

## Frequency of Complications of Measles, 1963

### Report on a National Inquiry by the Public Health Laboratory Service in Collaboration with the Society of Medical Officers of Health

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Recent advances in the development of measles vaccines give reason to expect that an acceptable, safe, and effective means of immunization will soon become available. But "the need or desire" for large-scale vaccination in this country is subject to debate (*British Medical Journal*, 1963b). One of the major sources of doubt about the need for immunization stems from the belief among many parents and doctors that measles is a mild disease in which serious complications are rare and almost never fatal in normal children. Deaths have indeed declined rapidly in recent years to about 2 per 10,000 notifications, and a recent study has shown that about half the deaths occur in persons with serious chronic disease or disability (Report, 1963). Little information is available, however, about the frequency of serious complications and consequent permanent disabilities which may result, especially from neurological complications, in patients who survive. Estimates based only on clinical impression are likely to be misleading and a numerically important minority may easily be overlooked. An investigation by a study group of the College of General Practitioners (1956, 1957), devoted primarily to a study of the place of chemotherapy and antibiotics in the management of measles, added much to knowledge of the disease, but it included fewer than 5,000 cases—too few to assess with confidence the public health importance of the complications of measles in relation to the need for immunization.

The aim of the present investigation was twofold: first, to estimate at the time of the attack the frequency of serious complications of measles, particularly of neurological complications, by means of a national postal inquiry into cases notified to medical officers of health during the 1963 epidemic; and, secondly, to investigate in a sample of patients the late consequences of the more serious complications. The results of the first part of the study are reported here.

#### Methods

The medical officers of health of 47 large county boroughs scattered throughout England and Wales agreed to participate in the inquiry. They first wrote to local general practitioners and medical superintendents of fever hospitals explaining the reasons for the investigation and the proposed procedure. Practitioners were invited to co-operate by completing simple record cards for cases of measles which they notified from 1 January to 30 April 1963. In 16 of the 47 boroughs where medical officers of health decided that they could not follow up all cases the inquiry cards were sent for a sample of notifications selected at random according to a plan decided at the outset in each borough. In one city cards were sent only to selected practi-

tioners, but as the results obtained were similar to those elsewhere they have been included in the analyses.

Record cards, with a brief covering letter reminding doctors of the purposes of the inquiry, were sent to practitioners one month after the date of notification for the sampled cases. Before dispatch the patient's name, age, and sex, and date of appearance of the rash as stated on the notification form were entered on the card. Doctors were asked to say whether any of the following complications occurred: encephalitis, impaired consciousness, behaviour changes, motor disturbances (including fits, involuntary movements, or paresis), pneumonia (or severe bronchitis), otitis media, deafness, and to give brief details of these or any other complications. They were also asked whether or not the patient was admitted to hospital.

If cards were not returned within two weeks of dispatch a reminder was sent to the doctors concerned, or, in some areas, information was obtained by a health visitor calling at the patient's home. On completion of the survey records were returned to the Epidemiological Research Laboratory for analysis.

#### Results

A total of 55,589 inquiry cards were sent to doctors for cases of measles notified in the 47 boroughs from 1 January to 30 April 1963. This represented approximately one in six of all cases reported to the Registrar-General in England and Wales during this period (Table I). The proportion fell slightly over

TABLE I.—Composition of Sample Studied

No. of cases notified in England and Wales from week ending 5 January to week ending 27 April, inclusive	341,961
No. of cases notified in selected boroughs from 1 January to 30 April, inclusive	89,095
No. of inquiry cards sent to doctors	55,589
No. of cards returned (percentage of cards sent in parentheses)	*53,008 (95)

\* 16 persons whose sex was not stated and who had no complications have been omitted from subsequent tables.

the course of the study, probably because the height of the epidemic came early in the winter in the north, where the proportion of cases studied was higher than for the whole country, and only later spread to the south-east, where the proportion was lower, mainly owing to the exclusion of London from the inquiry. The fall was not due to a decrease in the proportion of notifications sampled in the participating boroughs.

The response from practitioners was excellent. Of the 55,589 cards sent, 53,008 (95%) were completed and returned. The age and sex distribution of the patients is shown in Table II, with the exception of 16 uncomplicated cases whose sex was not recorded. Two-thirds of the patients were aged between 3 and 9 years, and less than 2% were under 6 months or over

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14 years of age. There was no difference in the age distribution for the two sexes, but the male/female ratio was 1 to 0.95.

TABLE II.—Age and Sex Distribution of Cases

Age	Males		Females		Total	
	No.	%	No.	%	No.	%
0-5 months ..	118	0.4	114	0.4	232	0.4
6-11 " ..	903	3.3	901	3.5	1,804	3.4
1 year- ..	3,067	11.3	2,985	11.5	6,052	11.4
2 years- ..	3,950	14.6	3,609	14.0	7,559	14.3
3-4 years ..	7,687	28.3	7,228	28.0	14,915	28.1
5-9 " ..	10,684	39.4	10,227	39.6	20,911	39.5
10-14 years ..	372	1.4	423	1.6	795	1.5
15-19 " ..	90	0.3	99	0.4	189	0.4
20 years or over	104	0.4	106	0.4	210	0.4
Not stated ..	163	0.6	162	0.6	325	0.6
All ages ..	27,138	100.0	25,854	100.0	52,992	100.0

### Frequency of Complications

The rate of complications by age and sex is shown in Table III. The complications included in this analysis were those specified on the inquiry cards, together with other serious disturbances attributed by the doctor to measles. Admission to hospital was also counted as a complication when the admission was on medical rather than on social grounds. Nearly 67 per 1,000, or about 1 in every 15 persons with measles in this survey, suffered from at least one complication. The most numerous were severe affections of the respiratory tract (38 per 1,000) and otitis media (25 per 1,000), followed by neurological disturbances (4 per 1,000) and a small number of others (2 per 1,000). Twelve of the children studied (0.2 per 1,000) are known to have died after measles, and 610 (11.5 per 1,000) were admitted to hospitals as a direct result of the disease.

TABLE III.—Age and Sex Frequency of All Complications

Age and Sex	Total No. of Cases	No. with Complications	Rate per 1,000 Cases
0-5 months ..	232	20	86.2
6-11 " ..	1,804	151	83.7
1 year- ..	6,052	435	71.9
2 years- ..	7,559	509	67.3
3-4 years ..	14,915	895	60.0
5-9 " ..	20,911	1,436	68.7
10-14 years ..	795	34	42.8
15-19 " ..	189	13	68.8
20 years or over	210	17	81.0
Not stated ..	325	22	67.7
Males ..	27,138	1,812	66.8
Females ..	25,854	1,720	66.5
All cases ..	52,992	3,532	66.7

Complications were most frequent in infants, particularly those under 1 year of age, and in adults; they were least frequent in the 3-4 years age-group and in those aged 10-14 years. There was no difference between males and females at any age and no distinction between the sexes has therefore been made in the table.

Details of the age and sex distribution for each group of complications are presented in Table IV. Persons who suffered

TABLE IV.—Age and Sex Distribution of Selected Complications

Complication	No. Affected*	Rate per Thousand Cases of Measles												
		All Cases	Males	Females	0-5 Months	6-11 Months	1-year	2-years	3-4 years	5-9 Years	10-14 Years	15-19 Years	20 Years or Over	Not Stated
Encephalitis or impaired consciousness ..	61	1.2	1.1	1.2	0	0	1.3	1.2	0.9	1.1	3.8	5.3	4.8	6.2
Behaviour changes ..	64	1.2	1.3	1.1	0	0	2.1	1.7	1.2	0.9	0	0	4.8	3.1
Motor disturbances :														
Fits ..	80	1.5	1.8	1.2	0	0.6	3.6	2.4	1.5	0.7	0	0	0	6.2
Other ..	13	0.2	0.3	0.2	0	0	0.2	0.4	0.3	0.2	0	0	0	0
All neurological ..	203	3.8	4.2	3.4	0	0.6	6.9	5.2	3.6	2.8	3.8	5.3	4.8	9.2
, respiratory ..	2,022	38.2	37.6	38.8	60.3	58.8	42.5	39.3	32.7	38.8	23.9	42.3	42.9	36.9
Otitis media ..	1,338	25.2	25.6	24.9	0	23.8	22.6	22.9	23.9	28.6	16.4	26.5	14.3	24.6
Others ..	117	2.2	2.4	2.0	25.9	5.5	3.0	1.9	1.6	1.7	5.0	5.3	19.0	0
All complications ..	3,532	66.7	66.8	66.5	86.2	83.7	71.9	67.3	60.0	68.7	42.8	68.8	81.0	67.7

\* Persons with more than one complication are included under each heading.

from more than one complication have been included under each heading, except that impaired consciousness associated with fits was ignored unless it was clear that encephalitis was also present.

### Respiratory Complications

More than half the complications reported in this inquiry affected the respiratory tract. This group included pneumonia, severe bronchitis, bronchiolitis, and croup; one of these complications was found in every 26 cases, or in 38 per 1,000.

The rate was the same in males and females, but it was much higher in infants than in older children and also a little higher in adults. Doctors were not asked to distinguish between pneumonia and severe bronchitis, but most did so; bronchitis was recorded more than twice as often as pneumonia but showed no age or sex differences. By contrast, croup was reported in 14 boys and in only three girls.

Six children are known to have died with pneumonia and one with severe bronchitis. One of those with pneumonia was a deaf-mute with spastic quadriplegia and severe mental deficiency, one had chronic encephalitis, and one had asthma. The child who died of bronchitis had mongolism and congenital heart disease. One child with severe fibrocystic disease had pneumonia and died from the original disease two days after discharge from hospital.

### Otitis Media

This was numerically the second most important complication and accounted for over one-third of the total. The rate was 25 per 1,000 cases and showed little variation with age or sex.

### Neurological Complications

Some neurological disturbance was observed in 4 per 1,000 cases of measles. Encephalitis or impaired consciousness was reported in one per 1,000, behaviour changes in one per 1,000, and motor disturbances—most often fits—in the remaining two per 1,000.

The age distribution for the various types of neurological complication differed: the frequency of encephalitis was greatest in persons over the age of 10; behaviour changes and fits were almost entirely confined to children from 1 to 4 years of age. There was also a small excess proportion of males with neurological complications, mainly because of a higher proportion of males with motor disturbances.

Of the 61 persons with encephalitis or impaired consciousness four were stated to have been in prolonged coma and four others died. One child, already mentioned, who died of pneumonia had pre-existing chronic encephalitis; another, with mental defect, had severe bronchitis with impaired consciousness.

ness but recovered. No other chronic neurological disease was reported in any patient with a neurological complication.

The commonest behaviour changes reported were excessive irritability, peevishness, or complaints that the child was difficult to manage. Other changes included screaming and excessive crying, confusion, reversion to infantile habits and incontinence, difficulty in getting the child to go to bed or to sleep, excitability, head-banging, and hallucinations.

In about a third of the cases with fits the doctor stated that these were associated with fever. Of the remainder, nine children had a history of epilepsy. One child who had no history of fits had had four attacks since recovery from measles and was under investigation; another child who had been a severe epileptic, having two or three fits a day, had had no attacks since having measles. One child reported to have had fits later died of bronchopneumonia. Six cases were reported with involuntary movements not associated with fits and seven with paresis, five of whom had strabismus, one palatal paresis, and two, including one of those with strabismus, leg weakness.

### Other Complications

There were few complications other than those already mentioned. Most of the patients in this category were those who were admitted to hospital because of the unusual severity of the attack of measles or because of some pre-existing or associated factor, such as congenital malformation, young age, concurrent gastro-intestinal symptoms, chronic respiratory or renal disease, or general debility, which placed the patient at special risk. Other than these, 21 children were reported to have had severe or purulent conjunctivitis requiring specific treatment, nine had acute appendicitis or mesenteric adenitis, and a further eight had abdominal pain. One child with acute leukaemia died; measles was given as a contributory cause of death.

### Admission to Hospital

Altogether 496 (14%) of persons with complications were admitted to hospital (Table V); a further 78 were admitted

TABLE V.—Age and Sex Distribution of Cases Admitted to Hospital

Age and Sex	Reason for Admission			Total	Rate per 1,000 Cases
	Complications	Social	Not Known		
0-5 months .. ..	14	4	0	18	78
6-11 ,, .. ..	51	5	5	61	34
1 year- .. ..	92	19	7	118	19
2 years- .. ..	84	12	5	101	13
3-4 years .. ..	101	19	9	129	9
5-9 ,, .. ..	136	12	9	157	8
10-14 years .. ..	5	0	0	5	6
15-19 ,, .. ..	0	1	0	1	5
20 years or over .. ..	7	6	1	14	67
Not stated .. ..	6	0	0	6	18
Males .. ..	259	50	18	327	12
Females .. ..	237	28	18	283	11
Total .. ..	496	78	36	610	12

for mainly social reasons and 36 for reasons unspecified. Thus 610 patients, just over 1% of those studied, were admitted as a direct result of having measles. In addition, 43 were in hospital when they developed measles, and their stay in hospital was probably prolonged as a result.

The age and sex distribution of those admitted is shown in Table V. The proportion was high in infants and adults and much lower in older children. In adults the high rate was partly due to a relatively large number of admissions for social reasons. There was no sex difference in those admitted for medical reasons, but in those admitted for social reasons there was a considerable male excess in most age-groups.

The admission rate for each category of complication is shown in Table VI. It is perhaps surprising that only just over a quarter of those with neurological complications were admitted to hospital, and even among those with encephalitis, impaired consciousness, or fits the proportion was only 40%. Of persons with respiratory complications 18% were admitted. Very few were admitted with otitis media and nearly all of them had in addition some other more serious complication which was probably the reason for their admission. The high proportion of patients with other complications who were admitted is explained by the inclusion in this group of those admitted with severe measles and associated conditions, as described above.

TABLE VI.—Admission to Hospital for Selected Complications

Complication	No. Affected	No. Admitted to Hospital	Rate per 100 Complications
Encephalitis or impaired consciousness .. ..	61	24	39
Behaviour changes .. ..	64	2	3
Motor disturbances :			
Fits .. ..	80	33	41
Other .. ..	13	0	0
All neurological .. ..	203	55	27
, respiratory .. ..	2,022	355	18
Otitis media .. ..	1,338	37	3
Others .. ..	117	87	74
All complications .. ..	3,532	496	14

### Electroencephalograph (E.E.G.) Studies

Studies in the United States have shown that E.E.G. abnormalities occur in a considerable proportion of patients, even with apparently uncomplicated measles, although the recordings usually quickly revert to normal once the illness is over (Gibbs *et al.*, 1959). Children with neurological complications, however, might show more prolonged or even permanent abnormalities. To investigate this possibility Dr. G. Pampiglione, of the Hospital for Sick Children, Great Ormond Street, London, kindly agreed to take E.E.G. recordings in a few children in this inquiry reported to have had encephalitis or impaired consciousness.

Sixteen children from nine boroughs close to three convenient centres in Lancashire and Yorkshire were examined by means of a portable E.E.G. machine set up in the local public health department. The children, who had been ill from a few weeks to six months previously, had all made reasonably good clinical recoveries. All but two of them showed definite E.E.G. abnormalities, but in none was the abnormality severe, even in one who had remained in coma for several days. Abnormal discharges in the form of spikes or complex waves were notably absent in all but one of the children tested. A detailed account of these investigations will be reported elsewhere by Dr. Pampiglione.

### Discussion

The results of this investigation show that serious complications of measles are commoner than is generally supposed and cannot be ignored in any assessment of the need for universal measles vaccination. In an average epidemic year more than half a million notified cases of measles may be expected in England and Wales; the number of cases studied in this inquiry was just over 50,000. Thus, if the results of this inquiry are generally applicable, to obtain an estimate of the number of complications occurring in the whole country during an epidemic the figures should be multiplied tenfold. This would mean that about 35,000 patients might be expected to have serious complications, and over 6,000 be admitted to hospital. Of the complications over 2,000 would be neurological, including some 600 cases of encephalitis; 20,000 would affect

the respiratory tract and 13,000 the middle ear. These estimates are subject to two minor sources of error, acting in opposite directions: they tend to underestimate the true picture because only about 80% of cases are notified; but they may overestimate figures for the country as a whole because the survey was conducted exclusively in the northern conurbations and other large cities where children tend to contract measles at a rather earlier age than those living in smaller towns and rural areas (General Register Office, 1963).

Most patients recover completely from complications, but in an important minority permanent disabilities may result. Those with encephalitis may suffer intellectual or physical damage; severe pneumonia, sometimes caused by the measles virus itself (Robbins, 1962), may result in permanent damage to the respiratory tract and chronic respiratory disease in later life; otitis media may lead to chronic middle-ear disease. Follow-up inquiries will show how often irreversible damage occurs.

Such is the formidable toll exacted by a measles epidemic. The figures may vary from epidemic to epidemic, and it has been suggested that the 1963 epidemic was exceptionally mild in its effects (*British Medical Journal*, 1963a). The incidence of serious complications may also be influenced by the use of antibiotics given prophylactically, although the study by the College of General Practitioners (1956) suggested that they conferred little benefit except in selected cases. In the course of further inquiry it is hoped to discover whether complications recorded in this investigation were modified by the use of antibiotics. In the meantime it can be said that the results reflect complication rates under the present conditions of medical practice, and on these grounds measles can scarcely be regarded as a mere inconvenience. Moreover, measles is an unpleasant disease that imposes considerable discomfort on nearly every child at some time, as well as a burden of anxiety and work on parents and doctors.

The age distribution of cases corresponds to the normal pattern in advanced countries (Langmuir, 1962). In each year of life except the first before school entry at the age of 5, the number of cases was almost the same. Under 1 year of age most children were apparently protected up to the age of 6 months and many in the second six months also. McDonald and Cockburn (1954) obtained similar evidence of passive immunity, presumably derived from maternal antibodies, during the first year of life; it will be interesting to discover how many mothers of such children give a history of having had measles.

Miller *et al.* (1956), in an extensive review of the world literature, largely based on hospital admissions, estimated the incidence of encephalitis at about 0.9 per thousand. The rate for patients admitted to hospital in the present survey was only 0.5 per 1,000 compared with 1.2 per 1,000 for all patients. The fact that more than half the patients with encephalitis were not admitted to hospital emphasizes that an investigation restricted to hospital in-patients may give an unbalanced picture of the damage caused by measles. It remains to be seen from follow-up inquiries how many patients suffered permanent damage as a result of their illness, but the results of the encephalographic investigations showed that apparent clinical recovery was not necessarily accompanied by full physiological recovery, as was reported by Gibbs *et al.* (1959). Greenberg *et al.* (1955), in reviewing all the measles cases in New York City between January 1949 and July 1954, also noted an increased

incidence of encephalitis with age, similar to that found in this study.

The proportion of patients admitted to hospital was low but the absolute number in an epidemic is considerable. Each epidemic must therefore impose a burden not only on the young patients, parents, and doctors but also on the nation's economy.

### Summary

A postal inquiry into the frequency of complications in 55,589 notified cases of measles in 47 large boroughs in England and Wales was carried out during the first four months of 1963. Information was obtained on 53,008 (95%) of the cases.

About 1 in every 15 persons with measles suffered from a potentially serious complication and 12 patients died. The incidence of complications was highest in infants and adults, but there was no difference between the sexes. Severe bronchitis or pneumonia was reported in 38 per 1,000 cases; the rate in infants was nearly twice that in older children. Otitis media, the second most common complication, occurred in 25 per 1,000 cases and showed little variation with age or sex. Neurological disturbances occurred in approximately 4 in every 1,000 cases and one of the four had encephalitis or impaired consciousness. Fits and other motor disturbances were commoner in males than in females. Other complications were few. Just over 1% of all cases were admitted to hospital. Admissions were most frequently in infants and adults.

Electroencephalographic studies of 16 children reported to have had encephalitis or impaired consciousness with measles up to six months earlier showed mild but definite abnormalities in all but two cases.

Further inquiry into the state of health before the onset of measles and the late consequences of serious complications in a proportion of patients is planned.

The Medical Officers of Health and their staffs in the following county boroughs kindly assisted in this inquiry: Birkenhead, Birmingham, Blackpool, Bolton, Bournemouth, Bradford, Brighton, Bristol, Cardiff, Carlisle, Coventry, Croydon, Darlington, Derby, Doncaster, East Ham, Gateshead, Huddersfield, Ipswich, Kingston-upon-Hull, Leeds, Liverpool, Manchester, Middlesbrough, Newcastle upon Tyne, Newport, Mon, Norwich, Nottingham, Oldham, Oxford, Plymouth, Portsmouth, Preston, Reading, St. Helens, Salford, Sheffield, Southampton, Southend-on-Sea, South Shields, Stockport, Stoke-on-Trent, Sunderland, Swansea, Wallasey, Walsall, and Wolverhampton. Thanks are due to them and to the many practitioners without whose full co-operation in completing and returning record cards this inquiry would not have been possible. The investigation was supported by a grant from the Medical Research Council.

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