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Whooping Cough and Measles

An Epidemiological Concurrence and Contrast

By WILLIAM BUTLER, M.B.
(*Brevet Lieut.-Colonel, Retd.*)

THERE is an intimate association of whooping cough and measles. They are coupled in the popular mind as affections of childhood, normally to be expected almost as inevitably as those of teething. Familiarity had bred a contempt which their comparatively low case fatality appeared to condone and yet at the time when this contempt most prevailed their respective contributions to child mortality were each of them higher than those of any other infectious disease. One hundred years ago, whooping cough exacted on an average each year in round figures 500 deaths per million population and measles over 400, to-day their mortality has fallen respectively to about 30 per million. The decline in mortality set in earlier in the case of whooping cough and its quinquennial rates have been uninterrupted in their progressive fall during a period of over 60 years. Measles, which lagged in its decline until the beginning of the present century and at the beginning was less steady in its fall, has nevertheless during the last quarter of a century sustainedly reduced the lead until now the respective annual mortality contributions are about equal. It has long been noted that the mortality among females was higher than that of males in whooping cough and lower in measles. The decline throughout a prolonged period in mortality for each sex in both diseases has maintained the respective sex ratios, though if the crude death-rates of each sex at all ages be taken, the positions with regard both to measles and whooping cough are reversed in the years of the first Great War.

Batch fatality rates.—It is an obvious advantage to have recorded the case fatalities from current diseases continuously throughout the period of their occurrence. A rate relating deaths to the actual cases from which they derive, where that is possible, is the most reliable statement of case fatality.

The batch fatality rate computed by the method described in a paper on "The Fatality Rate of Measles" (*J. R. statist. Soc.*, 1945, **108**, Pts. 3 and 4) gives, I believe, a very close approximation to this result. It is true of the batch fatality rates advancing *seriatim* week by week with the returns that they assume the character of a moving average picking up belated deaths and dropping others which later are ascribed as fatalities of subsequent batches. This has the effect of slightly flattening the curves described by the varying rates but, if the pre-fatal interval obtains in anything like the proportions I have assumed on the bases of the somewhat limited analysis which has been available, the instances which do not strictly belong to the batch period must be very few in number. In any case, the rates do exhibit, very closely to what is actually occurring, fluctuations which with the same approximate accuracy are shown by no other method with which I am acquainted.

In an analysis made between thirty and forty years ago of 196 deaths from measles and of 187 deaths from whooping cough I found that while in measles 93% of the deaths had occurred by the end of four weeks from onset, only 75% of the deaths from whooping cough had occurred within that period. For this and for other reasons I considered that in the case of measles it was sufficiently near the facts to assume that if a fatal termination were to occur it would do so within five weeks of onset, which gave a batch period of nine weeks and a fatality term of five weeks and on this assumption the formula for calculating the batch fatality rate was constructed (*J. R. statist. Soc.*, 1945, **108**, Pts. 3 and 4). The error in the case of measles was negligible so far as the few cases dying outside these limits was concerned. In the case of whooping cough the difficulty of determining a period within which all fatalities would occur was greater. 25% of the fatalities occurred beyond the fourth week of onset of the disease and it is practically certain that not all—if even the greater part—of the remaining fatal cases would die within another week as might be practically assumed of the smaller residue in the case of measles. On the other hand the further the batch period was extended beyond that within which the bulk of the remaining fatalities actually occurred, the less definite was the relationship of the batch to the deaths to which it was presumed they were specifically related. Moreover, the deaths ascribed to whooping cough are more inclusive of all fatalities from this disease than are the returns of measles of the actual cases of death from morbilli, and for this reason: the chief causes of death from either of these affections are pulmonary complications. The diagnostic evidences of measles disappear with the eruption but those of whooping cough obtrude themselves for weeks after the onset of the disease. As a result pulmonary affections are recognized as secondary in higher proportion in the case of whooping cough: in measles the primary affection may never have been recognized, its diagnostic evidences having disappeared before medical aid was sought. It follows that the number of cases of whooping cough dying at the more remote periods from onset are recognized as such in greater proportion than in the case of measles. In assuming that whooping cough has a six weeks' fatality term, necessary for practical purposes, it has to be recognized that a higher, though relatively a small, proportion of the deaths which should be totalled in the six weeks' fatality term from cases occurring during the batch period of eleven weeks are carried over and included in succeeding fatality terms. This has the effect greater than in the case of measles of slightly flattening the curve of case fatality rates. Nevertheless it remains approximately correct and is a useful, though not an exact, figure. The batch fatality rates of measles and of whooping cough have been calculated for each week over the six complete years, 1940-45, during which these diseases have been notifiable (Table I). They are based on the Registrar-General's returns for London and the Great Towns and the respective formulæ used were:—

FORMULA FOR CALCULATING BATCH FATALITY RATES

Where serial cases and deaths are recorded week by week as in the Registrar-General's weekly returns of notifications, the batch fatality rate at the terminal week of each successive—Measles: 9-weekly, whooping cough: 11-weekly—period is:—

MEASLES

$$\frac{\text{The sum of the deaths during last five weeks} \times 1{,}000}{\text{(Half the sum of the cases of the first four weeks + all the cases of the middle week + half the sum of the cases of the last four weeks)}}$$

WHOOPING COUGH

$$\frac{\text{The sum of the deaths during last six weeks} \times 1{,}000}{\text{(Half the sum of the cases of the first five weeks + all the cases of the middle week + half the sum of the cases of the last five weeks)}}$$

TABLE I.—MONTHLY AVERAGES OF BATCH FATALITY RATES PER 1,000, LONDON AND GREAT TOWNS.

	Measles						Mean of monthly averages 6 years	Whooping cough						Mean of monthly averages 6 years	Whooping cough. Multiples of measles B.F.R.	
	1940	1941	1942	1943	1944	1945		1940	1941	1942	1943	1944	1945			
Jan. ..	4·1	3·4	1·7	2·4	2·9	2·6	2·8	13·0	15·8	14·2	15·3	15·7	17·5	15·2		5·0
Feb. ..	5·4	3·9	2·6	2·4	1·3	2·1	2·9	29·4	22·5	14·8	16·8	14·0	18·6	19·3	6·0	6·6
March ..	3·2	3·7	3·4	2·7	2·1	2·1	2·9	30·0	22·9	13·1	14·7	11·3	13·1	17·5		6·1
April ..	2·1	3·9	2·3	2·5	1·4	1·7	2·6	28·1	20·2	16·3	14·4	11·3	11·7	17·0		6·5
May ..	2·2	2·7	2·3	1·8	1·8	1·4	2·0	19·3	15·4	16·2	12·4	13·4	10·7	14·5		7·2
June ..	1·6	2·5	2·4	1·2	1·4	1·2	1·7	10·8	13·6	11·8	10·6	14·1	9·4	11·7	7·2	6·9
July ..	1·7	2·1	1·4	0·6	1·1	1·2	1·3	12·4	13·4	9·3	8·4	10·8	5·9	10·2		7·5
Aug. ..	1·6	1·4	1·2	1·3	1·6	0·8	1·3	8·9	12·0	8·7	8·5	10·6	8·0	9·4		7·3
Sept. ..	2·5	1·8	1·0	2·6	0·8	1·6	1·7	10·3	11·2	11·0	10·5	9·5	8·1	10·1		5·7
Oct. ..	3·4	3·0	2·0	2·7	1·8	1·6	2·4	13·9	11·0	14·4	12·3	13·8	8·0	12·2		5·1
Nov. ..	4·0	4·1	1·8	3·4	2·4	4·0	3·3	15·0	9·3	12·7	10·4	11·9	9·0	11·4	4·8	3·5
Dec. ..	2·7	3·1	2·2	3·2	2·6	1·9	2·6	12·0	10·4	14·3	15·3	13·7	13·0	13·1		5·0
Mean Annual ..	2·9	3·0	1·9	2·2	1·8	1·9	2·3	16·9	14·7	13·6	12·5	12·5	11·1	13·5		
Mean of two years	2·9		2·0		1·9		2·3	15·8		13·0		11·8		13·5		
Whooping cough. Multiple of measles B.F.R.								5·8	4·9	7·2	5·7	6·9	5·9			
								5·4 times		6·5 times		6·2 times				

Seasonal variations in fatality.—Perhaps the most outstanding feature of the batch fatality rates as well of measles as of whooping cough is the regular, and in the uniformity of behaviour, definitely characteristic variations with season.

As will be seen from Table I and fig. 1 there is a close correspondence in the seasonal variations of fatality in the two diseases. In both, fatality is lowest in the warmer months of the year. Measles falls below the mean earlier (May) than whooping cough (June) and the case fatality of whooping cough appears to be less adversely affected by late autumn than that of measles.

EXPLANATION OF GRAPHS

The graphs are of the differences, expressed as a percentage above or below the six-yearly mean, between the weekly numbers of cases averaged for each month and the weekly numbers of cases averaged for six years. The course of incidence, just as if of the actual monthly mean of weekly numbers, is shown in three successive biennial periods, either singly for each biennial span or by superimposition of three successive biennial graphs. The composite graphs are of the means of the cases so graphed and respectively comprised in the three successive biennial periods.

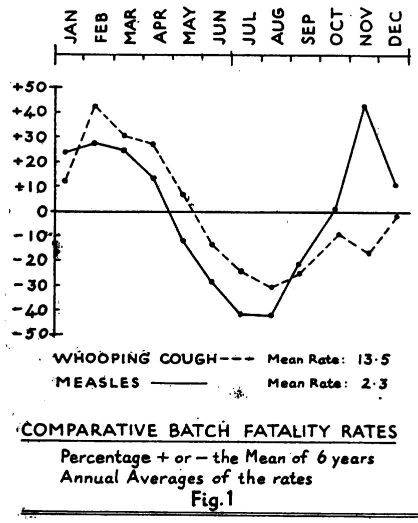


FIG. 1.

MEASLES

Fig. 5. Superimposed biennial distribution — 6 years ⟶

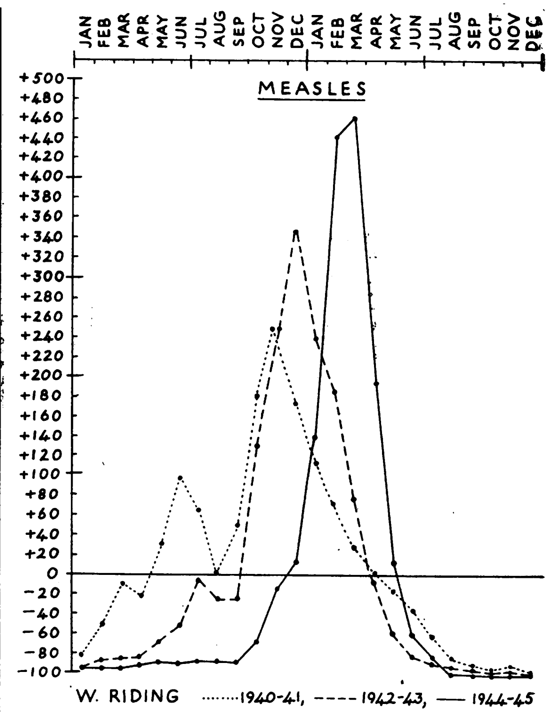


FIG. 5 (*see also* fig. 4).

Taking consecutive months in each third of the year, the four months, May to August, are more favourable to measles than to whooping cough which, in its batch fatality rates averaged for the period, has a multiple 7·2 times the batch fatality rates similarly averaged for measles. The first four months of the year are next more favourable to measles with a whooping cough ratio 6·0 times the average batch fatality rates of measles, while in the last four months, measles is relatively much more adversely affected, the multiple of whooping cough to measles average batch fatality rates falling to 4·8 times.

In Table II are set out the maximal and minimal rates among the serial batches of each year and the months in which they occurred:

TABLE II.—WHOOPING COUGH AND MEASLES MAXIMUM AND MINIMUM BATCH FATALITY RATES PER 1,000.

		Maximum during year	Month of occurrence	Minimum during year	Month of occurrence	The averaged mean of monthly B.F.R.s each year
1940	Whooping cough	32·9	February	8·1	August	16·9
	Measles	6·4	November	1·4	August	2·9
1941	,,	23·8	February	8·3	December	14·7
	,,	4·3	November	1·2	August	3·0
1942	,,	18·0	May	7·8	August	13·6
	,,	4·2	February	1·0	September	1·9
1943	,,	17·3	March	7·6	July	12·5
	,,	4·7	October	0·4	July	2·2
1944	,,	15·8	January	8·7	September	12·5
	,,	4·6	January	0·3	September	1·8
1945	,,	20·1	February	5·3	July	11·1
	,,	5·8	November	0·2	August	1·9

Yearly decline in case fatality.—Throughout the six years, the batch fatality rates both of measles and of whooping cough are unexpectedly low. The continuing decline from previously accepted rates to the low figures of the notification years is still to be observed as a process common to both diseases. During the notification period the measles batch fatality rate has declined by about one-third, that of whooping cough by about one-fourth.

If we turn from batch fatality rates to case fatality calculated on the annual totals of cases and deaths from either disease during each successive year, confirmation of this trend is disclosed and the behaviour of the rates not only of London and the Great Towns but of England and Wales also can be observed (Table III). Although case fatality rates calculated on these data, comparable over so prolonged a period, differ slightly from the batch fatality rates averaged for similar periods (Table I), they both tell the same tale.

TABLE III.—RATIO OF ANNUAL TOTALS OF DEATHS TO CASES FOR ENGLAND AND WALES AND LONDON AND GREAT TOWNS, MEAN ANNUAL BATCH FATALITY RATES, LONDON AND GREAT TOWNS AND WHOOPING COUGH MULTIPLES OF CORRESPONDING MEASLES RATES.

		London and Great Towns			London and Great Towns			England and Wales		
Years		C.F.R. Annual totals Deaths per 1,000 cases	Wh. C. multiples of measles C.F.R.	2 yrs. mean	B.F.R.	Wh. C. multiples	2 yrs. mean	C.F.R. Annual totals Deaths per 1,000 cases	Wh. C. multiples	2 yrs. mean
1940	Whooping cough	13·3	5·1		16·9	5·8		12·6	6	
	Measles	2·6			2·9		5·4	2·1		5·4
1941	„	15·4	4·5	4·8	14·7	4·9		13·7	4·9	
	„	3·4			3·0			2·8		
1942	„	13·6	8·0		13·6	7·2		12·1	7·6	
	„	1·7			1·9		6·5	1·6		6·6
1943	„	12·3	4·7	6·4	12·5	5·7		11·6	5·8	
	„	2·5			2·2			2·0		
1944	„	12·3	7·2		12·5	6·9		11·2	7·5	
	„	1·7			1·8		6·2	1·5		7·2
1945	„	11·5	6·4	6·8	11·1	5·9		11·0	6·9	
	„	1·8			1·9			1·6		

It is to be noted, however, that the high batch fatality rates of whooping cough in the early months of 1940, never afterwards approached, are, relatively to subsequent rates, probably exaggerated. Statutory notification of whooping cough and measles, recently imposed, was almost certainly less complete in the earlier months of its operation than later. There is, in the case of whooping cough, an additional lag due to the fact that notification is usually delayed until late when the whoop has developed. The diminution due to this delay is, when notification has got into its stride, in some measure, compensated by the legacy of preceding similarly-acting deferment. It is probably for this reason also that the annual averages of the monthly batch fatality rates give for the year 1940 a rate very considerably in excess of the case fatality calculated from the smoothing annual totals of cases and deaths. The year 1940 is the only one in the six years' series, in which there is a difference in the annual rates calculated by these respective methods, so great that it would show to the first place of decimals in rate, as commonly expressed, of deaths per 100 cases.

Measles fatality, it will be seen from the tables, is falling more rapidly than the case fatality of whooping cough both in the Great Towns, and in England and Wales. This retardation, relative to that of measles in the decline of whooping cough fatality, is the more clearly seen if, in the successive two-yearly periods in which the measles epidemics respectively run their course, the ratio of the fatality rates of the two diseases in the relative years is compared.

Case fatality in hospitals—M.A.B. and L.C.C.—The most reliable figures of case fatality in the pre-notification period come from hospitals where the numbers of cases and deaths are known precisely (Table IV). Unfortunately, however, owing to the selective character of the cases, these, in many respects, are not comparable with figures which would have been yielded by corresponding cases and deaths among the general population.

TABLE IV.—CASE FATALITY IN M.A.B. AND L.C.C. HOSPITALS.

Years	Whooping cough case fatality rate per 1,000	Measles case fatality rate per 1,000
1910–14 ..	108	116
1915–19 ..	123	109
1920–24 ..	100	90
1925–29 ..	130	69
1930–34 ..	91	52
1935–39 ..	57	28
1940–44 ..	34	6·4

Figures by courtesy of Sir Allen Daley.

Measles fatality has declined in hospital more rapidly than whooping cough though both continue to fall; and right up to the present time, as shown also by batch fatality rates, the reduction in case fatality is for both a striking and even an astonishing feature.

Persistent as for many years, within the limited field of observation possible, has been the decline in case fatality, notification revealed, at least in the case of measles, a fall which must be regarded as abrupt. This I have already discussed (*J. R. statist. Soc.*, 1945, **108,** Pts. 3 and 4). With regard to whooping cough, in a personal communication from Sir Allen Daley he says "that the sharp fall in case fatality in 1939 was shared by the whole community" and in support of this says, "Some comparison of the incidence of whooping cough in 1938 and 1939 can be made from the reports of cases noted by head teachers at schools, though these reports ceased to be complete after the middle of 1939, owing to the dispersal of school children. For the first six months of each year the figures are 2,025 in 1938 and 7,125 in 1939. Thus in the first half of 1939 the incidence was three times as heavy as in the same period of 1938. Deaths in the first half of 1939 were 91 compared with 72 in the first half of 1938, whereas the expected figure on 1938 case mortality would be in the region of 250". Case fatality on the above figures shows a fall of from 35 to 13 per 1,000 and is thus quite as striking in whooping cough as in measles.

In measles there seems good reason to believe that the decline in case fatality is in considerable measure due to changes in age-incidence, and it is possible that whooping cough fatality, which has behaved in like manner may be similarly accounted for. Dispersal of children which was so marked a feature of 1939, diffusing infection of measles, of whooping cough and other diseases among persons normally less in contact with infection and of higher age-periods than school children, hitherto the most intensively exposed, may well account for the abrupt fall in case mortality in both diseases. Stocks has shown that the dispersal of children had the effect in certain regions of keeping down the whooping cough rate in the evacuation towns, but in the reception areas evacuees with a higher incidence were mingling with an adult population less protected than that from which the children had been evacuated. It is not the whole story. There are other factors persistently modifying the course and character of these familiar epidemic diseases, but the dispersal of juveniles both in the evacuation and in the reception areas at the outbreak of war was calculated to produce just such striking results as we have observed.

Age distribution of cases.—So far we have considered the behaviour of case fatality at all ages. It has for long been established that both diseases are much more fatal in early than in later life and the case distribution according to age becomes important on this account, since case fatality will be higher the greater the proportion attacked at the more vital age-periods. I have been able to cull a random sample of some 15,000 cases of whooping cough and 33,000 cases of measles from recent annual reports of those relatively few Medical Officers of Health who have set out their analyses.

TABLE V.—AGE DISTRIBUTION OF APPROXIMATELY 15,000 CASES OF WHOOPING COUGH AND 33,000 CASES OF MEASLES.

(*a*) In County and Municipal Boroughs and Urban Districts.
(*b*) In Rural Districts.

	Whooping cough				Measles			
	All ages	0–1	0–5	5 and over	All ages	0–1	0–5	5 and over
(*a*) Urban	13,238	1,694	9,320	3,918	28,970	1,472	15,747	13,223
Percentage All ages = 100		12·8	70·4	29·6		5·1	54·3	45·6
(*b*) Rural	1,593	137	931	662	4,090	116	1,632	2,458
Percentage All ages = 100		8·6	58·4	41·6		2·6	38·9	60·1
Totals (*a*) and (*b*)	14,831	1,831	10,251	4,580	33,060	1,588	17,379	15,681
Percentage All ages = 100		12·3	68·8	30·2		4·8	52·6	47·4
Comparative sample Measles taken earlier in notification period.					25,628	1,087	13,495	12,133
						4·2	52·6	47·4
England and Wales 1944*		10·8	64·0	36·0		3·9	47·7	52·3
,, ,, ,, 1945†		10·7	66·7	33·4		4·3	52·7	47·0
,, ,, ,, 1946†		9·4	66·4	33·5		4·6	53·8	46·8

*Figures in Ministry of Health C.M.O. Rep. on the State of the Public Health, 1939–45.
†Figures in Registrar-General's Quarterly Returns.

The figures relate to cases of whooping cough and measles taken at random throughout England and Wales. In place and period their respective occurrence was identical. Those relating to Rural Districts are small but sufficient, I think, to reflect with approximate truth the differences between urban and rural incidence of these diseases. I have added to the table the figures of another and quite different random sample I had previously recorded (*J. R. statist. Soc.*, 1945, **108**, Pts. 3 and 4) of measles notifications similarly distributed. The almost identical proportions of distribution in these different samples is presumptive that they are characteristic. I think the figures demonstrate some important features in the recent behaviour of the two diseases.

(*a*) Whooping cough attacks infants in much higher proportion than does measles and both have higher incidence upon urban than upon rural infants.

(*b*) The proportion of persons attacked over 5 years of age is considerably higher in measles than in whooping cough and is much higher in the former than, before notification came into operation, one would have expected. Again the proportion is higher in rural districts than among urban populations.

During the first 6 months of life infants are little susceptible to measles but no such protection is afforded against whooping cough, in fact susceptibility to this disease in early childhood appears to be exceptionally emphasized. In the 0 to 5 age-group children are attacked in very much greater proportion in towns than in rural districts, as might be expected. Since liability to attack when exposure occurs must, in children not already protected by previous attack, be pretty much the same in both diseases and since opportunity of exposure must, in the more prevalent measles, be greater, it is difficult to understand why early childhood should be selected to bear the brunt of whooping cough and even though no congenital immunity in the early months of infancy safeguards the baby from this disease its native seclusion should afford sufficient protection save when other members of the family become affected. I have also included in the table the ratios of age-incidence of measles and whooping cough for England and Wales. It will be seen that the proportions to those at all ages, at the respective age-periods given in the random sample, are in agreement with those shown by the much more comprehensive figures, which, in fact, give ratios intermediate between those of urban and rural districts, not distinguished in the figures for England and Wales.

Sex incidence.—The ratios of male to female cases in all age-groups in 1944–46 are distinctive for the two diseases, and show very little variation with age except in the over 15 age-group in which the numbers of cases are small.

Unfortunately corresponding distribution of deaths is insufficiently available to enable case fatality at age-periods to be calculated on a scale that is adequate. London hospital figures (M.A.B. and later L.C.C.) show how at each age-period case fatality has been declining during the last thirty years.

TABLE VI.

	Whooping Cough				Measles		
1910–14	Cases	Deaths	Case fatality per 100	1910–14	Cases	Deaths	Case fatality per 100
0–1	675	165	24·4				
0–5	4,113	501	12·2				
5 and over ..	646	14	2·2				
All ages ..	4,759	515	10·8	All ages	11,925	1,388	11·6
1935–38				1935–39			
0–1	1,628	362	22·2				
0–5	8,194	636	7·8				
5 and over ..	1,217	21	1·7				
All ages ..	9,411	657	7·0	All ages	25,954	739	2·8
1939–40				1940–44			
0–1	871	77	8·8				
0–5	3,867	115	3·0				
5 and over ..	540	3	0·5				
All ages ..	4,407	118	2·7	All ages	18,286	118	0·6

TABLE VII.—ENGLAND AND WALES.

Whooping Cough and Measles Notifications. Proportional Age and Sex Distribution on Totals of 1944, 1945 *and Six Months of* 1946

	All ages	0–1	1–3	3–5	5–10	10–15	15 and over
				Whooping Cough			
Sex ratios 100 F/M	112	101	108	112	112	120	331
Proportion all ages =	100	M 11·1	28·3	27·5	30·1	2·4	0·8
		F 10·1	27·5	27·6	30·8	2·6	2·3
				Measles			
Sex ratios 100 F/M	100	97	94	97	99	110	203
Proportion all ages =	100	M 4·3	22·6	26·1	40·5	5·0	2·8
		F 3·9	21·2	25·2	40·2	5·5	4·2

As already pointed out hospital figures in many respects are not comparable with those relating to the general population. For well-known reasons they are higher, but there can be little doubt that they reflect at the times to which they relate, and in their respective age proportions, analogues in rates which differ from those of the general population principally in their order.

One fact of great interest remains unaffected by recent data. The established high fatality of both diseases in the first two years of life, greater in the case of whooping cough and especially in infants, is perhaps, from the point of view of preventive practice, the most significant feature in their behaviour. That whooping cough is more deadly even than measles in the first year of life is in part due to the fact that while most infants have a respite from measles during the first six months no such congenital immunity is extended to whooping cough. Approximately whooping cough has twice the opportunity in time to claim its fatalities in the first twelve months of childhood. There is for the young infant no compensatory protection from whooping cough which the sex of the mother predisposes her to contract and—whether on this account or not—in higher proportion than the male sex to die of the disease. Immunization of the mother by actual attack appears not to be as in measles congenitally transmissible even for a brief period. Moreover as Stocks has pointed out (*J. Hyg.*, 1932, **32**) "the loss of acquired latent immunity is more rapid than in measles and little or none remains after a year". In measles apparently it lasts for two or three years. Not only the acquired latent variety but the active immunity conferred by attack appears subject to the same rule. I myself have been the victim of three attacks of whooping cough at intervals approximately of twenty-five and forty-five years respectively between the first and second and the second and third occurrences. This is doubtless very exceptional though I have known of a number of adults who have suffered attack notwithstanding that in childhood they had undergone a primary salting. In measles second attacks are rare; in whooping cough acquired immunity is permanent to a lesser degree than the high protection extended usually for life in the case of measles.

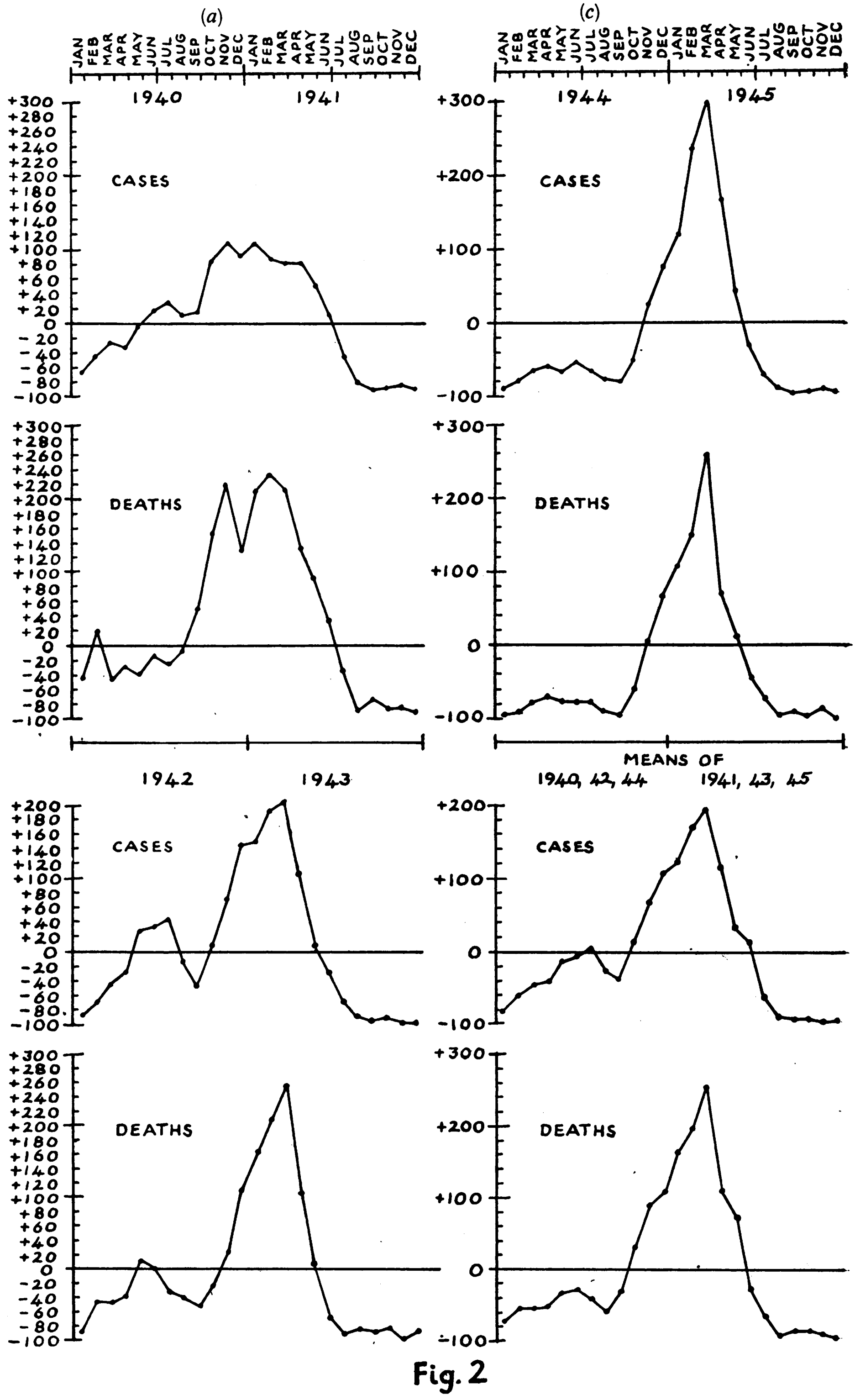
Immunities, congenital, latent or active following fully developed attack are co-determinants of epidemic developments and endings. With apparently universal susceptibility to whooping cough from birth, and to measles after six months of congenital protection, these diseases are the commonest and most widespread of the scourges of childhood. Deferred to the ages and seasons of low fatality, therapeutically cared for on a scale co-extensive with that of diffusion, there is, as a growing trend reflected in lower and declining fatality demonstrates, a prospect of protection to the community at a sacrifice which is but a fraction of that hitherto claimed. It is neither practicable nor desirable wholly to prevent diffusion throughout the community of ever-present infections to which all, until immunity has been acquired, are highly susceptible. It looks as though the time may not be distant when such immunity may be conferred by specifically directed measures. Till that is possible preventive efforts should consist, not in futile attempts by time-honoured but inappropriate means aimed at limiting immediate diffusion from cases, for this purpose belatedly coming to knowledge, but rather in noting the natural behaviour of these diseases by appropriate social and other administrative adjustments, so arranging that as far as possible the inevitable personal attack befalls when it is least dangerous to the patient.

EPIDEMIC BEHAVIOUR

The epidemiologist is concerned with the incidence of communicable diseases as seen affecting masses of the population. Their prevalence may be sporadic, epidemic, endemic or of a mixed description as when, between epidemic exacerbations there is a sub-epidemic activity maintaining at lower levels an endemic continuum. To this latter type both whooping cough and measles belong and in this respect differ from intermittent invaders such as, in Europe, are cholera, plague, smallpox and other occasional visitors. A succession of Registrar-Generals, and their medical advisers, have given voluminous, invaluable records, mostly in terms of deaths, of the courses and other epidemic features of measles and whooping cough in England and Wales. Six years of statutory notification of measles and whooping cough on an inclusive basis throughout England and Wales have placed for the first time at the disposal of investigators a store of facts which enables case distribution to be shown on a scale not only not hitherto available but on one sufficiently comprehensive to give a presumption of the distribution being characteristic. The six years' notification records relate to a period—war and post-war years—in which conditions affecting prevalence have been far from normal. It is possible, therefore, that we are dealing with somewhat atypical epidemic occurrences and so it would be wrong to assert of observed fact anything but its current truth. Nevertheless the broad features at least of measles epidemics appear not to have altered. I have made (*see Monthly Bull. Min. Hlth.*, April 1946) a comparison of graphs showing the composite weekly means of notified cases of the three epidemics of measles, London and the Great Towns 1940–1945, and the composite weekly means constructed from deaths and school-notified cases of three epidemics, London 1908–1913. As may be seen by reference to the graphs (reproduced with the article) the respective epidemics follow a common course in which resemblance in all outstanding features is very striking. Measles more than whooping cough exhibits repetitive epidemic features, though it is possible that in the case of whooping cough the gamut of the notification period is insufficient for the development of periodicity analogues, if, in fact, they occur.

Differences in the epidemic course, shown respectively by deaths and cases.—Comparison of corresponding graphs of cases and of deaths similarly plotted bears out what would be expected from consideration of the differences in seasonal case fatality. Taking the extreme range in the case fatality exhibited, that between the end of August 1945 and the end of January 1946, the batch fatality rates were found to vary from 0·2 to 7·6 per thousand. "A given number of deaths would at the lower rate yield a total of cases 38 times the number calculated at the higher rate" (*Monthly Bull. Min. of Hlth.*, May 1946). With a mean number of weekly deaths of 15 the calculated number of cases per week would, with this range of case fatality, vary from 2,000 to 75,000 and this potentially wide range of error, where a flat rate of fatality had to be assumed, inevitably must greatly disturb seasonal distribution when deaths are translated into calculated cases. The monthly distribution respectively of cases and of deaths each as a proportion of their respective six years' means does not, however, as may be seen from the diagrams, so greatly vary the main epidemic features that they are not in each series clearly exhibited. Taken separately either for the two-yearly periods within which each of the three epidemics ran its course (fig. 2, *a*, *b*, and *c*) or, for the average figures (fig. 2, *d*), seen in the six-yearly composite graphs, these features, characteristic of measles, are easily perceptible whether the graphs be of deaths or of cases. Alike, in contemporary and in successive epidemics, the minor and the major phases, the summer maximum of the minor phase, the autumnal notch, the re-commencing ascent in September–October, the maximum peak of the second year and thereafter the rapid fall and maintenance for several months in late autumn and early winter of a low, practically uniform level of sub-epidemic or endemic prevalence are common to all graphs. Nevertheless, differences and distortions of proportionate prevalence are shown in the death graphs as compared with those of actual cases. In the winter months, except when anomalous low fatality occurs, the graphs of deaths are relatively much higher and in the months of low case fatality proportionately lower than the graphs of cases. This has the apparent effect in the deaths graphs of greatly reducing the volume of the minor phases which attain their maxima in the summer months of low fatality, when cases are represented by few deaths, and of lengthening the peaks of the major phases which coincide with months of high case fatality when a given number of cases are represented relatively by more deaths. This, of course, is what we should expect and without more than indicating the kind and magnitude of these differences we may pass to consideration more fully of the graphs in which they are displayed.

The graphs.—During the six completed years within which statutory notification has operated—1940–45—all the epidemics of measles have bestridden the calendar divisions between years in each of all three successive biennial periods. The complete course of an epidemic, therefore, could be exhibited only in a span which included parts at least of two successive years. It was found that the beginning of the first year of each such span coincided approximately with a commencing epidemic rise, immediately following a sub-epidemic level sustained during several preceding months. Commencing at the beginning of one year each epidemic attained maximum incidence in the next and, some months before the end of the year, subsided, to just such a level as that from which it sprang.



MEASLES. LONDON AND GREAT TOWNS. Respective graphs of cases and deaths.

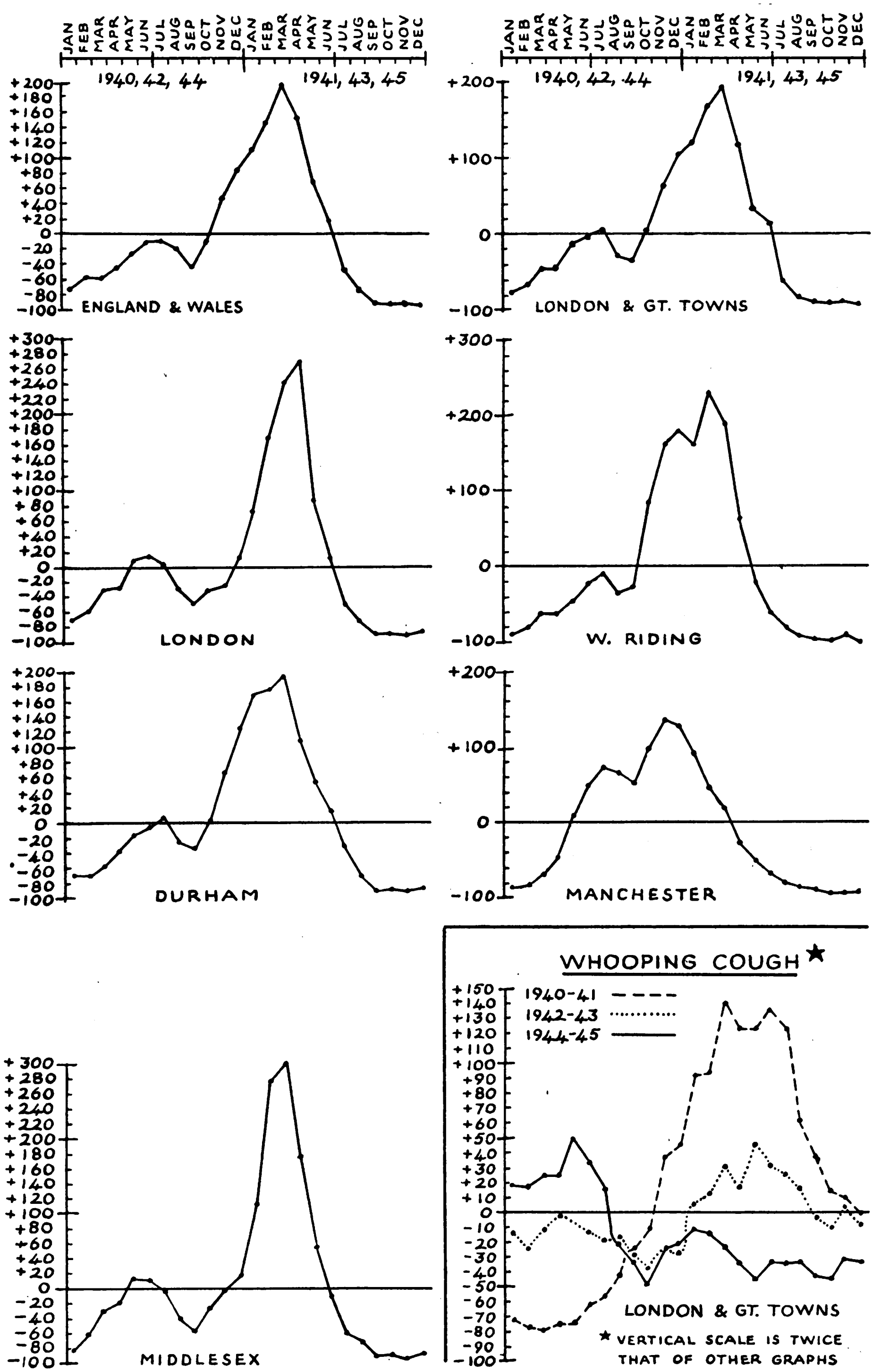


Fig. 3

MEASLES. Composite of Three Epidemics. Years 1940-1945.

It followed, therefore, that within each of three successive two-yearly spans into which the six years' notification period was divisible there were comprised an epidemic and a succeeding inter-epidemic period, each virtually complete. And this is so, as illustrated in the graphs whether the notifications for England and Wales, London and the Great Towns, counties such as Middlesex, the West Riding, Durham, Lancashire and Cheshire or great cities such as London, Manchester and Liverpool were severally subjected to such an analysis. While the course of a measles epidemic is thus displayed within a two-years' span, its actual duration falls well within that time. In none of the graphs does it exceed twenty months from the perceptible rise in January of the first year of epidemicity to its fall to sub-epidemic levels in August of the year following. And, indeed, there is little departure from this rule. It may, of course, be argued that within this span we are dealing, as has often been taken to be the case, not with a single, but with two epidemics. I think that the graphs render this view untenable, but this will be the better appreciated when we have considered more fully the features disclosed.

Epidemic beginnings.—The commencing point of each epidemic coincides approximately, as has just been said, with the beginning of the year of its initial development. But in the first, 1940–41, of the three series of epidemics which six years' notification has disclosed, already at the beginning of January a rise above sub-epidemic levels has been attained, but to a height which, if the curve be retrojected[1], places the start only a few weeks in advance of the commencing year. In the January, two years later, the level is a little lower and lower still, in fact barely perceptible, in the first month of the third two-yearly span. This means that each epidemic started just a little later in each succeeding epidemic period. This is not uniformly true of all the graphs, but is readily seen in those both of England and Wales (fig. 4*a*) and London and the Great Towns (fig. 2). The time of commencement does, presumably, make a difference to the subsequent development of an epidemic; the older it is, the sooner, *ceteris paribus*, its course is likely to be unfolded and completed. A procession of commencing dates and later developmental features in serial epidemics, should they, by more prolonged observations, be established, would greatly modify recurrent periodicities if they are, as they may be, chronologically, rather than seasonally, determined.

In the Statistical Review of the Registrar-General, 1921–25, attention is called to some notable changes in the seasonal curves of deaths from measles in which during a number of years "the gap between winter and spring peaks had filled up completely for London and almost completely for England and Wales. . . . The stages of this change for London are shown in the weekly returns from which it appears that in 1891–95 the February depression was pronounced, but that by 1911–15 its last traces had disappeared". It is the fact of these changes in peaks and gaps at the seasons named to which I wish to call attention. Neither the winter peak nor the February depression between it and the still surviving March maximum are generally to be recognized in the graphs of notifications with which we are dealing, though a cleft in the February of the major phase of the cases graph—England and Wales, 1942–43 epidemic (fig. 4*a*), and a similar depression corresponding in phase in the 1940–41 Durham epidemic (fig. 4*d*)—suggests that in these atavistic vagaries there may be a recent representative of the earlier notch. If over long periods certain valleys may be exalted and certain peaks laid low, the process, conceivably, may be one with a procession, a recession or an oscillation in the season of beginning epidemicity.

Epidemic phases.—The course of measles, graphed as above described, shows within each two-year span a minor and a major phase of epidemicity, separated by what I have called the autumnal notch and terminated by a spell of continuous sub-epidemic activity. Conformity to type is always a variable quantity and it is in accord with the proclivities of the typical that, in particular instances, wide departures may be shown amounting at times to total absence of a specific characteristic feature. In measles, epidemic types are no exception in their possession of aberrant members. For instance, the minor phase in the West Riding epidemic, 1944–45 (fig. 5, *see* p. 386), was wholly lacking and the epidemic, commencing in October, normally the eighth month of epidemic prevalence, continued thereafter in general conformity to the customary course, attaining its maximum in March—unlike its two predecessors with erratic maxima respectively in November and December—and completing its subsidence by August. But, lacking the minor phase, the epidemic is shortened to a single pinnacle of unwonted altitude, in this resembling the London epidemic of the same period where a minor phase, not lacking, but aborted, was followed by a similar pinnacle, the highest of any in the epidemics examined. Again in Manchester in the epidemic, 1940–41 (fig. 4*c*), the minor phase commencing late was merged completely with that of the major, the dividing autumnal notch being wholly absent and the customary low incidence of August replaced by a maximum peak in which the only tribute to the usual depression of

[1]Notification had come into operation only shortly before this and could not yet be said to have got into its stride.

that month was the break, not in the ascent but in its steepness previously uninterrupted from April to July. In the epidemic, 1942–43 (fig. 4*c*), again in Manchester, which acts to-day as England may to-morrow, the customary minor phase in May attained a maximum higher than that reached in the December of what usually is the major phase. That in London again the minor phase of the epidemic, 1940–41 (fig. 4*b*), was atypical, almost lacking in fact, was due no doubt as were other atypical developments of the epidemic to the very extensive evacuation of children which then characterized the metropolis.

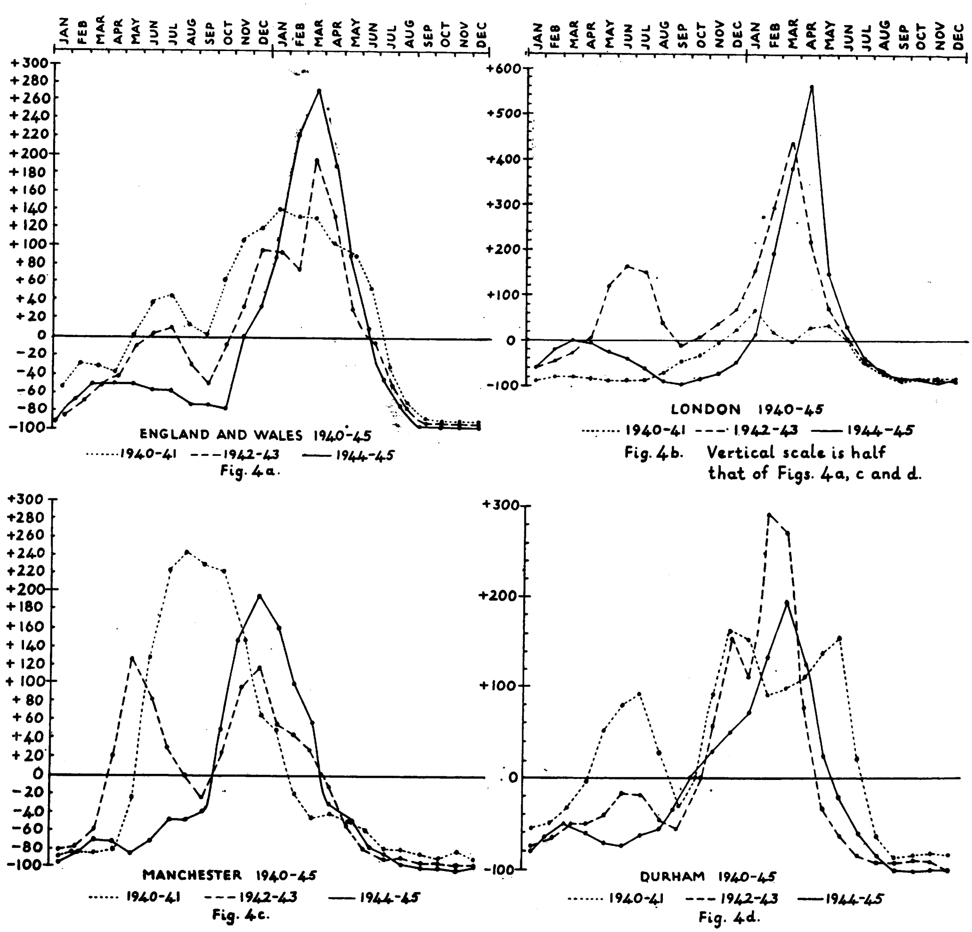


FIG. 4 *a*, *b*, *c* and *d*.—MEASLES. Superimposed biennial distribution—6 years.

It is to be noted that in none of the instances, in which these aberrant forms were presented, did the composite graph of the other two of the three epidemics depart from the type to which the others in the six years' records of the prevalence conform. Further, the chronological order of development in the aberrant types may vary and in their maximal incidence revert exceptionally to a season noted in the past as common and yet in general feature resemble what is claimed as the unmistakable type of current measles. It is as though, if one may import an animism, that when conformity to type was thwarted, a corrective reaction marked subsequent activities.

The sub-epidemic phase.—There is one other feature of the graphs of measles to which attention should be directed, a negative one, but different from the others in that it does not vary and so is common to all the graphs. In the September of the second year of epidemicity, incidence has fallen rapidly as a rule, to a level from which on the scale on which the graphs are drawn there is scarcely a perceptible change for the rest of the year. The monthly averages, ranging within the low sub-epidemic limits of between 80% and 90% below the mean, are represented from September to December by what is virtually a straight line. The earlier September level, following the minor phase in the first year of epidemicity is also, almost with the same invariability, the lowest, after the initial stage and before that reached with the final fall, in the whole course of epidemic prevalence, but unlike the fall in the September following, it is immediately, in October, followed by resumption of the ascent which had been interrupted by the autumnal notch. This difference in the behaviour of measles at the conclusion respectively of the minor and the major phases is, perhaps, as convincing an evidence that they are phases and not alternating minor and major epidemics, as any presented by the graphs. If the phases be conceded features of a single epidemic, biennial periodicity remains a suitable description of epidemic recurrences so related, even more appropriate because more embracing than when applied only to biennially recurring peaks separated by a void. On the other hand, if the minor phase be regarded as in no sense one of epidemic prevalence, either of one or of separate epidemics, it becomes a nondescript incidence, somehow relegated to sub-epidemic levels to which discernibly it rarely descends. Should one be able to rest in such a contradiction he would be free to regard the surviving major incidence exclusively as an epidemic, relatively short-lived and alternating with a year of non-epidemic mixed flat and undulating prevalence. This, usually, is what is meant by biennial periodicity. Yet again the minor phases as such may cease and, if enlarged and separated by definite sub-epidemicity from what follows, be regarded justly as completed epidemics. In that case, of course, biennial periodicity disappears and is replaced by annual recurrences. But in the graphs of incidence of recent years there is seen to be comprised within a single span of four-and-twenty months the proportioned phases not alone of epidemic prevalence but also of the low levels of intercurrent sub-epidemicity. Thus seen, periodicity ceases to be a biennial recurrence of punctual maxima and becomes a periodic repetition of like prevalences each in its due season, once within two years. Ultimately the present forms of measles prevalences may be shown to be, as presented, impermanent; they may prove to be transitional stages to or from such a form of biennial periodicity as, hitherto, for the most part, it has been conceived. If the movement be towards a single peaked form recurring biennially, the minor phase together with the autumnal notch will each disappear and be reduced to levels uniformly sub-epidemic; if away from such a biennially periodic type and towards that of annual recurrence, the minor phase will expand, the autumnal notch deepen, and there may thus emerge annually recurring epidemics separated by sub-epidemic phases, long and short in alternate years. Exceptional forms of prevalence among those examined may be said to be illustrative of either trend.

Epidemic behaviour of whooping cough.—So much for the serial distribution of measles: what of whooping cough? Similarly treated to exhibit features of prevalence, the graphs are not helpful. So far from conformity to design being established, type has not even emerged. In his account of the epidemiology of whooping cough, Professor Bradford Hill sets out the seasonal differences in deaths and, so far as then known, in cases. Except for the bearing upon them of seasonal case fatality, notification has added little, so far, to this aspect of whooping cough epidemiology. That the graphs suggest no law of incidence, no definite periodicity of recurrence, no characteristic case distribution and no rule in seasonal quiescence, may be due to the longer time-span required for their development. Certainly, neither in their annual nor in their biennial features do they show aught but a law unto themselves.

Dr. J. B. Russell, a former Medical Officer of Health of Glasgow, says (Public Health Administration in Glasgow. Studies in Epidemiology. Edited by A. K. Chalmers. Glasgow, 1905): "Estimated simply by the numbers of its victims, whooping cough is by a long way the most formidable infectious disease known to Glasgow. We might probably generalize and say the most formidable infectious disease of industrial cities. It shoots up into an epidemic at intervals of two to five years. . . . *But whooping cough never subsides to a low level. Its line of mean prevalence is high.*" This is true to-day. It is the high level of sub-epidemicity which is an outstanding feature of whooping cough, in the steady maintenance of which it contrasts with measles. Owing to this fact its endemicity is probably of more importance than its epidemic exacerbations recurring as they do at intervals normally much longer than those of measles. One sharply-defined epidemic only, and another of lower incidence, but more extended duration, occurred during the period (whooping cough graph, fig. 3). The first, commencing in April 1940, continued till the end of 1941, by which time it had fallen only to the mean level of six years' cases, having during the greater part of two years' epidemicity consistently maintained a high degree of prevalence. The second, commencing in December 1942, attained its first low peak in May 1943, and after a gradual decline and reascent, reached a slightly higher peak in May 1944, terminating as an epidemic by October of that year. For the rest of the six years, the incidence was that of a high endemicity, by no means of uniform level and subject to variations in weekly incidence not unlike those of its epidemic periods.

Inter-epidemic prevalence.—The low levels of incidence to which, between epidemics, whooping cough relatively and measles positively sink, have an interest for the epidemiologist not less than the striking, occasionally violent, outbursts which from time to time dominate attention.

In measles, a just-continuing persistence, in whooping cough, an apparently erratic sub-epidemicity, are the reservoirs from which spring the spectacular outbreaks apt to monopolize observation to the neglect of the no less important, though less obtrusive, modes of prevalence.

Not apparently seasonally determined, though, as seen in the measles graphs, regularly from September to December, in alternate years, seasonally exhibited, they are an enduring source from which, when circumstances favour, are started the rising prevalences that culminate in epidemics. Whooping cough shows little proclivity to regular periodicity either in its general or inter-epidemic features and measles, in this phase of prolonged quiescence, is in contrast with its seasonal behaviour in alternate years, when, in the same months, following the autumnal notch, there is, normally, a rapid and continuing rise to epidemic heights.

It cannot be that identical months exhibit seasonal influence in so diverse a manner, and alternating seasonal exhibition of these opposed phases of incidence can mean only that they are determined otherwise than by seasonal influences. But the significance of the continuing lowered incidence between epidemics of measles and whooping cough is that in this endemic diffusion the train is laid so that never are the potentially explosive foci arising with each cessation of epidemicity far removed from the smouldering embers so readily converted to igniting sparks.

In neither of these affections is there reason to believe that the *materies morbi* have an independent, extra-corporeal career. Proliferation of the virus is almost certainly synonymous with microbial cytogenesis within the bodies of its increasing victims. When Brownlee (*Proc. R. Soc. Med.*, 1919, **12**, 77) speaking of measles announced that "An epidemic is due chiefly to the properties of the organism causing it and that the periodicity of epidemics which occur at regular intervals depends for the most part on the life-history of the organism" he may have been prepared to accept the proposition that there was no reason to believe that at any time in its life-history was the measles organism saprophytic, and, if this be so, the significance of endemic continuity needs no emphasis. And we may, in passing, inquire as to whether periodicities or other features of epidemics can properly be spoken of as determined mainly by the properties of the organism causing them or, conversely, as due to co-ordinate qualities, the necessary proportionate correlative vulnerability in the populations threatened. The antithesis is false, for apparent variations in virulence of the organism are meaningless save in terms of implicit constants of susceptibility or alternatively of corresponding changes in immunity of infected persons. Infective, susceptible—obverse aspects of the same phenomenon, how shall we say of either that it is the chief; upon which of two reciprocals, for the most part, depends a result to which both are indispensable? The cause of an epidemic is never wholly the diffusion of organisms of constant or changing pathogenicity, never alone an accumulation of relatively susceptible persons, but always the two together. Without one and the other you cannot have the resultant cases.

Conclusion

Though whooping cough and measles are kindred epidemiologically, in many of their features, clinically, they are most dissimilar. Measles, one of the exanthemata akin to small-pox with which its affinities are so close that for long the diseases remained undistinguished one from the other, is in a category removed from the non-eruptive disease that has taken its description from its mastering, paroxysmal cough. Initially more catarrhal, more sharply febrile, brief in its duration if uncomplicated, measles spends itself selectively in inflammatory epithelial lesions.

Whooping cough, more insidious in its onset, prolonged in its growing distress, less prone primarily to involve the tissues in extensive inflammatory changes, is almost devoid of pathological histology. Increasingly, as it matures, its symptomatology is that of neural disturbance. The paroxysmal neurosis dominates, sharing in wider, less terrorizing functional disturbances unaccompanied by perceptible structural neural changes, the selective toxins of whooping cough in this differing from those of diphtheria which so often result in late organic paralyses.

That two diseases, clinically so unlike, each presenting fundamental contrasts of behaviour, measles notably in its biennial cycles of recurrence, whooping cough in this and other respects in erratic disunity, should yet otherwise exhibit so close an epidemiological concert and together have travelled so far toward a common destiny, is an unexpected result from so strangely assorted a yoking. Preventive technique must aim not, as in such epidemic diseases for instance as typhus and typhoid, at attempting to prevent their prevalence, but at cultivating the immunizing process of which they have ever been the active, and in this respect collectively speaking, beneficent agents. Until this can be reliably effected by the promising prophylaxis of the immunologists, the path of still further fostering the natural course, the diseases themselves exhibit must be followed. Since the passing of the Public Health Act of 1875 the annual mortality they exact has fallen for each from over 400 to about 30 per million population, unaccompanied, so far as we can judge, by any corresponding or even positive fall in prevalence. This, the most signal feature in their behaviour, brings into striking relief the epidemiological importance of their case-fatality and marks the goal of the inevitable partnership they have imposed upon the human race, a more benign schooling to their wellnigh universal endemic-epidemic sway.

Dr. J. Alison Glover: Colonel Butler has, I think, triumphantly vindicated the epidemiological value of the notification of both diseases. Its practical value has, of course, been somewhat obscured during the war years by the shortages in medical, nursing and health visitor staffs and will become more obvious as these are restored to full strength.

In the decennium in which I began to study medicine, on an average 12,500 persons died each year of measles, and 11,500 of whooping cough. In the decennium ended 1945 the corresponding averages were 986 and 1,284. These impressive figures represent the saving each year of many thousands of lives and also a much lower incidence of those complications which, even when they do not kill, so often permanently damage health. There is little doubt that the immediate deaths form only a part of the mortality ultimately due to these two diseases.

The case fatality of measles, though it has varied greatly in different epidemics, used to be reckoned at about 4%. In 1945, though this was an epidemic year and 446,828 cases were notified, it was only 0·16%, about one-seventh of the immediate fatality rate of whooping-cough in the same year. Contrast this with 1918 when a modified system of notification (of the first case only in each family) was enforced, 414,346 cases were then notified, though of course there were many more. The number of deaths was 9,856 (nearly fourteen times as many as in 1945). Even if we assume that on average two cases occurred in each family, though probably this would over-estimate the actual number, the fatality rate must have been many times as great as that of 1945[1]. Colonel Butler has pointed out the very interesting sex ratio in the relative mortalities of the two diseases. It is an interesting point which I have not seen emphasized elsewhere that another disease, bacillary dysentery, resembles measles in that male infants and young boys show a higher notification of, and a much higher mortality from, dysentery than female infants and young girls, although in dysentery this higher young male incidence is much more pronounced and persists to a later age.

[1]Rep. of Chief Medical Officer of the Ministry of Health, 1945, 4. H.M.S.O. 1947.