in the acute stage of the illness.

The most obvious feature during the examination was the degree of spontaneous muscular pain present; movements of the affected parts during the examination were resented and had to be done very gently. In many cases straight leg raising caused severe pain before the leg had been raised more than an inch or two and the hamstrings went into spasm. Gentle palpation of the affected muscles was difficult as the overlying skin was highly sensitive and light touch was interpreted as an unpleasant cutting sensation in the severe cases.

Palpation of the affected muscles frequently revealed the presence of a few palpable and tender nodules in the muscle substance, which gave a gritty sensation to the touch.

Pain in the low back was the main myalgic manifestation in some cases, the pain being aggravated by standing, or bending, or attempted straight leg raising, but not by coughing or sneezing, and sufficiently severe for these patients to take to their beds and lie without moving, in case they aggravated the pain.

Pain in the neck was sufficiently severe for the patient to send for me in the middle of the night. The picture was similar to that seen in acute torticollis but other more general manifestations of the disease were also present, and the patient was also in a disturbed emotional state with marked depressive tendencies.
Neurological examination at this stage was largely negative. The superficial reflexes were normal, and the tendon reflexes were normal or diminished. A slight degree of weakness in the flexors of the thigh was seen in a few instances at this early stage. No overt weakness in the extrinsic muscles of the eye was seen, but the diplopia on upward or lateral gaze, which occurred in a considerable number of cases at this stage, argued the presence of some degree of weakness in the muscles responsible for the upward and lateral movements of the eye.

No organic changes were found to account for the subjective phenomena commonly present.

The mental state in the early stages was one of apathy and somnolence, later followed by a labile emotional state and depressive tendencies; inversion of the sleep rhythm occurred in a number of cases. A short period of sleep would be followed by a restless night, with dreaming a marked feature of the short snatches of sleep which were obtained during the remainder of the night. Dreaming was extremely common during the course of this illness, excessive dreaming occurring also in those who were accustomed to dreamless sleep.

The dream content was usually fanciful and absurd; it was always vivid and in some instances of a nightmarish nature. This tendency to nightmares was more marked in children, who would wake up screaming in terror, and who would not thereafter stay in their room alone.

The projection of the dream into the first ten minutes or so of waking was found in six cases. The patients were conscious they were in bed in their own room, but around the bed, and peopling the room were the creatures and persons of their dream,
whom they were able to see and hear and to whom they could speak. Full return to reality took about ten minutes to take place the process being gradual with the vision fading slowly, rather in the manner of the Cheshire cat.

Progress of the disease in cases of abrupt onset:

In the majority of these cases the symptoms began to abate from the third or fourth day following the onset and by the end of a week from the onset the patient began to feel that life was worth living again, although minor degrees of headache and myalgic pains and the liability to waves of dizziness persisted usually for several weeks further, as did paraesthesias and muscle cramps.

No serious motor dysfunction was observed and the patients returned to work two to three weeks following the onset in these milder cases, although they had to take things very quietly for another month or more as easy fatigue ability was the rule.

In a smaller number of cases the disease had a more protracted course. The acute symptoms diminished in intensity, and the febrile patients usually became afebrile by the third or fourth day, with episodes of low grade fever recurring for a day or two at a time, during the subsequent month.

The symptoms and signs in these cases where the onset was abrupt, and the disease followed a more protracted course than in the majority, were similar in the later stages to those seen in the more severe cases of insidious onset.
Symptoms and Signs in cases of insidious onset:

In this mode of onset the patients complained that for a period which varied up to six weeks prior to the time they consulted me, they had been feeling off colour and that they had experienced some or all of the following symptoms in varying degrees and at varying times.

(1) **Excessive tiredness**, and finding their normal work a burden to them.

(2) **Sweatings**, which were often sudden in appearance and unrelated to work being done, or the ambient temperature.

(3) **Difficulty in keeping warm**; cold hands and feet.

(4) **Bouts of dizziness and unsteadiness**.

(5) **Intermittent headaches** and **neuralgic pains** which were most common around the eye and fairly frequently referred posteriorly to the ear and down the neck.

(6) **Insomnia**.

(7) Some loss in **clarity of thought** and in **concentration**.

(8) **Aching in the legs and back** of an intermittent nature, a feeling of heaviness in the legs, and pins and needles in the hands and feet.

(9) **A hard dry cough**, or **hoarseness** or **partial aphonia**.

(10) **Blurred vision**.

These patients usually stated they thought they had got a "chill" or "a touch of 'flu", which had not affected them to any extent and which they proposed to work off. The symptoms often did ease off after a few days, only to appear again, and the reason they eventually consulted me in most instances was that they had felt their symptoms were persisting too long.

In a few cases they had been frightened by the feeling of loss
of power in their legs, which had manifested itself by limiting the distance they could walk. One such case walked about a mile to visit a friend, and on the way back they found it very difficult to keep the legs moving and got home only after stopping many times, and being almost unable to bring one leg past the other by the time the home was reached.

Another case customarily took a can of tea and some sandwiches across a field each afternoon to where her husband was working, and thought nothing of the wall. Five weeks after developing what she had thought was a short cold, which had left her tired and liable to attacks of dizziness, she found walking was getting very tiring, and on going across the field with the customary tea and sandwiches she was unpleasantly surprised to find she had great difficulty in reaching the place her husband was working and further difficulty in getting home - her legs, as she said, "gave out."

On examination:

The general appearance was one of tiredness and anxiety. The colour was pale, and the skin felt cold, moist, and rather greasy. A skin eruption of recent development and resembling acne was seen on the chin and around the mouth in several adult female cases.

The temperature was usually subnormal, but in three cases it was raised to 99°F. The pulse varied from 80 - 90/min. in the majority of cases, but in several instances the rate was as high as 120/min.

The tongue, as in the cases of acute onset, was always coated but to a lesser extent, and at this later stage the coat was often a milk white in colour and less dry than in cases of
acute onset. There was rarely much inflammation in the nasopharynx, but the inflammatory reaction in the larynx and trachea was sufficient to produce laryngitis in some cases, and an irritating spasmodic cough, without much sputum production, in others.

There was no evidence of involvement of the bronchi or the lungs in these cases.

The Abdomen:

As in the cases where the onset was acute, small plaques were found in the muscles of the abdominal wall, which were tender to palpation and gave a feeling of grittiness to the touch.

The costal liver margin and the spleen were tender to palpation, and in three cases the spleen was considered to be enlarged. Tenderness was usual on deep palpation in the right iliac fossa, which, as in the cases of acute onset, was found to extend down over the inguinal ligament and distal to the saphenous opening.

Constipation was a commonplace finding.

Blood Picture:

The alteration in the blood picture that has been described previously, was found in a higher proportion of these cases, than in cases of abrupt onset. In two cases the picture was considered very suggestive of glandular fever, although the Paul Bunnell test was negative. Further films, however, taken a fortnight later in these two cases showed only the relative lymphocytosis and eosinophilia, with morphological changes in the lymphocytes, which were seen in other cases of this disease.
Lymph Glands:

Tender enlargement of glands in the cervical chain and, to a lesser extent, in the inguinal saphenous and axillary groups was noted, as in cases where the onset was abrupt. The degree of tenderness and enlargement was, however, less marked than in cases of abrupt onset.

The urinary system was unaffected, and no skin rashes developed, except for the acne-like rash, that developed on the face, in several female cases, which has already been mentioned.

Blurred vision, which was considered worst for several hours after rising, was a constant complaint as it was in the more severe cases of abrupt onset.

A minor degree of conjunctivitis, with the formation of phlyctenules was seen in most of these patients.

Joints and Muscles:

Joint pains were noted in some of these cases of insidious onset; joints that were painful in various cases included the knee joint, the ankle, elbow, wrist, metacarpophalangeal and interphalangeal joints. In two cases bilateral hydorarthrosis of the knee joints occurred, with slow resolution.

A fairly frequent complaint was a feeling of tightness or distension in the hand, with aching in the metacarpophalangeal and interphalangeal joints. This was associated with fusiform swellings around the interphalangeal joints in some instances. In three cases, loss of 40° of extension occurred at the proximal interphalangeal joint. The skin over the fingers in these instances appeared taut, of rather a cyanosed colour, shiny, and felt cold.
Muscles:

A dull but persistent acheing was a feature of the myalgia experienced in these cases of insidious onset. The lower limb was usually affected to the greatest extent, the commonest sites for complaints of pain being in the calf muscles and the flexors, abductors and adductors of the thigh. Myalgia pain was also found in the back, the shoulders, the neck and the upper limbs, but this was not so severe as in the acute stage of the abrupt onset. Palpation of the muscles tended to trigger off an attack of cramp in the muscle palpated, although in the muscles of the lower limb cramps were in any case of frequent spontaneous occurrence.

Hyperaesthesia of the skin overlying the aching muscles was commonly noted, but not to the same degree of intensity as that found in cases of abrupt onset.
Neurological signs and symptoms encountered in cases of insidious onset and in the later stages of cases of abrupt onset:

Neurological disturbances that were present included:

(1) Paraesthesiae.
(2) Hypoesthesiae and Hyperesthesiae.
(3) Impairment of taste and smell.
(4) Vertigo.
(5) Blurred vision.
(6) Loss of concentration, or depression.
(7) Poor recent memory, and diminished powers of abstract thought.
(8) Impairment of co-ordination and unsteadiness.
(9) General weakness.
(10) Inversion of the sleep rhythm.

The Cranial Nerves:

Impairment acuity of the sense of taste and smell was present in most cases and abnormal perception of various tastes and smells was also commonly found.

Visual acuity was considered to be impaired by some cases, but no objective evidence was found to support this complaint. Blurred vision, not due to refractive errors, was commonly found, as was diplopia which was usually elicited on upward and lateral gaze. No gross weakness of the extrinsic muscles of the eye was found.

Pupils: These were frequently sluggish in their reaction to light and accommodation, and in two cases a dilated fixed pupil, with ptosis of the lid occurred unilaterally. There was no accompanying squint.

Neuralgic pain was commonly complained of, the site of the pain frequently being around the eye and cheek, extending back
to the ear and down the neck, earache and toothache being the focal complaints.

**Unilateral facial paralysis** occurred in two cases.

**Diminished auditory acuity** occurred in two cases and was associated with a severe degree of **vertigo**. **Hyperacusis** was a common but transient phenomenon. **Vertigo** developed to a greater or lesser extent in all **severe** cases and persisted for a period of many months in three cases.

**Nystagmus** was present in not more than half a dozen cases, it was usually associated with severe vertigo, and was lateral in form, and transient in nature.

**Hoarseness and recurrent partial or complete aphonia** occurred in three cases. In one of these cases, examination of the oropharynx and larynx by an E.N.T. consultant showed no evidence of a local lesion responsible for the condition and examination of the other two by myself gave a similar negative finding.

**Motor Dysfunctions:**

**General muscular weakness** was a frequent complaint. More specifically complaint was made that walking proved fatiguing and that the distance that **could** be walked was considerably limited, compared with their normal walking distance; similarly the powers of lifting and carrying were much limited.

Partial loss of power in individual muscles was found in 30 patients. The muscles most frequently affected were tibialis anteriors, the flexors, abductors and adductors of the thigh, the deltoid, and the interosseus and hypothenar muscles of the hand. Atrophy of muscles was not a frequent occurrence, but was noted in 8 cases. The dorsal interossei of the hand,
notably the 4th, and the hypothenar muscles were most affected, but the process proved reversible in most of these instances recovery of power and substance being complete in six months.

In one case partial atrophy of the affected muscles in the leg has now been present for two and a half years.

In only one case, however, was the partial loss of muscular power persistent or disabling enough to interfere with the return to normal work after an initial period of recovery - which, however, was a year in two cases.

Alterations in speech were noted in four cases, the voice becoming flat and monotonous in two cases, nasal in one case and jerky in the fourth.

Nominal aphasia developed to a marked degree in two cases, and difficulty in finding the right word, especially the name of a person, was encountered in many instances.

Ataxia was found in varying degree in cases showing other neurological signs. Romberg's test was commonly positive in these cases. Four of these patients had falls as a result of the unsteadiness. In three other cases falls were due apparently to abrupt loss of consciousness rather than unsteadiness. One man fell suddenly at work lacerating his head on a brick, another fell without warning in a 'bus queue, and a third was similarly affected, but at home.

The period of unconsciousness varied from five minutes to half an hour. In the first two cases scalp and facial lacerations occurred. There was no clinical evidence of any epileptiform tendency in any case, and the E.E.G. was normal, except in the first case, which displayed the abnormal activity in the occipital leads which has been mentioned earlier.
Tremor, which was accentuated by doing purposeful movements, was intermittently present in about half the cases showing other neurological signs, and usually disappeared after the passage of several months, but remains intermittently present in two cases nearly two years from the onset.

Co-ordination.

This was impaired in all cases showing neurological disturbances and was sometimes the main abnormality.

Breakage of crockery showed a marked rise in incidence in households, the housewife's complaint being that the plate, or other object being held, had hit the floor before she was aware she had dropped it.

Other evidence of inco-ordination and impaired judgment of distance was given by the frequency with which familiar actions, such as pouring tea into a cup, or walking through a doorway, were poorly performed.

Frequently it was found that at the first attempt, the tea would go into the saucer or on the table, while bumping into the frame of the doorway when passing through was a common happening; occasionally the collision was severe enough to produce bruising.

Reflexes.

A variable reflex state was found during the course of the illness.

In the acute stage in cases of abrupt onset, the reflexes, both superficial and deep, were normal or diminished. In the later stages, in cases where the illness was protracted, the reflexes were normal in some cases, but in the larger number, the tendon reflexes became brisk, with knee and ankle clonus occasionally found. The abdominal reflex was absent or diminished in these cases and the plantar reflex normal. In two cases the
tendon reflexes were sluggish, clonus could not be elicited and the abdominal reflexes were absent, but a marked unilateral plantar extensor response was present. The response obtained was immediate and brisk, and flexion at the knee and the hip occurred. This response persisted for a period of six and eight weeks respectively.

Reflexes in cases of insidious onset were either normal or brisk, and the abdominal reflex was often sluggish or absent.

**Pupils.**

Reaction to light and accommodation was often sluggish in protracted cases of abrupt onset, and also in some cases of insidious onset.
Sensory Disturbances:

Subjective sensory disturbances were complained of by most cases. These included the following abnormal sensations:

(1) Tingling, or "pins and needles."

(2) Numbness, and a feeling of heaviness in a limb.

(3) Pressure feeling on the scalp, as if wearing a tight skull cap.

(4) Feeling as of drops of cold water trickling down the affected area.

(5) Feeling as of insects creeping over the skin.

(6) Abnormal perception of small and taste, and an abnormal feel in the mouth of a normally familiar article of diet.

Of these disturbances of sensation, pins and needles and numbness, affecting various areas, often the extremities, were the most frequent cause of complaint, and often co-existed in time in the same patient.

The feeling of pressure on the scalp was also common, as was the abnormal perception of taste and smell. Abnormal perception of the texture of foodstuffs in the mouth was less common, as was the feeling of cold drops of water trickling over an isolated area of skin. The feeling as of insects creeping over the skin was uncommon, occurring in only six patients and in these cases the sensation was confined to the extremities.
Objective Sensory Disturbances:

Objective evidence of sensory disturbance was found to be present in a much smaller proportion of cases than might have been suggested by the numbers of patients complaining of subjective sensory disturbances.

Objective sensory disturbances that were found included:

1. Hyperaesthesia.
2. Hypoesthesia.
3. Hypoalgesia.
4. Impairment of position sense.
5. Impairment of joint sense.
6. Impairment of vibration sense.

Hyperaesthesia was observed in the skin overlying the painful muscles during the acute myalgic phase, and to a lesser extent was sometimes observed over the more chronically aching muscles of cases of insidious onset. In the acute phase light touch on the skin over the affected muscle was resented; the lower limbs were the sites most commonly affected by this phenomenon.

Hypoesthesia & Hypoalgesia:

Diminished sensitivity to light touch with cotton wool and to pin prick was present in 18 cases, of patchy distribution below various levels. In 4 cases the diminished sensitivity was confined to the ulnar distribution of the hand, and in 2 cases pressure pain was also diminished in the same area as diminished sensitivity to light touch and pin prick was found.

Position sense and joint sense were impaired in not more than 20 cases and a large proportion of those showing diminished sensitivity to touch and pin prick were also present in this group.
Romberg's test was positive in most of the cases showing evidence of impairment of position or joint sense.

Impairment of vibration sense was found in two cases only, but not all cases were tested for vibration sense.

Disturbances pertaining to the Autonomic Nervous System:

Abnormal coldness in the extremities.

Complaints that the hands and feet felt cold and that general susceptibility to cold weather was more marked, were of frequent occurrence in cases where the illness was more protracted. In the majority of patients making this complaint, objective evidence that the skin temperature was lower than normal in the extremities was given by the feeling of cold gained by the presumptively normal examining hand. Instrumental evidence was lacking as a thermo-couple for measuring skin temperature was not available.

Sweating.

Apart from the drenching nocturnal sweatings that were common in the acute phase of the cases of abrupt onset sweating was readily provoked, or of spontaneous occurrence, during the course of the more protracted illnesses.

Eyes.

Sluggish pupillary reactions have already been mentioned as being seen in many cases in whom the illness was more protracted.
Mental State:

The mental state was commonly affected in this illness. Such affects included:-

1. Depression.
2. Loss of energy.
3. Retardation of thought processes.
4. Impairment of concentration.
5. Impairment of memory.
6. Disorders of sleep.

**Depression.**

Depressive tendencies, often with weeping, appeared early in the course of the disease and were a persistent feature of it. In general, the depression engendered was not severe enough to require treatment other than could be given at home, but four cases were of a greater degree of severity and required psychiatric attention as in-patients. One woman in her middle thirties, with a previous history of instability, developed a severe depression very rapidly and committed suicide.

**Loss of Energy.**

Energy loss was complained of in all but the lightest cases, and, in varying degree of severity, proved a persistent sequel to the infection.

**Retardation of Thought Processes.**

Work involving abstract thought was found to be much more difficult to perform than prior to the illness in all who had protracted illnesses or recurrences of the illness. This is illustrated by two cases: **Case 1** - a secondary schoolgirl was
due, several months later, to sit examinations for distinction in three subjects, having already passed her school leaving examinations at ordinary level the year before.

During the convalescent stage of her illness she attempted to keep up with the work she would ordinarily have been doing at school, but found that she could not think with her normal clarity. Her concentration was also impaired as was her immediate retention. She had to force herself to work, which was unusual for her, and was readily distracted. On reading a page she would find that she had little recollection, by the time she reached the end of the page, of what the beginning of the page was about.

These symptoms, coupled with a labile emotional state and outbursts of weeping, proved remarkably persistent and eventually forced her to give up the idea of sitting the examinations.

Case 2 - this case was a middle-aged business woman. She, amongst other features of the disease, developed depression with outbursts of weeping, and retardation of thought, with impairment of concentration and of the capacity of retention. She had bookkeeping to do at home, as she ran a home club, and she attempted to keep the bookkeeping up-to-date from the early stages of the illness. She found, however, that the arithmetic involved, which had never troubled her before, proved difficult of execution and she was much slower in her calculations. Orders that had been memorised to be written down at home were forgotten and had to be retaken, and subsequently she found she had to note full details immediately or they would not be remembered.
In cases where the illness was protracted, it was found that the 7 from 100, or serial seven, test was poorly performed in many instances and it was rare to find it performed without at least one error. The level of intelligence in these people appeared normal, and most of them would have had no difficulty with simple addition or subtraction. They began the test confidently, but many of them after successfully subtracting twice, got bogged down, and even after further attempts rarely got past three or four successful subtractions.

These patients were unpleasantly surprised at their lack of success in the test, and would save face by saying that they were never much good at arithmetic at school, anyway, or that they could ordinarily have done it easily, but that since the illness they couldn't think straight.

Impairment of concentration:

Persistence in an activity was found difficult to maintain and these cases were also readily distracted from what they were doing. Reading was a case in point; a magazine or paper would be taken up, read at random for a few minutes, and then put down, with or without an excuse, and the patient would be able to give only the vaguest idea of what he had read.

Persons who ordinarily took pleasure in solving the daily crossword puzzle found, for a period during and subsequent to their illness, that the concentration, abstract thought and persistence of effort required to do this was altogether too much for them.

Female patients who ordinarily took pleasure in knitting and tried to pass the time doing some knitting, in the later stages of the illness, found that errors frequently crept into their work, which then had to be taken down past the error;
as the errors recurred despite attempts at further concentration on the pattern, and the knitting had to come down each time, this activity was usually given up in disgust, and sometimes in tears.

**Impairment of memory, recent retention and recall:**

Severe memory defect occurred in two cases only during or subsequent to this illness, both being cases of nominal aphasia. One recovered from this defect over a period of several months, the other dying a year or so later after a terminal illness lasting three weeks, in which sudden deterioration had occurred at the beginning of the period of three weeks, and death was found to be due to numerous small haemorrhages in the mid-brain.

Further details of this case were given in the section on morbid anatomy.

It was found, however, that less severe disturbances of the memory were common in the later stages of this illness or subsequent to the return of the patient to usual activities.

It was found by these people that items of work to be done, or purchases to be made, or other activities to be undertaken, had to be listed and consulted as occasion arose, as memorising these details proved unreliable. It was commonly complained that the memory was now like a sieve.

One such case, a housewife, duly made out a shopping list and went into the town, forgetting to take her list. She went into a shop, looked for her shopping list, found she did not have it, and without it was totally unable to recall what she had come for, and had to abandon shopping for that day.

Names of persons, even of those reasonably well known, to the patient often enough could not be recalled when wanted, with
embarrassing results at times. The name wanted would usually be remembered perhaps half an hour after the encounter.

Disorders of Sleep:

Inversion of the sleep rhythm was commonly noted. In many cases this disorder disappeared shortly after the cessation of the acute symptoms in the less severe forms of the illness, but where the illness was more protracted, a feeling of excessive tiredness and somnolence persisted by day, and at night, after a short period of deep sleep, restlessness persisted until the morning.

In children, nightmares and night terrors commonly occurred, and in children of 2 - 5 years, and, in a few instances, of up to 10 years, fear of being alone at night developed to such an extent that they often would not stay in their own room alone at night.

In adults, dreaming was a constant feature of the short lived snatches of sleep. Hallucinations occurred on waking in six cases, the hallucinatory episode not lasting more than 10 minutes, and the liability to the development of these episodes usually lasted only over a period of three or four days. The hallucinatory episodes were usually found towards the latter part of the first week from the onset in cases of abrupt onset.

Behaviour disorders in children:

Mention has already been made above of night terrors in children and the subsequent fear of being alone at night. This fear was calmed only by bringing the child's cot or bed into the parents' room, and in several cases many months elapsed before the fear of being alone at night had diminished.
sufficiently for the child to return to his or her room to sleep alone.

Temper tantrums were of frequent occurrence in younger children following the illness, and in older children unsociability and lack of attention and effort at school resulted in a marked lowering of their standards at school. Weeping was common for the slightest check on behaviour in a small number of children in the 5 to 12 age group. In a considerable proportion of children who developed the illness, complaints were made by the parents that the child had become difficult to manage following the infection. Traits that tended to develop, in varying degree and combination, included:

1. Nocturnal enuresis, in those previously unaffected in this manner.

2. Disobedience in the school and in the home.

3. Unmotivated acts of aggression, directed at other children, and wilful damage to property.

4. Unsociability.

5. Facile lying in children previously given to a normal degree of truthfulness.

6. Rapid changes of mood and readily produced weeping.

In several children these traits persisted for longer than 18 months, but in the remainder affected in this way gradual return to their normal pre-infective behaviour took place over several months.
Complications:

Recurrences or Relapses.

The most prominent complication was the development of recurrences of the symptoms of the original attack in a number of patients. At least 20% of cases were affected this way, and probably more, as the patients knew there was no specific therapy, and if the return attack was not too severe, a further number of patients would have endured it, with perhaps a couple of days in bed, without sending for me. I found this to be true in several instances when visiting a household to see another member, ill with another complaint, on inquiring into the health of the member of the household who previously had been infected by the epidemic disease, and finding that a recurrence of symptoms had in fact occurred.

The recurrence of symptoms was usually of short duration, and the attack milder than in the first occurrence. A low grade fever was sometimes present, but the patients were usually afebrile during the recurrence. In a few instances, the original attack was mild and the subsequent episode or episodes much more severe.

In 12 cases the liability to recurrences of symptoms has persisted over periods varying from 18 months, to two and a half years, with symptoms which include headache, dizziness, extreme tiredness, depression and myalgic pain, recurring at varying intervals up to 6 months.

Respiratory Complications.

The nasopharynx, larynx and trachea were commonly involved in a mild inflammatory reaction, in the early stages of the illness. Involvement of the lungs was rare, although one case
developed a frank lobar pneumonia, shortly after the onset, pneumococci being recovered from his sputum. Three cases of bronchitis occurred.

Myocarditis.

The heart rate was accelerated during the course of the illness, and the rate was raised out of proportion to any pyrexia that might be present.

In three cases a persistent tachycardia developed; the rate varied from 12- to 150 per minute, and dyspnoea on slight effort, cyanosis of the lips and oedema of the ankles appeared. The heart sounds were soft, and the blood pressure was lowered. The heart was not enlarged. These effects persisted for over 12 months in these cases, and in a fourth case, similarly but less severely affected, recovery took place in four months.

Blood Pressure.

A persistent rise in the level of the blood pressure occurred during and subsequent to the illness in four cases. The raised levels varied between 180 - 220 mm.Hg. systolic, and 110 - 130 mm.Hg. diastolic, and a return to a lower blood pressure occurred slowly over a period of many months.

Jaundice.

Jaundice occurred in 5 cases, towards the end of a week from the onset of symptoms, and was accompanied by marked tenderness of the liver and spleen. The jaundice was obstructive in type, and resolved in 6 or 7 days.

Venous Thrombosis.

Thrombosis of the deep femoral vein occurred in two women in their sixties, 8 and 10 days from the time of onset. In one case, the thrombosis was bilateral.

Orchitis was a complication in three cases.
Two types of rashes occurred:

1. A maculo papular rash, resembling that seen in rubella.
2. An urticarial type of rash.

Five children were affected by the maculo papular rash which was centripital in distribution, and caused considerable itching. The rash disappeared in 24 to 48 hours, without residual staining, or desquamation.

Three children and four adults developed urticarial wheals. In two of the adults the lesions were widespread and persistent; as older lesions cleared, new lesions appeared elsewhere, and this tendency to the production of urticarial lesions persisted in these two cases for five months. In the remainder, the tendency to produce urticarial lesions disappeared in less than a fortnight.

Mental changes and neurological manifestations.

The psychogenic phenomena, and the neurological manifestations, which were largely subjective, consistently complicated the course of the illness and the post infective state in the more severe cases, and have already been mentioned.

Sequelae:

Psychogenic disturbances were the most commonly met and disabling sequel to the illness, and they persisted over periods of many months in the more severely affected cases. The types of disturbances encountered have already been described. A further sequel to contracting the disease was the liability experienced by a number of cases to recurrence of symptoms of the illness over a prolonged period.
Diagnosis.

The diagnosis was made on clinical grounds in the absence of any specific diagnostic test and the failure to isolate a causative organism.

In the milder cases the clinical picture was possibly not sufficiently definite to warrant a diagnosis, apart from the occurrence of these cases in association with cases of greater severity during the epidemic.

In the more severe cases a definite pattern began to emerge, which provided evidence of the presence of a generalised infection, which involved chiefly the reticulo endothelial system and the central nervous system.

Diagnosis of this disease was made when the following features were present in the clinical picture:-

1. Dizziness.
2. Headache and extreme lassitude.
3. Drowsiness and lethargy by day and restlessness at night.
4. Thickly coated tongue, dry mouth, sore throat and dry cough.
5. Blurred vision, diplopia on upward and lateral gaze, and a mild conjunctival reaction.
6. Spontaneous severe pain in the back of the neck and the lower limbs, and frequently also in the back and upper limbs.
7. Muscle tenderness and some loss in muscle power.
8. Paraesthesiae and some degree of sensory impairment.
9. Tender enlargement of lymph glands in the neck, inguinal region and axillae.
10. Splenic and hepatic tenderness and subcostal pain.
11. Depression, with feelings of foreboding, and a labile emotional state.
12. Low grade fever, or subnormal temperature, and mild tachycardia.
An abrupt mode of onset in which the above features appeared rapidly, following a short initial period lasting a few hours to 2 or 3 days, during which the main features were dizziness, headache, stiff neck and muscular pains, and an insidious mode of onset in which the above features appeared gradually over a period of several weeks of steadily increasing malaise, proved to be definite characteristics of the disease, and as such, were of use in considering the diagnosis.

**Differential Diagnosis.**

Illnesses which had to be considered in the differential diagnosis included:-

1. Glandular fever.
2. Influenza.
3. Poliomyelitis.
4. Illness caused by the adenoviruses.
5. Coxsackie disease.
6. Illness due to ECHO viruses; a septic meningitis.
7. Psittacosis.
8. Q Fever, mumps, toxoplasmosis.
9. Viral encephalitides and encephalitis lethargica.

**Glandular Fever.** was initially suspected in view of the enlarged lymph glands that were characteristic of the disease, and the presence of a sore throat. The Paul Bunnell test was consistently negative, however, and the blood picture, although showing a relative lymphocytosis and eosinophilia, with morphological changes in the lymphocytes, in 30% of cases, developed a picture thought to be characteristic of glandular fever in only two cases.

**Influenza.**

The initial symptoms of the illness were not dissimilar
from those seen at the onset of influenza but could be distinguished by the greater degree of weakness and prostration in the severe cases of the present illness than that usually encountered in influenza, considered in relation to the low degree of fever usually present, and the accelerated pulse. The reticulo endothelial involvement in the disease under study was a further distinguishing factor. Serological studies also proved negative for Influenza A, B and C, using acute and convalescent serum samples for the complement fixation tests.

**Poliomyelitis.**

Headache, pain and stiffness in the back of the neck, and acute muscle pain in the back and the lower limbs, associated with a febrile state, which were common manifestations of the present illness, made it necessary to exclude poliomyelitis as the cause of the illness.

In the present illness, however, although the back of the neck was tender and stiff, there was no true rigidity and Kernig's sign was negative. In the later progress of the disease sensory manifestations were frequently present, and where muscle weakness occurred muscle wasting of the lower motor neurone type did not ensue. The reflexes initially normal or diminished in the illness under discussion later became brisk, and were never absent, in contrast to the loss or partial loss of reflex activity in regions of motor weakness in poliomyelitis.

A further point in differentiating the two illnesses was the characteristic reticulo endothelial response in the present illness.

Laboratory evidence was also of service in differentiating
the two diseases. The cerebro spinal fluid in the cases examined in the present illness was normal in all respects, compared with the changes in the spinal fluid usually found in poliomyelitis. Furthermore, the virus of poliomyelitis was not grown in tissue culture following inoculation of the tissue cultures with suitable material obtained from the cases of the present illness, when successful isolation of poliovirus had been obtained, using similar methods, in cases of typical poliomyelitis.

The Adenoviruses.

Infection with the A.P.C. group of viruses produced a clinical picture somewhat similar to that seen in some of the milder cases of the present illness, but was distinguished by the greater degree of emphasis in the adenovirus illness on respiratory and conjunctival symptoms; the protracted and recurrent nature of the more severe cases of the present illness, as well as the mental and neurological findings in these cases, were further distinguishing features of the present illness, compared with illness due to the adenoviruses. Serological examination in more than 50 cases also excluded the possibility that the disease was due to a member of this group. Adenoviruses were also not grown in tissue culture using methods which were successful in isolating these viruses from specimens from cases giving a more typical picture of adenovirus infection.

Coxsackie and ECHO virus infections.

The presence of acute muscular pain and spasm as characteristic features of this illness suggested the possibility that the disease was due to infection with a
Coxsackie virus, especially in view of the protracted course, with recurrences of symptoms that marked the more severe cases.

Against this possibility was the lack of any meningeal reaction in the cerebro spinal fluid examined, and also the failure to produce any reaction in suckling mice by inoculations with suitably treated faecal suspensions and throat washings obtained from patients with the present disease.

The presence of the neurological and psychogenic phenomena of the present illness was also not indicative of Coxsackie disease.

**ECHO Viruses.**

Outbreaks of illness due to members of the ECHO virus group have been reported with some frequency recently. One such report (Rotem 1957) concerned the first 100 cases of aseptic meningitis admitted to the Leicester Isolation Hospital in 1956.

The symptoms and signs in this outbreak included pyrexia, headache, neck rigidity, back stiffness, vomiting, maculo papular rash, photophobia, drowsiness, abdominal pains, sore throat, enlarged lymph glands and constipation. There were no abnormal neurological signs in any of the patients, no hallucinations, disorientation or unconsciousness, but recovery was slow and tiredness and mild depression were common.

Similar outbreaks occurred in Belgium between June and November, 1956, with large numbers of persons affected (Nihoul & Quersin-Thiry, 1957). The manifestations were similar to those described by Rotem with the additional feature of occasional conjunctivitis described. A relapsing tendency was described as being a notable feature of the disease.
No mortality occurred in these outbreaks.

Signs of meningeal involvement were prominent features of the outbreaks and investigation of the cerebro spinal fluid characteristically showed a very pronounced pleocytosis, with cell counts ranging from 50 to more than 3,000 cells per c/mm.

Virus isolation was easily accomplished, the virus strains being isolated in tissue culture using monkey kidney. These viruses were shown to be differing but immunologically related strains of ECHO virus group 9, to which the patients showed a rising titre of neutralising antibodies from the acute to the convalescent sera.

The clinical picture in the present illness resembled in a number of respects the picture in illnesses ascribed to viruses of the ECHO group, but the cardinal point of meningeal irritation was lacking both clinically and as shown in the cerebro spinal fluid where no pleocytosis was found in any specimen examined. ECHO viruses were also not isolated from a large number of specimens inoculated into tissue cultures, with one exception. The isolation of an ECHO virus in one case out of the number examined was considered by the Virus Reference Laboratory, Colindale, to be a random finding of no aetiological significance.

A further differentiation from the clinical features ascribed to the ECHO virus infections was the protracted course of the present illness in a number of the severe cases, with the perseverance of subjective neurological phenomena, with evidence of some objective impairment, both sensory and motor, and the prolonged psychogenic sequelae seen in some cases.

The lack of a meningeal reaction, and the normal cerebro
spinal fluid, were arguments also against the disease being caused by the virus of acute lymphocytic choriomeningitis. 

Psittacosis.

The coincidence of a disease, with a heavy mortality affecting budgerigars during the epidemic period of the present disease required that psittacosis should be considered as a possible cause of the human and avian disease, especially in view of the upper respiratory involvement and general prostration found in cases of the human disease, and the frequently protracted course of the illness.

Involvement of the lungs was not found, however, nor were the skin manifestations of psittacosis seen.

Serological tests were, moreover, negative for psittacosis and the lympho-granuloma venereum group of viruses.

Other serological tests excluded Q Fever, Mumps and toxoplasmosis as possible causes of the illness.

Louping-ill was considered as a possible cause, in a country district near the Border, where there is extensive sheep farming, especially on the hill farms. There was, however, no evidence of any undue preponderance of the infection amongst farm workers, and the winter onset of the epidemic was an argument against the possibility of the disease being a virus encephalitis transmitted by insect vectors.

The normal cerebro spinal fluid was a further point against the possibility of the present disease being caused by such an infection.

Encephalitis Lethargica.

The more severe cases of the disease bore some resemblance to the clinical picture ascribed to encephalitis lethargica but
in a very much lower degree, while the case mortality was nil and the subsequent invalidism was negligible in comparison.

Nevertheless in the case of one woman residual changes are present, after a period of 21 months, consisting of weakness of hemiplegic distribution, flexion of the bodily stance, a shuffling gait, and an intermittent rhythmic tremor of the hand on the affected side. The face is expressionless and the skin had become oily, with the development of an acne-like rash.

She has fallen several times, the affected leg giving way without warning, and she remains physically unfit for anything but light housework.

References:
Treatment.

1. Preventive Measures.

Preventive measures that were advised were those applicable to infectious diseases in general. Patients were advised to avoid crowds as much as possible, especially in cinemas, and to avoid getting excessively fatigued or chilled, as in several instances a severe attack appeared to be precipitated by excessive physical exertion, with sweating and subsequent chilling. Cases were isolated and sent to bed as they occurred, and were advised to see no visitors for a week. Soiled articles were disinfected before washing, or burnt, and frequent washing of the hands was advocated for those attending the patient; masks should have been worn by those attending the patient, to avoid direct droplet infection, but this unfortunately was a counsel of perfection. As the causal organism of the disease was unknown the question of a vaccine did not arise.

2. Palliative Measures.

No specific cure for the disease was found. From the nature of the complaint, antibiotics and chemotherapeutic agents were considered unlikely to be of any assistance, which proved to be the case, with the proviso that, in several cases in which tetracycline was tried, the symptoms appeared to be ameliorated temporarily, although the disease was not terminated thereby, or the liability to recurrence suppressed. Penicillin was used in cases of secondary infection of the throat due to susceptible organisms and in the few cases that occurred of bronchitis and the single pneumonia. Treatment with drugs resolved itself into attempts to obtain
symptomatic relief.

Compound tablets of aspirin, phenacetin and codeine proved effective in alleviating muscular pain in most instances, in a dosage of two tablets every three or four hours, although some patients, who also were experiencing nausea, could not tolerate them, and in a few cases of acute muscle spasm their action proved negligible and had to be supplemented by pethidine or morphine, at the height of the pain.

Promethazine or "Phenergan" was found to be useful in many cases. It was first instituted in cases where an urticarial type of skin manifestation had appeared and had been tried when several other anti-histamines had been tried, including mepyramine maleate, and found of little value. A slow but steady improvement in the urticarial lesions occurred with Promethazine, 25mgms. twice daily, and as a side effect, one of the patients, who was also experiencing severe vertigo and waves of nausse, was pleased to say that the vertigo and nausea had also eased. Subsequently I used Promethazine in all cases complaining of dizziness or nausea, with variable effects, but in general, some degree of amelioration of these symptoms occurred.

General Management.

Bed rest was the most important factor. In the mild cases a week was often sufficient, but in the severe cases longer periods were required, one case requiring bed rest for three months. Too early mobilisation resulted in setbacks and recrudescence of symptoms in the more severe cases. The room was kept warm and well ventilated and the bed clothes light. Changes of night clothes were frequently needed because of the frequency of drenching sweatings, and sponging also proved
comforting. The diet for the first few days was often fluids only, glucose in fruit drinks being given liberally, as the patient was thirsty but had no appetite. The aberrations of taste and smell also played a part in the dislike of food.

As solid food was added to the diet it was found best, therefore, to exclude any article of diet which had a pronounced taste or smell, as the taste or smell might prove unpleasant enough to induce nausea. Constipation was common and had to be treated. The oily preparations were not well tolerated and such preparations as Senokot and Veracolate were found useful.

Insomnia and general restlessness at night had to be treated in some of the more severe cases and the administration of compound aspirin tablets, in conjunction with three grains of sodium amytal or seconal was usually sufficient to give a reasonably quiet night, although a marked tendency to dream was present. A dry irritating cough that came on towards evening was often present and responded to treatment with syrup codeine phosphate as indicated.

Convalescence.

Convalescence was slow in the more severe cases. In the milder cases, patients were back to school or to work in less than a month, but a number of these patients complained of excessive tiredness, difficulty in concentration, and headaches for several months after going back to work.

In the more severe cases recovery was more protracted; in both the severe and the mild cases recurrences of symptoms complicated the convalescent and the post convalescent period. Weight loss in children, of half a stone and sometimes more,
was seen in some cases, over a period of 6 - 8 weeks during the acute and convalescent stages of the illness.

The presence of psychological symptoms was fairly general in the convalescent period; most often the symptoms were depressive in nature, with features of anxiety present. Reassurance coupled with sodium amytal gr. 1 thrice daily was usually sufficient treatment and the symptoms gradually disappeared. In several cases, however, the depressive tendencies were very severe and required in-patient treatment in the psychiatric wards.

These cases responded fairly well to electro convulsive treatment. Several other patients required psychotherapy which, as their condition was not so severe, they received as out-patients.

Three children attended the child guidance clinic as they had developed behaviour disorders, and had become very backward at school following their illness. Similar but milder cases of psychogenic upset in children, following the illness, were treated at home without special psychiatric attention.
Prognosis.

The illness under study is one of variable duration, with a tendency to the appearance of recrudescences of symptoms in a significant proportion of cases, during the course of the illness.

The prognosis for life has been excellent. In the majority of cases the disease was mild, with little objective evidence of neurological involvement, and these cases recovered sufficiently to return to work within a month, with no objective evidence of residual neurological involvement.

In a small number of cases residual neurological involvement is still present many months from the onset, and the damage may be permanent.

Persistence of symptoms, such as excessive tiredness, intermittent pains in various sites, recurring headaches and waves of dizziness, lack of ambition, irritability and depressive tendencies, has been a marked feature of the post infective period, in a number of cases, and, in some, persists up to the present day.

The prognosis for this disease, therefore, is that it is excellent for life. Most persons affected by it can expect to recover completely, but in a few instances, permanent neurological involvement may result. All cases of a moderate to severe degree of intensity may expect to have persistence of the symptoms mentioned above, for a variable post infective period, and a proportion of cases will be affected by recrudescences of the disease.
Discussion.

W.N. Pickles (1939) in his book 'Epidemiology in a Country Practice' considers that nothing so disrupts orderly medical practice as the occurrence of an influenza epidemic. While agreeing with this dictum - with all the more feeling, as I try to complete this thesis in the midst of an influenza epidemic - I would suggest the acute and unfamiliar infectious disease, which appeared in my single handed country practice in 1955, and affected over 200 patients during the course of 7 months, falls little short of influenza in disrupting power.

During the early stages of the epidemic I recognised that the disease was not conforming to any familiar pattern and this recognition was forced upon me by the recurring picture seen in some of the more severe cases, which has been described earlier. If all the cases had been mild or relatively mild, the clinical features seen would have formed too vague a clinical picture for the emergence of a recognisable syndrome; the individual cases would then have been treated symptomatically and as the prognosis for the mild cases is in general full recovery in 3 or 4 weeks, the condition would have been ascribed, no doubt, to whatever infective disease the individual case bore most resemblance. That this was not done was due to the sign posting or spot lighting of the characteristic features of the disease by the more severe cases of the illness, which caused me to examine the milder cases of the disease with the picture seen in the more severe cases well fixed in my mind.

Having become epidemiologically minded, mistakes in diagnosis were made, and in some instances, the early manifestations of other diseases were ascribed to the epidemic disease, through
over enthusiasm on my part.

It is also possible that some of the milder cases in whom the full picture was not present may have been abortive attacks of other illnesses, although in the great majority of these milder cases serological tests were negative for the common infections.

One had also to remember that in the post-infective period, adenitis and minor symptoms of the disease often persisted for a considerable time, and that during this time other illnesses, such as the common cold, might occur. One had then to avoid the temptation to ascribe the episode to a recurrence of the original infection. It was found, moreover, that an extraneous infection such as the common cold, or, for instance, cystitis caused the reappearance of symptoms of the epidemic complaint in some cases that had been free of such symptoms for months.

When the general pattern of the disease, as it appeared in individual cases, was becoming reasonably clear, I sought help in identifying the complaint, as I could not identify it from my own knowledge or with the aid of text-books, from the clinical features I had found characteristic of the disease. I turned to the Public Health Laboratory for technical aid, and I would like to pay tribute to Dr. D. G. Davies, the Director of the Carlisle Laboratory, for his consistently helpful and supporting attitude and thank him for the large amount of laboratory work which was subsequently done.

Serological tests and bacterial examination of material supplied excluded the possibility of the disease being one of a number of illnesses for which it might be thought to have some resemblance. At the time of the epidemic tissue culture
facilities were not available in the Public Health Laboratory at Carlisle, but the Virus Reference Laboratory at Colindale undertook to examine a considerable number of faecal specimens and throat washings by tissue culture methods, at Dr. Davies' request, and they also examined over 50 serum samples for evidence of adenovirus infection; in both instances the results of the investigation were negative.

Examination of the cerebro spinal fluid showed that there were no abnormalities present in the samples examined. I would have liked a greater number of samples of spinal fluid examined but I was dependent on the hospitals for this as I did not think it justifiable to subject the patients to lumbar puncture in the home. In several instances, cases were sent to hospital for observation, as in their particular instances there was a certain similarity to poliomyelitis present. In these instances I requested that a diagnostic lumbar puncture be done, but was informed that it was not desirable to perform a lumbar puncture if there was a possibility that poliomyelitis might be present. In the end several samples of spinal fluid were obtained from patients under aseptic conditions at an out-patient clinic, through the kindness of a hospital colleague.

Haematological investigation excluded the likelihood of glandular fever being the cause of the epidemic in the absence of specific changes in the blood picture and the negative Paul Bunnell test.

Changes, not noted in connection with any specific disease, were present in 30% of the blood films examined. The white cell count was usually on the low side of normal, and in the 30% of cases in which the blood picture was abnormal there was a
relative lymphocytosis and an eosinophilia, with abnormal lymphocytes and occasional Turk cells present, of the type described as being present in various virus infections. The hematologist examining these films formed the opinion that these changes made a recognisable and characteristic picture, which was most commonly seen in blood films from the Dalston cases, but which he had also encountered in a few other blood films sent from cases occurring elsewhere in Cumberland and Westmorland; the accompanying history and clinical details of these cases showed much similarity to the clinical pictures seen in the Dalston outbreak.

This opinion, and the findings suggestive of a similar disease occurring in a few cases elsewhere, were interesting but not of value in establishing the diagnosis of the disease.

Laboratory investigations, therefore, failed to be of aid in establishing a diagnosis, although they provided presumptive evidence that the epidemic disease was not one of a number of diseases, for which serological and other tests were negative.

The diagnosis of the disease, therefore, had to be made on the epidemiological and clinical features present. Further medical opinion was therefore sought, and an epidemiologist on the staff of the Central Public Health Laboratory, London, came to Dalston to view the situation. He was shown a number of cases, most of whom were, unfortunately, from the point of view of diagnosis, in the convalescent stage, and he was given the history of the outbreak up to the time of his arrival. He came to the conclusion that an unusual infective disease was present in the district, which gave a clinical picture which he did not recognise, but which had some features in common
with clinical features described in two outbreaks of infection in America, where the causation was shown to be due to a member of the A.P.C. group of viruses, or adenoviruses. He advised laboratory investigation into the presence of the adenoviruses in cases of the present illness; this was done with the negative results already mentioned.

The Medical Officer of Health, Dr. K. J. Thomson, who has always been helpful and shown interest in the epidemic and sporadic disease in the Dalston practice, examined some of the cases with me, but like myself, he was unable to arrive at any firm diagnosis.

Perhaps because of a certain lack of liaison, lack of time or possible differences in personality, consultant medical opinion rather clearly showed disinterest in exploring the possibility that an unusual disease was afoot, an implication being that a hypothetical mountain was being erected on an imagined molehill, and that the cases could readily be explained on conventional grounds by a competent person.

I understand, however, since obscure illnesses have become respectable, following the outbreak of an obscure illness at the Royal Free group of hospitals, with subsequent reports and leading articles in the medical press, that such diagnoses are now made in certain instances by the consultant in question.

The mental sequelae of the condition, notably depression, caused me to call in consultant psychiatric opinion in a proportion of cases, several of whom had to have psychiatric treatment as in-patients.

The psychogenic sequelae of the present illness, including the behaviour disorders seen in some childish victims of the
disease, were considered affective disorders which were likely to regress with the remission or disappearance of the disease. The psychiatrist was interested in the condition, and was of much help to me in its investigation. He also later informed me that he was finding a few instances of similar psychogenic disturbance in his out-patient clinic both in Carlisle and West Cumberland; a history of an infective complaint prior to the psychogenic disturbance, with clinical features similar to those he had seen at Dalston was elicited from these patients.

In view of the mental disturbances found in a number of these patients he arranged for electro-encephalographic investigation in more than 20 instances, with the results given earlier, a non-specific but definite abnormality being found, in the tracings from the occipital leads in a considerable proportion of those examined.

One case in which the illness was protracted, with marked fluctuations of symptoms and signs, was referred by the psychiatrist, Dr. J. K. Stuart, to the Royal Victoria Infirmary, Newcastle, for a consultant neurological opinion. This was given by Dr. H. G. Miller who commented - "Although objective neurological signs are scanty, I think her condition is neurological rather than psychiatric. Her case is very similar to those reported from the Royal Free Hospital, London, and the vagueness of the neurological findings is in keeping."

Electro-diagnostic facilities are not as yet available in this region, and, therefore, no information was gained by means of electro diagnosis, which was unfortunate in view of the widespread involvement of muscles seen in cases both in the epidemic and sporadically.

My experiences during and since the epidemic in quest of a
diagnosis for the disease have, on the whole, been frustrating. I now know, after two and a half years work, what it is not, but what it is remains elusive.

An appraisal at this period of time from the onset of the disease shows that -

(1) It is infectious.

(2) All ages are affected by it and both sexes, children and adolescents being most affected.

(3) The mode of transmission is not known. It appears probable that spread is by direct contact and droplet infection but this has not been proved.

(4) The reticulo endothelial system and the central nervous system are chiefly involved by the disease process.

(5) The main clinical features are dizziness, somnolence, muscular pain and weakness, lymph gland enlargement, a tender liver and spleen, neurological disturbances and mental affects.

(6) A protracted course, with recurrences or relapses, and persistence of minor symptoms, is usual in severe attacks.

(7) In the majority of cases, the disease produces a relatively mild reaction, with little objective evidence of neurological involvement, recovery occurring in under one month.

(8) No fatalities have occurred as a result of the disease.

(9) A causal agent has not been discovered.

The reaction to infection varied widely in intensity in individual hosts. In some, it was a transient affair with slight enlargement of lymph glands, dizziness for a day or two, while feeling off colour, and in less than a week the episode was
In the majority of cases the illness was more severe than this, with a marked reticuloendothelial reaction and subjective neurological manifestations in the form of paraesthesiae, but little objective involvement, and acute myalgia. Some of these cases had a severe illness in which the main weight of the attack appeared to be on the reticuloendothelial system, with little evidence of neurological phenomena, and several of these cases developed jaundice.

A minority of cases developed objective evidence of neurological involvement, and in these cases the neurological involvement was remarkable for the fluctuation, or transience, of some of the signs and symptoms that occurred, and for the complex nature of the involvement as shown by its effects.

Muscular weakness was usually paraplegic in distribution, the patients complaining that "their legs had gone from them," but was also seen in hemiplegic and monoplegic form. The tendon reflexes were usually normal or rather sluggish in the initial stages of the disease, later remaining normal or becoming brisk. In several instances knee and ankle clonus could be elicited in the affected limb over a period of a few days. In two cases a crural monoplegia developed, in each case during the convalescent stage, following an attack that was not very severe. There was no loss of consciousness and no evidence of weakness in the other limbs. In both instances there was considerable loss of power in the affected limb, the muscles were hypotonic, the tendon reflexes were diminished and the plantar response was extensor; cutaneous hypoesthesia was present in the foot and ankle. Recovery of power in the limb took place over a period of several months, while the tendon reflexes became normal.
and the plantar response became flexor after intervals of 6 or 8 weeks respectively. No spasticity developed.

Although the muscle weakness generally appeared to be of the upper motor neurone type the muscles were not hypertonic. Wasting of muscles was uncommon but it has been observed, affecting the dorsal interossei of the hand, particularly the 4th interosseus muscle, and in one case the muscles of one leg show a definite wasting and hypotonus.

A picture is therefore seen of neurological involvement in which motor weakness is usually of the type associated with upper motor neurone disease, but in which hypertonicity of the affected muscles is not present; but in which a few cases also offer evidence of lower motor neurone dysfunction with muscular wasting and loss of tone.

The sensory changes, both subjective and objective, have already been described.

The agent responsible for the disease thus appears to possess properties of causing an irritative host reaction which varies from a short mild irritative reaction in the reticuloendothelial system, to a more prolonged and severe reaction in that system combined with a mild irritative reaction in the central nervous system, and thirdly to a combination of irritative reactions affecting the reticuloendothelial system and the central nervous system in greater or lesser degree, and in the third instance paralytic signs may also be produced.

The third type of reaction was met in a minority of cases but these were the cases in which the disease ran a more protracted course.

It is fair to consider that the third type of reaction, in
which the central nervous system is involved to a varying extent, is an encephalo-myelitis, but these cases were in the minority, and the bulk of the cases showed only mild evidence of neurological involvement, the weight of the reaction to infection falling on the reticulo endothelial system and the muscles; nevertheless the encephalo-myelitic manifestations must be considered the most serious feature of the epidemic.

**Encephalomyelitis of unknown origin.**

During the past decade outbreaks of obscure illnesses simulating poliomyelitis have been reported from various parts of the globe. In the last outbreak only, that in the Royal Free Group of Hospitals in London in 1955, was poliomyelitis not initially suspect.

These outbreaks may be placed in the order of their occurrence:-

2. **Adelaide, Australia, 1949.** Reported by Pellew, 1951.

The peak incidence of these epidemics has been in the summer, with the exception of the initial outbreak at Akureyri which occurred in the autumn and winter months.

The clinical features that appeared in these epidemics bore a close resemblance to each other with slight variations and consisted of:-
An initial stage of malaise, sore throat, headache, pain in the nape of the neck, lassitude and sometimes nausea or vomiting.

A low grade pyrexia was usually present, but not infrequently the illness was apyrexial.

Muscle tenderness and pareses which appeared usually after several days and were not usually associated with wasting.

Little disturbance in muscle tone or reflexes.

Sensory symptoms consisting of spontaneous muscular pain, and paraesthesiae, with objective findings of sensory impairment also present in many cases.

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Cranial nerve involvement.

Emotional lability and psychogenic sequelae.

Involvement of the reticulo endothelial system, which was observed in the Royal Free Hospital outbreak.

Little change in the cerebro spinal fluid in most outbreaks.

Recurrences were frequently a feature of the disease.

In none of these outbreaks was the causal agent isolated. Pathological information on the morbid anatomy of the disease was not available in the absence of any fatalities in the outbreaks.

The clinical features common to these outbreaks are also similar to the clinical features observed in the more severe cases occurring in the Dalston epidemic.

While the diagnosis rests on clinical grounds, however, it is not possible to do more than draw attention to this similarity as any confirmatory evidence of a true association is lacking.

It is hoped, however, that confirmatory evidence will
eventually be forthcoming with the isolation of the causal agent of the disease.

Further virus studies to this end are to be made at the Public Health Laboratory, Carlisle, and specimens taken from patients affected by this disease are held in "deep freeze" pending further attempts at virus isolation in tissue culture, using human amnion cells, and other types of cells that have not as yet been used in attempts to isolate a virus.
Conclusion.

An infectious disease occurred in epidemic and sporadic form in a rural practice in Cumberland in 1955 and subsequent years.

The aetiology of the disease remains obscure as laboratory investigations were negative and there were no fatalities.

The clinical features of the disease show some similarity to clinical features reported from outbreaks of encephalomyelitis of unknown aetiology that have occurred in various parts of the world during the past decade.

In the absence of the isolation of a causal organism, and the lack of pathological material, a firm diagnosis cannot be made except on clinical grounds.

References:

APPENDIX
ILLUSTRATIVE CASE HISTORIES.

Case 1:

Patient - Male, aged 51.


19.1.55. Aching pains continued in back, and legs now aching with tingling sensation in the feet. Complains of loss of power in legs, but no objective evidence of this or of sensory loss. Reflexes normal.


26.1.55. No headache and no pain in the back, but the legs feel heavy and ache intermittently. Occasional tingling in the hands and feet. Slight loss of power in both lower limbs. No sensory impairment. Reflexes normal. Still tender subcostally.

1.2.55. General improvement, but felt dizzy on getting up, and generally weak.

Further course: Gradual improvement over the next two weeks following which he returned to work. Depression occurring in convalescent stage cleared slowly over 2 months and occasional
w-\-aves of dizziness and intermittent muscular pains were felt during this period. Muscular power normal by the end of this period.

Recurrences: None.

C.S.F: Not examined.

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Case 2:
Female, aged 32.


31.1.55. Headache only intermittently. Muscular pains improved. Still a little dizzy. Vision blurred, cannot read more than a few lines as the print blurs. Diplopia on upward and lateral gaze.

4.2.55. Feeling much better and allowed up.


Further course: Tremor disappeared within one week. Depression and emotional lability persisted with intermittent headache and muscular pains and paraesthesiae for 6 weeks.

Recurrences: Four recurrences of symptoms have occurred. No neurological sequelae, but remains emotionally labile and complains of poor memory for details in everyday life and of poor concentration.

C.S.F. Not examined.
Case 3:

Patient - Female, aged 8 years.

9.2.55. Date of onset. Felt unwell for previous week. Tired, listless, dizzy. At onset complained of headache, sore eyes and stiff neck and pains in the legs. Tongue coated and dry, throat slightly inflamed, glands visibly enlarged in posterior cervical group and tender. Eyes watering a little, no conjunctival injection. Subcostal tenderness. T.100.5. P. 110/min.


Further course: Gradual recovery in a month, no loss of muscle power evident at the end of that period. Glands remained palpable but not tender. Remained easily tired, emotional and given to tears, for a further 2 months. Lost 7 lbs. in weight during illness.

Recurrences: None.

C.S.F. Not examined.
Case 4:

Patient - Male, aged 7 years.

3.2.55. Date of onset. Has been tired and complained of a headache and dizziness two days previously. At the onset complained of sore throat, headache, aching in the neck, back and legs, and pains in the abdomen. Anorexia. Tongue coated, throat mildly inflamed, with two ulcers on the palate, eyes watering and rather pink, painful enlarged glands along the sterno mastoid muscles, marked tenderness in the upper abdominal quadrants and muscles of lower limbs tender to light palpation; cutaneous hyperaesthesia in lower limbs. Reflexes normal. No sensory loss. T. 100°F. Pulse 112/min.

10.2.55. "Pins and needles" in feet and hands. Complains of earache, but examination of the ear negative. Sleeping poorly and waking in fright.

14.2.55. Headache improved, neck and glands still tender, subcostal pains diminished but aching in muscles below the knee still persisting. Patchy cutaneous sensory impairment in lower limbs to cotton wool and pin prick.


Further course: Gradual recovery over 2 months, but rapid mood swings, irritability, "touchiness" and lack of concentration persisted longer.

Recurrences: Recurrences of symptoms occurred three times in the subsequent 18 months, dizziness, excessive tiredness, aching muscles, incoordination and paraesthesiae being prominent.
2.

Features of the recurrences. No neurological sequelae.

10.5.57. Referred to child guidance clinic, as the child was worrying excessively about his school work.

Psychiatric opinion was that the condition was a post-infective state, in a child of normal intelligence, the prognosis being favourable.

C.S.F. Not examined.
Case 5:

Patient - Female, aged 33.

1.3.55. Date of onset. Had been below normal two or three days, then developed dizziness, headache, sore throat, stiff aching neck, a painful back and limbs, waves of nausea. Tender enlarged glands in the cervical and inguinal regions. Liver and spleen tender. Tingling in arms and legs. Feels very sleepy. Temperature 99.5°F. Pulse 90/min. Reflexes normal.

3.3.55. Patchy diminution of sensation to cotton wool and pin prick along right ulnar distribution. Cutaneous hyperaesthesia lower limbs.


Further course: Steady improvement and recovered in three weeks.

Recurrences: Two recurrences of symptoms in succeeding 18 months, symptoms being milder at each recurrence.

C.S.F. Not examined.

Blood Picture: Leucopenia with relative lymphocytosis and eosinophilia. Abnormal lymphocytes present.

Paul Bunnell: Negative.
Case 6:

Patient - Female, aged 70.


10.3.55. Acute pains in right upper and lower limbs and back. Tingling in hands and feet. Tender subcostally. Reflexes sluggish. Vision blurred, diplopia on upward and lateral gaze.

15.3.55. Moderate degree of loss of power in right lower limb, and right hand grip. Diminished response to cotton wool and pin prick below right knee. Temperature 97. Pulse 80/min.

20.3.55. Sleeping badly at night, waking frequently and dreaming persistently when asleep. Depressed. Still sweating intermittently. Muscular pains persistent but diminished.

25.3.55. Apyrexial, pulse rate slightly raised, muscular pains and weakness, paraesthesiae. Depression persisting.

Further course: Slow recovery over 3 months, muscular power being regained. Remained depressed and easily tired for 6 months.

Recurrences: Three recurrences of symptoms over 18 months - myalgia, headache, dizziness and swollen painful glands occurring.

C.S.F. Not examined.

Blood: Paul Bunnell negative. Little change in blood picture.
Case 7:

Patient - Male, aged 51.

23.3.55. Onset of urticarial reaction, preceded during the previous fortnight by increasing malaise, vertigo, frontal and occipital headache, and acute myalgic pains in the neck, shoulders, and upper and lower limbs. Paresthesiae present. Throat slightly inflamed, tongue coated and dry, cervical glands tender and enlarged. Eyes watering and slight conjunctival injection present, movements of the eyes painful and diplopia present on upward and lateral gaze. Fine lateral nystagmus present. Suboccipital tenderness and guarding; spleen tender and slightly enlarged. Cervical and axillary glands palpable and tender. Moderate degree of weakness in both lower limbs. Muscle tone normal, reflexes brisk and equal, but no clonus present. Abdominal reflexes sluggish and plantar response could not be elicited. Hyperaesthesia affecting back and lower limbs. Irritating urticarial wheals present, in a scattered manner, on the shoulders, back and limbs and seemed to appear in regions subjected to pressure when lying in bed. Temperature 100°F. Pulse 118/min.

25.3.55. Vertigo severe, even at rest, and exaggerated by any movement of the head. Mucosa appearing in waves but has vomited only once. Marked depression present.

28.3.55. Restless at night and confused at times when waking. Numb feelings, tingling in the extremities, and cramp in the muscles of the legs. Vision blurred. Patchy diminution of sensation present to cotton wool and pin prick in the lower limbs and impairment of vibration sense.
Further course: Slow improvement occurred over one month, the nausea and vertigo becoming more tolerable, and the muscle pains diminishing, but a complication appeared in the development of bronchitis and bronchospasm, and myocarditis. The bronchitis and bronchospasm responded well to suitable treatment, but evidence of myocardial weakness remained over a period of many months. Urticarial wheals appeared intermittently over a period of 3 months. Vertigo slowly diminished in intensity and after 2 months became intermittent; it could, however, be readily induced by looking upwards or turning the head quickly. Sensory and motor impairment in the lower limbs was persistent. The reflexes at the knee and ankle, at first brisk and equal, became somewhat sluggish, especially so on the right side and slight wasting occurred in the calf muscles of that side. The plantar response remained absent. Return to work did not take place for 12 months. Readily induced fatigue, intermittent myalgic pains and paraesthesiae, headaches, depressive tendencies and lack of concentration were sequelae of the illness.

Recurrences: Five exacerbations of symptoms occurred during 9 months from the onset.

C.S.F. Not examined.

Blood: Paul Bunnell negative. Leucocytosis, with relative lymphocytosis and marked eosinophilia seen in blood picture.
Case 8:

Patient - Male, aged 44.


5.4.55. Muscular pains and tenderness in right leg. Subcostal tenderness and muscular guarding. Dizziness, anorexia, and nausea persisting.

Further course: Fluctuation of symptoms and signs with gradual recovery over 2 months. Remained easily tired, and liable to attacks of depression and anxiety over next 2 years.

Recurrences: Two episodes of recurrence of symptoms during the next 12 months.

C.S.F. Not examined.

Blood: Paul Bunnell negative. Relative lymphocytosis seen in blood film, with abnormal lymphocytes present.
Case 9:

Patient - Female, aged 63.

2.4.55. Date of onset. Headache, vertigo, aching neck, sweatings and aching pains in the back of the legs following 4 weeks increasing malaise, intermittent headaches, muscular pains and dizziness. Cervical and inguinal glands markedly enlarged and tender. Marked tenderness of liver and spleen. Cutaneous hyperesthesia lower limbs. Temperature 97°F. Pulse 88/min.


8.4.55. Jaundice developed, and paraesthesias affecting the extremities. Muscles very tender in legs.

12.4.55. Jaundice almost clear. Little improvement otherwise.

Further course: Recovery protracted, over 3 months. During convalescence developed a femoral thrombosis. Remained easily tired and with numerous complaints of aches and pains for the remainder of the year.

C.S.F. Not examined.

Blood: Paul Bunnell negative. No change in blood picture.
Case 10:

Patient - Female, aged 40.

2.4.57. Insidious onset of symptoms over past month, these consisting of general malaise, frontal headache, stiff aching neck, dizziness and pains in the back and lower limbs and weakness in the lower limbs. Depression, apathy and general fatigue present.

Temperature 99°F. Pulse 88/min.


Further course: Intermittent febrile state, up to 99.5°F., persisted for 3 weeks. Paraesthesiae consisting of tinglings and numbness appeared and were persistent. Motor weakness gradually improved over 2 months, and general recovery occurred but was very protracted, leaving residual symptoms of insomnia, paraesthesiae, sweatings, fits of depression, impaired memory and concentration, and liability to readily induced fatigue.

Recurrences. Four recurrences of symptoms occurred in the ensuing 2 years.

C.S.F. Normal.

Blood: Paul Bunnell negative.

Blood Film: Relative lymphocytosis and eosinophilia with abnormal lymphocytes present.

Electroencephalogram: Non-specific abnormality in tracings from occipital leads.
Case 11:

Patient - Male, aged 11 years.

3-4-55. Date of onset. Developed frontal headache, dizziness, aching neck, sore throat and muscular pains in back and both legs, following two or three days feeling tired and disinclined for any exertion.

Cervical and inguinal glands markedly enlarged and tender. Throat slightly inflamed. Tongue coated. Eyes watering slightly, vision blurred, diplopia on upward gaze and pain felt in upward rotation of the eyes. Tender, with some guarding, subcostally. Reflexes sluggish.

Temperature 99°F. Pulse 90.

6-4-55. Dizziness, aching neck, aching in thighs, and tingling in feet. Restless at nights and sleeping poorly.

9-4-55. General improvement, but lower limbs ache persistently.

Further course: Gradual and complete recovery over four weeks.

Recurrences: None.

C.S.F. Not examined.

Blood: Leucopenia. Abnormal lymphocytes present.
Case 12:

**Patient** - Female, aged 19.

8.4.55: Date of onset. Acute onset of vomiting and diarrhoea lasting 12 hours and followed by frontal headache, vertigo and general malaise, and acute muscular pains in the neck, back and lower limbs. Tongue coated, throat little inflamed, cervical glands enlarged and tender, tingling in hands and feet, and hyperaesthesia in lower limbs. Subcostal tenderness.

12.4.55. Slow improvement, but sleeping poorly, general feeling of weakness and muscular cramps present in legs. Depressed.

**Further course:** Slow recovery over four weeks, and easily tired and emotionally upset for 3 months.

**C.S.F.** Not examined.

**Blood:** Paul Bunnell negative.

**Blood Film:** Relative lymphocytosis, with presence of abnormal lymphocytes.
Case 13:

Patient - Male, aged 13.


Temperature 99.2. Pulse 96/min.

17.4.55. Rash disappeared. No staining. Tingling felt in extremities and legs aching. Reflexes sluggish.

20.4.55. Improved and symptoms disappearing.

Further course: Gradually regained strength over a month, but was easily tired and subject to headaches for a further couple of months.

Recurrences: None.

C.S.F. Not examined.

Blood: Paul Bunnell negative.

Blood Picture: Several abnormal lymphocytes seen.

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Case 14:

Patient - Female, aged 34.

4.5.55. Date of onset. Acute onset of stiff aching neck, sore throat and acute myalgic pain in the back and the legs. Dizzy and tired. Pharyngitis, enlarged, tender, posterior cervical glands, subcostal tenderness and acute myalgic pain were the main features. The eyes were watering a little and felt irritable. Temperature subnormal and pulse 84/min.


Further course: Symptoms disappeared in a fortnight, but depression and emotional lability persisted.

Recurrences: Four recurrences of symptoms occurred, one with a low grade pyrexia for several days, and in one of the recurrences acute spasm developed in the right sternomastoid muscle which was severe enough initially to require morphine.

Psychogenic sequelae of depression, impairment of concentration and emotional lability have been marked features in this case.

C.S.F. Normal.

Case 15:

Patient - Male, aged 35.

24.5.55: Date of onset. Onset of frontal headache, stiff neck, dizziness, retro-orbital pain, acute myalgia in lower limbs and back following three days increasing general malaise. Throat slightly inflamed, tongue coated, eyes watering slightly, palpable and tender enlarged cervical glands. Subcostal tenderness. Muscles of calves of legs extremely tender to touch. Cutaneous hyperesthesia. Reflexes normal.

26.5.55. Tingling in right foot. No sensory loss.

29.5.55. Muscular pain abating and no headache. Feels extremely tired.

2.6.55. Recurrence of pain in right leg. Slight weakness.

Further course: Gradual improvement, being fit to return to work by the end of the month. Found himself easily tired, and liable to attacks of depression for a further couple of months. Fond of fell walking but found his legs could no longer carry him the usual distances, during the subsequent 6 months.

Recurrences: One recurrence of symptoms 9 months later, which persisted for one week.

C.S.F. Not examined.

Blood: Paul Bunnell negative.
Case 16:

Patient - Male, aged 8 years.

3.7.55. Date of onset. Acute onset of upper abdominal pain, nausea, and headache, followed by mild conjunctivitis, and photophobia, sore throat and complaints of pain in the neck, back and lower limbs. Very sleepy and presented examination. Cervical and inguinal glands were enlarged and tender. Subcostal tenderness and guarding were present and muscular spasm was present in the calf muscles. The reflexes were sluggish, and cutaneous hyperaesthesia was present in the upper quadrants of the abdomen. Temperature 99.5°F. Pulse 100/min.

5.7.55. Complaining of pins and needles in his feet and hands. Headache and muscular pains still present. No sensory loss. Has been having drenching night sweats.

7.7.55. Restless at night with night terrors. Labile emotional state. Headache and myalgia diminishing.

Further course: Gradual recovery occurred during the course of a month.

Recurrences: These were a marked feature in this boy and continued to occur during the next 18 months, five recurrences of symptoms, with headache, myalgia and tender enlargement of lymph glands occurring. Psychogenic disturbances of impairment of concentration, emotional lability and behaviour disorders were persistent features in this case and caused him eventually to be sent to the Child Guidance Clinic for attempted correction of these features.

C.S.F. Not examined.

Case 17:

Patient - Male, aged 34.

15.7.55. Acute onset of diarrhoea and vomiting, which persisted for less than 24 hours, and was associated with severe headache. Followed by stiff neck, sore throat, and acute myalgic pains affecting the back, abdominal wall and lower limbs. Waves of dizziness present and a mild conjunctivitis. Reflexes sluggish. Kernig negative. Temperature 99°. Pulse 90/min.

18.7.55. Tender enlargement of cervical, inguinal and axillary glands, and acute pain and guarding subcostally in the right lower quadrant of the abdomen. Acute muscle spasm in the right thigh. The acute tenderness and guarding in the right lower abdominal quadrant simulated appendicitis, and, as a precaution, I had this patient sent into hospital for observation. The pain gradually diminished and he was discharged home after a week, feeling extremely tired and lethargic.

Further course: One recurrence of symptoms, 2 months later, which was much less acute than the initial attack. Further observation was not possible as the patient left the district following this attack.

C.S.F. Not examined.

Blood: Paul Bunnell negative.

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Case 18:

Patient - Male, aged 31.

12.8.55. Headache and general malaise for several days followed by frontal headache, dizziness, aching neck, back and limbs, sore throat and sore eyes. Pins and needles in extremities. Tender, enlarged, cervical and inguinal glands. Temperature 100°F., Pulse 110/min.

15.8.55. Developed unilateral orchitis. Severe myalgia in lower limbs, lethargic and sleepy.

18.8.55. Improving but complained of weakness in the lower limbs and cold feet, and feelings of numbness. Reflexes normal.

Further course: Gradual resolution over three weeks, but leaving lethargy and depression present for the subsequent 2 months.

Recurrences: One recurrence of symptoms of headache, myalgia and dizziness in the subsequent 3 months.

C.S.F. Not examined.

Blood: Paul Bunnell negative. Serum also negative for mumps.
Case 12:

Patient - Female, aged 17.

7.2.56. Headache, frontal and occipital, stiff neck, myalgic pains in the back and upper and lower limbs followed after two days of feeling excessively sleepy through the day, and dizziness. Sore throat, retro-orbital pain, eyes watering, slight conjunctivitis, and tender enlargement of the cervical glands. Dry irritating cough present. Temperature 99.5°F. Pulse 100/min.

12.2.56. Sleepy tendency persists and tingling in the extremities and cramps in the muscles of the lower limb developed.

16.2.56. Spasm in the muscles of the shoulder girdle with cutaneous hyperesthesia. Impairment of sensation to touch with cotton wool and to pin prick of ulnar distribution. Reflexes normal. Markedly depressed, and emotional.

23.2.56. Remains very tired and apathetic. Continuance of myalgic pains, paraesthesiae and slight sensory impairment in right hand. Upper limbs have developed fine tremor.

Further course: Sufficient improvement in 5 weeks to return to school, but sequelae of loss of concentration and impairment of retention and immediate recall made preparation for examinations extremely difficult.

Recurrences: Three occurrences of symptoms of headache, dizziness, acute myalgic pain and depression, associated with enlargement of cervical glands, during next 9 months. No eventual neurological sequelae.

C.S.F. Normal.

Blood: Paul Bunnell negative. Relative lymphocytosis with
abnormal lymphocytes present.

E.E.G. Non-specific abnormality in tracings from occipital leads.
Case 20:

Patient - Female, aged 52.

11.2.55. Insidious onset during the past three weeks of sore throat, mild laryngitis with intermittent periods of aphonia, headache, mild conjunctivitis with slight degree of watering of the eyes, dizziness and muscular pains in the neck, back and upper and lower limbs, most marked in the right arm and leg. Tingling in the right hand and foot. Pharyngitis present and slight degree of conjunctival injection, mainly palpebral. Pupils equal, concentric and react slowly but equally to light and accommodation. Complaint that light used in testing the pupils caused pain. Vision blurred. Diplopia present on upward and lateral gaze, but no overt weakness of ocular muscles, other than that. Tender enlargement of lymph glands along sternomastoid muscles and in posterior triangle of neck. Tender in upper abdominal quadrants, but liver and spleen not enlarged. Tender nodes present in abdominal muscles. Muscle power diminished in the right leg and power of the right hand grip lessened compared with the left; muscle tenderness present, tone normal. Reflexes brisk but equal. No clonus. Plantar response flexor; abdominal reflexes diminished. Impaired sensation to cotton wool and pin prick below the right knee, and affecting the ulnar distribution of the right hand. Temperature normal. Pulse normal.

18.2.55. Sleeping badly, with much dreaming, and feels extremely tired. Muscle pain persistent, most severe in the right thigh. Coarse tingling felt in right lower limb.
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Depressed and emotionally labile.

25.2.55. Pharyngitis and laryngitis improved considerably and headache now intermittent and mainly occipital.

Dizziness still present with unsteadiness on changing position suddenly. Romberg test positive. Reflexes normal.

Further course: The illness followed a fluctuating course.

The initial episode gradually settled over a further month but leaving sequelae of impairment of concentration and memory, depression and attacks of vertigo.

Recurrences: Recurrences of symptoms have occurred four times to date and have lasted three to four weeks. Ataxia affecting the right upper limb developed during the first recurrence, and has been a feature of subsequent recurrences, while reverting almost wholly to normal in the periods between recurrences.

Reflexes have remained brisk but equal, muscle tone has not been affected, but residual weakness in the right lower limb has resulted in a gait in which the right lower limb is swung from the hip, the foot dragging and tending to catch. She has fallen twice with the right lower limb giving way suddenly without warning. Paraesthesiae consisting of numbness and tingling are still experienced. Depression, lack of concentration and initiative, and readily induced fatigue persist at the present date. The face has become almost expressionless, the skin greasy, with an acne-like eruption, and the voice is husky and has developed into a monotone. All actions, including speech production, are done with deliberation.

C.S.F. Normal.

E.E.G. Normal.

Blood: Paul Bunnell negative.
3.

**Blood Film:** Relative lymphocytosis, with abnormal lymphocytes present.

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MAP OF DALSTON
and its
ENVIRONS
ORDNANCE SURVEY
Scale 1:25,000 or about 2 3/4 Inches to 1 Mile
Summary:

An epidemic disease occurred in a rural practice in Cumberland in 1955. The peak of the epidemic was reached in the latter part of March and April. Cases of the disease have appeared sporadically to the present date.

Over 200 cases were affected during the epidemic period. Both sexes and all age groups were affected; the age groups most affected were children and adolescents. A high incidence of infection was found in a small closed community in the district.

The mode of transmission of the disease has not been proved, but is thought to be by person to person contact. The incubation period appeared to be 5 to 7 days.

The illness was mild in many cases, with recovery in less than one month, but other cases were more severe and the course of their illness was protracted and of fluctuating intensity.

Recurrences or relapses were found to be a feature of the disease, occurring in the same person several times, in some instances.

Full recovery occurred eventually in almost all cases, but two are still disabled, and one is unfit for work. There were no fatalities directly due to the disease. Residual psychogenic sequelae and minor physical complaints proved remarkably persistent in the post infective period.

Treatment was symptomatic. Antibiotics with the possible exception of tetracycline were not of use. Compound tablets of aspirin, and promethazine were the drugs used most commonly. Electro convulsive treatment was required in several cases of severe depression following the illness.
Laboratory investigations were not able to incriminate any causal agent and tissue culture methods were used without success in attempts to isolate a virus.

Changes in the blood picture occurred in 30% of cases but were of a non-specific nature, of the kind that have been associated with various virus infections.

Electroencephalographic studies showed an abnormality in the occipital leads, of non-specific nature, in a fairly high proportion of the cases that were examined in that way. Electro-diagnostic techniques of investigation were not available. The clinical features of the disease provided evidence of a varying degree of reticulo endothelial involvement in all cases, and in 20% of cases there was also objective evidence of involvement of the central nervous system. The involvement of the central nervous system took the form of an encephalo myelitis which was present in all cases in which the disease was protracted, and was the most serious feature of the illness.

Attention is drawn to a degree of similarity between the clinical features of the present disease and clinical features of outbreaks of encephalo myelitis of unknown etiology that have been reported from various parts of the world during the past decade.

No conclusion is drawn as to the identity of the present disease with the outbreaks of encephalo myelitis mentioned above, as positive proof of identity rests on identification of the causal agent of the disease which so far has proved impossible of attainment in this, and other, obscure outbreaks.