THE MILROY LECTURES ON CHANGES OF TYPE IN EPIDEMIC DISEASES.

Delivered at the Royal College of Physicians.

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LECTURE III.

Prevalence determined by External Conditions.—Not accompanied by Change of Type.—Milk Epidemics.—Water Epidemics.—Seasonal Prevalence.—Accumulation of Susceptible Persons.

ALTHOUGH change of type is an important factor in determining the fluctuations in prevalence of epidemic diseases, it is not the only factor. Wide diffusion may take place without increased severity; and, indeed, it is not an uncommon experience to find that sudden epidemic extension is accompanied by apparent lessening of average severity and lowering of the case mortality. This involves no real exception to the general rule, that the tendency to epidemic diffusion is greatest when the intensity is at its maximum. There are obviously three principal classes of conditions upon which epidemic prevalence depends: (1) the energy of the contagium itself, its power of withstanding hostile influences and of overcoming resistance; (2) the facilities for transmission of infection to susceptible persons; (3) the susceptibility of the individuals upon whom the contagium is to be grafted.

The conditions which come under the second head include the varying degrees of proximity, from the closest contact to complete isolation; atmospheric states favourable or unfavourable to diffusion; and transmission by other media, such as water or milk. These are constantly changing, and however orderly the rise and fall of intensity may be, the prevalence will be modified at every phase by a multitude of extraneous conditions. Without any change in the real infectiveness of a disease, an epidemic, or at all events prevalence, may be brought about by sudden increase in the facilities for infection of susceptible persons; or conversely the conditions may become unfavourable, and the prevalence thereby be lessened without any loss of intensity in the type of the few attacks which occur. Such mechanical outbursts or interruptions, due to causes which are in a sense accidental, and usually temporary in character, have one important feature in common, which presents a conveniently sharp contrast to the broader cycles determined by altered quality of the contagium. They are attended by a lowered case mortality. If, during the course of an epidemic or in an inter-epidemic interval, a sudden increase of prevalence be brought about by accidental circumstances of weather, or food infection, or the like, the proportion of fatal attacks during that exceptional prevalence will be less than in the more normal periods which precede and follow it. Such a relation is antecedently probable, and is in harmony with actual statistical observations.

It seems reasonable to assume that those persons who are most susceptible to attack will be most readily singled out for attack; and moreover that among such persons the attacks will on the whole be more severe than among the less susceptible. If therefore a wide extension of prevalence occurs, it will be mainly at the expense of persons whose susceptibility is not of the highest order, and whose chance of recovery is greater for that reason. The aggregate case mortality will therefore be lowered, if the energy of the contagium remains unaltered. Perhaps the converse proposition is even more self-evident. If an epidemic, instead of being widely diffused, is narrowed down to a small fraction of the population, it is probable that the few who are still subjected to attack owe their selection partly to a higher average susceptibility, and that among these specially susceptible persons the attacks will be more severe. In a mixed community small-pox attacks the unvaccinated in far larger proportion than the vaccinated, and with far greater case mortality. If, therefore, the disease, instead of being limited to the former

class, extends in some degree to the latter, the gross case mortality will be lowered by this change, which involves an increased average resistance in the persons attacked. Another simple illustration is afforded by milk epidemics of scarlet fever, such as that which occurred at Wimbledon in 1886-7. The disease was not left to follow its usual course, and pick out the more susceptible portion of the population for attack. Infection was imparted to the milk, and by that means forced as it were upon a large number of persons selected at random. Some of them resisted attack altogether, others suffered slightly, a few more severely. There were only three fatal cases among 600, a case mortality of 0.5 per cent. That milk epidemics of scarlet fever are rarely severe in type was pointed out several years ago by Sir George Buchanan and Mr. Power; and the observation has been amply confirmed by later experience, although in exceptional instances (at Halifax in 1881 for example), the fatality has been high. Milk epidemics of enteric fever also seem to be attended as a rule with low average case mortality, although there are notable exceptions. It was only about 10 or 12 per cent. in the Armley, Moseley, Marylebone, and other well known outbreaks, and little more than half of this at Eagley and Bolton in 1876, and at Glasgow in 1875. As regards diphtheria, it is scarcely possible to fix upon a standard for comparison, but the recorded case mortality in milk diphtheria epidemics on the whole seems to be somewhat lower than that observed in diphtheria epidemics due to other causes.

The question is not always a simple one. Now that bovine scarlet fever, diphtheria, and perhaps enteric fever have come to the front, we have to bear in mind the possibility of attenuation (or the reverse) of the disease by passage through the cow, as well as the suspicion that the character of the attack may be modified by the magnitude of the dose of poison. Then, again, Mr. Power has given reasons for believing that the diphtheria poison may multiply in milk if left standing for some hours, possibly increasing in virulence as well as in quantity. But these elements of uncertainty leave untouched the general proposition that if compared upon equal terms, the average case mortality is lowered by this as by other mechanical facilities for the diffusion of infection, so far as it is merely mechanical. Milk epidemics, as a rule, are of very brief duration, dying out speedily without lighting up any lasting prevalence; and from a theoretical standpoint it is to be anticipated that such would be the case. Their occurrence (unlike the beginnings of an ordinary outbreak), does not presuppose the existence of other external conditions favourable to wide extension. It seems, too, that the infectiousness of individual cases of this kind is not great.

Similar considerations apply to water epidemics. They are usually attended with low case mortality, although the uncertainty as to the dose of poison is a disturbing influence, and indeed it may be open to question whether the mildness of attack which characterises great water epidemics may not be due in part to minuteness of the dose forced upon the persons consuming the water. When the volume of water polluted is limited, the concentration may be supposed to be excessive and the dose large. Dr. Barry has found that when enteric fever arises from pollution of a well the attacks are often severe; but that water epidemics on a large scale, as at Bangor, and more recently in the Tees Valley, a low average case mortality has prevailed. In the Caterham epidemic of 1879, investigated by Dr. Thorne Thorne, 14 died out of the 305 attacked, the percentage being, therefore, 4.6 only. At Mountain Ash, in 1887, an epidemic of enteric fever occurred, which Mr. Spear found to affect very unequally the persons living respectively inside and outside a certain small area supplied by a particular water main. Within this special area, 179 per 1,000 were attacked, outside it 6 per 1,000 only. Only 6 per cent. of the cases were fatal.

A third and still more important kind of prevalence is that which from its constant relation to season is assumed to be connected with weather and climate. So far as scarlet fever, enteric fever, and small-pox are concerned, these seasonal changes prove upon investigation to be simply changes in prevalence, without any real alteration in intensity; but, on the contrary, the maxima are attended with a somewhat lower case mortality than the minima. They are, in short, "super-added" waves, like milk epidemics and water epidemics.

If the average seasonal curve of attacks, or even cases admitted to hospital, be compared with the seasonal mortality curve of the same disease, it will be found that the former, while closely parallel with the latter, is somewhat in advance of it at every phase. The attack curve, moreover, has a wider range than the other; it rises higher and falls lower. Since the seasonal maximum of attacks does not carry with it a proportionate excess of deaths, it follows that the attacks at that phase are on the average less fatal; and conversely, as the falling off in number of attacks at the lowest phase is not attended by a corresponding reduction in the number of deaths, the comparatively few attacks then occurring must be somewhat more fatal than the average. In the Annual Summary for 1890 the Registrar-General gives charts which illustrate these points, especially as regards enteric fever and small-pox. In making the comparison, two cautions are necessary. The Registrar-General has pointed out that the mortality curve will naturally be somewhat flatter and less acute than the other, since the deaths arising out of a group of cases admitted or notified in a given week may be spread over several successive weeks, and especially in diseases of long average duration. Dr. Longstaff¹ calls attention to the possibility that limits of hospital accommodation may at times of maximum prevent the admission curve from rising as high as it otherwise would. But after making due allowance for these sources of error (which tend in opposite directions, so far as the present comparison is concerned), the contrast is marked. In the charts referred to the Registrar-General compares in respect of each disease the average seasonal curve of mortality with that of admissions to the various isolation hospitals in London. The admission curve of enteric fever rises 100 per cent. above and falls 50 per cent. below the mean, while the death curve has a range little more than half of this (+50 per cent. and -30 per cent.).² As regards small-pox, too, the difference is strongly marked, the admission curve reaching +70 per cent. and -60 per cent., and the death curve only +30 per cent. and -40 per cent.; but owing to the periods of record being different the two curves are not altogether parallel, the winter maximum being far more prominent in the death curve, based upon fifty years' statistics, than in the hospital curve, which relates only to fifteen years, 1876-90.

In an earlier chart³ of similar character the concurrence is closer, the admission curve being calculated upon five years' experience only. In both instances the contrast as to range between the admission and death curves is obvious, and confirms the relation between maximum seasonal prevalence and lessened average fatality of attack. We may conclude from the difference between the two admission curves referred to, that small-pox since 1880 has somewhat altered its seasonal curve, the spring maximum having become much more pronounced and the winter maximum less so. The differences between the death curve and admission curve for scarlet fever are slight, and notification statistics⁴ afford a clearer contrast. Still the attacks, measured in either way, rise higher above their mean in autumn, and fall further below it in spring, than do the deaths, and the same inference of lessened case mortality in time of seasonal prevalence may be drawn. As regards measles, there are few data for comparison, but Dr. Harvey Littlejohn⁵ has given us the seasonal curves of attacks and deaths for the ten years 1880-89 in Edinburgh. They are closely parallel, and, so far as the principal maximum in spring is concerned, there is no indication of altered case mortality, the crests in the two curves being of equal height, but the attack curve falls rather lower than the death curve at the minimum, and the smaller maximum in December is more marked in the attack curve than in the

other. The epidemiological character of measles is such as render it unlikely that any strong contrast would appear. The epidemics are brief and widespread and the attacks in the intervals are few. Hence the data are made up almost exclusively of the records of epidemics, the attacks and deaths which occur during the intervals being too few to materially affect the averages or to afford any basis for comparison.

Among certain diseases of mobile type, and particularly those which are dependent upon changes in the soil, the seasonal curve has a different meaning. The seasonal maximum of prevalence is the result of increased virulence, and of necessity the average severity of attack is greater at that time. The lowered case mortality of enteric fever during the autumnal prevalence divides it sharply from the purely telluric group in this respect. Diphtheria again is liable to rapid change of type, and it may be that seasonal conditions bring about intensification as well as wider diffusion of the contagium. The notification figures quoted by Dr. Thorne Thorne,⁶ lend some support to the idea that the case mortality in diphtheria is on the whole increased during the period of maximum seasonal prevalence, but further evidence is needed.

It would seem that, in small-pox at all events, the seasonal curve is of wider range during periods of greater epidemic intensity than at other times. Buchan and Mitchell⁷ found that this was the case in 1870-71-72 to a very marked degree, as compared with the other years for which records were available. Indeed the figures given by them show a gradation in this respect in successive quinquennia, from the point of minimum mortality in the fifties to the great epidemic of the early seventies, a gradation which is in keeping with other indications of progressive change in the character of small-pox during that period. In the following table the range of the seasonal curve is measured roughly by the percentage excess of the January maximum over the September minimum.

Small-pox Deaths in London.

	Deaths in First Four Weeks in January.	Deaths in Last Four Weeks in September.	Percentage Ex- cess of Maximum over Minimum.
During 1840-44 ...	485	345	41 per cent.
" 1845-49 ...	462	288	60 " "
" 1850-54 ...	317	207	53 " "
" 1855-59 ...	263	217	21 " "
" 1860-64 ...	324	233	39 " "
" 1865-69 ...	406	228	78 " "
" 1870-74 ...	984	372	165 " "

From this it appears that as the destructiveness of small-pox increased in the sixties, so did the range of its average seasonal curve. If however the quinquennia are traced backwards from the time of least mortality, in the direction of the previous great epidemic of 1838, the otherwise accordant indications are interrupted by a conspicuous lessening in intensity of the seasonal curve in the years 1840-44. Another point of some interest in connection with the seasonal curves of infectious diseases is that they are often of wider range where climatic changes are more intense and more orderly. This is seen for example upon comparing the curves of small-pox, measles, diphtheria, and enteric fever (not however of scarlet fever or whooping cough) for London and New York respectively.⁸

The varying incidence of infectious diseases at different seasons is no doubt dependent directly or indirectly upon climatic conditions. It has been suggested that social relations have much to do with it, there being closer aggregation indoors in the colder months, but this explanation is negated by the want of uniformity among the diseases in ques-

¹ *Studies in Statistics*, p. 403.

² In the Annual Summary for 1880 the Registrar-General states that "it appears from the records of the London Fever Hospital 1848-57 that out of an equal number of cases of enteric fever, about as many die in one quarter of the year as another; the spring quarter, however, showing a slightly greater fatality among its cases than any one of the other three." It is not to be anticipated that hospital cases would include a full proportion of the slighter attacks, but it seems from the above observation that even among those of sufficient severity to bring them into hospital there is some indication of higher case mortality at the period of the spring minimum.

³ Registrar-General's Annual Summary, 1880.

⁴ *Trans. Epidem. Soc.*, 1887-8, p. 176.

⁵ *Ten Years' Compulsory Notification of Infectious Disease in Edinburgh.*

⁶ *Diphtheria, its Natural History, etc.*, p. 32.

⁷ *Journal of the Scottish Meteorological Society*, 1875, p. 193.

⁸ Buchan and Mitchell, *Journal of the Scottish Meteorological Society*, 1878.

tion. Some infectious diseases are most prevalent at the beginning of winter, others at the end. Scarlet fever reaches its maximum in England in October, in Germany and Scandinavia in January, in New York in April or May. And, further than this, the rise begins long before the maximum is reached; so that if it be alleged that the commencement of winter conditions causes the maximum of scarlet fever prevalence to be reached in October, it still remains to be explained why the rise begins as early as May, and continues throughout the summer.

Perhaps the most unequivocal instances of "seasonal" waves dependent upon social conditions are those which arise from the difference in risk of exposure to infection on Sundays as compared with other days of the week. Thus the rash of small-pox has been stated to appear most commonly on Sundays among domestic servants, the usual interval between infection and rash being fourteen days, and the chance of outdoor infection being often limited to Sunday. The notification records of Nottingham show a very decided minimum in the number of onsets of scarlet fever occurring on Wednesdays, corresponding, as it would seem, to a minimum risk of infection on Sundays.

ON THE ESTIMATION OF SUGAR IN URINE BY THE PICRIC ACID METHOD.

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I AM anxious to explain to the profession my reasons for making a slight modification of the standard-colour solution, which for some years I have used in estimating the amount of sugar in urine. I have recently discovered that the manufacturer of my micro-saccharometer has been in the habit of graduating the tube by *external* linear measurement, and not by its *internal* capacity. The tubes employed not being of uniform calibre throughout their length, the result has been inaccurate graduation.

The standard colour was arrived at by imitating the tint given by a four-grain to the ounce solution of pure glucose, boiled with picric acid and potash, according to the method described by me in my two lectures on Albumen and Sugar Testing (Smith, Elder, and Co.), and in the chapter on Sugar Testing, in my *Medical Lectures and Essays* (J. and A. Churchill), and subsequently diluting four times in the graduated tube.

Now, as the upper divisions of the tube were more capacious than the lower, the result was a slight degree of over-dilution and a somewhat paler colour than would have been produced in an accurately graduated tube. Inasmuch as the same tube and the same method of procedure were adopted in analysing urines, the results obtained by me have been practically correct.

In order to avoid any error in future, I have corrected the standard colour solution by imitating the tint produced by diluting a solution of pure glucose in an accurately graduated tube, made for me by Mr. C. E. Müller, of 148, High Holborn, W.C., who will guarantee the accuracy of all graduated tubes supplied by him for my micro-saccharometer.

The corrected formula for the ferric acetate standard is as follows: R Liq. ferri perchlor. fort. (P.B. sp. grav. 1420) 3j; acid. acet. glacialis (P.B. sp. grav. 1058) 3iv; liq. ammoniæ (P.B. sp. grav. 959) 3ij; aquam destill. ad 3iv. The only change in this formula consists in the addition of π xx of liq. ammoniæ in the 4 fluid ounces. Since this method of analysis gives extremely accurate results, it has appeared desirable to indicate even so slight a source of error as that which I have here described.

THE late Signor Siro Valerio has bequeathed 1,130,000 lire (£45,200) as the nucleus of a fund for the foundation or transference to Milan of a university for the study of the sciences, or at least some section of them—preferably medicine and surgery.

ON THE RESTORATION OF THE FUNCTION OF MICTURITION.¹

By REGINALD HARRISON, F.R.C.S.,
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At a meeting of the International Medical Congress at Copenhagen in 1884,² I brought under discussion a method of dealing with the enlarged prostate when, in addition to retention of urine, it had caused other serious symptoms of obstruction and inflammation which were not at all, or imperfectly so, relieved by ordinary catheterism. This method consisted in puncturing the membranous urethra on a median grooved staff so as to obtain access to the interior of the bladder, as in Cock's well-known and useful operation. This preliminary having been accomplished, the prostate was dealt with in one of three ways, according to the circumstances elicited by exploration with the finger: (1) By division of the prostatic bar or floor of the gland; (2) by the enucleation or removal of some portion of the prostatic ring or outgrowth, or (3) by the mere stretching or divulsion of the canal with the index finger or sound. Whatever method of dealing with the canal as it passed through the prostate was adopted, the introduction and retention of a suitable drainage tube invariably followed. For the first few days a gum-elastic tube of some rigidity was selected, which gave place to one specially made of india-rubber for the purpose. The process of drainage was then continued for varying periods of days, to two or three weeks. A short time ago I had occasion to inquire into the results I had obtained, and to follow out as far as it was possible the later history of these cases. I found I had operated in somewhere about thirty-five cases of advanced prostatic obstruction in persons about 60 years of age, excluding, as far as I could ascertain, malignant growths, for the general reasons already assigned. In eighteen of these cases the floor of the prostate was divided, or a portion of the gland removed, whilst in eighteen drainage alone was effected. Without going into details which have already been published, it is sufficient for my purpose to state that in ten of these instances I was able to satisfy myself that the function of micturition had been restored, in addition to the immediate relief to retention the operation universally gave.

About the same time that I was engaged upon these observations I described³ a method of puncturing the bladder from the perineum, which has since been referred to as "tunnelling the prostate." This proceeding was also followed by more or less bladder drainage by means of the cannula that was used instead of a drainage tube. In illustration of this kind of practice I published the particulars of a case, where, in a man 84 years of age, shrinkage of the hypertrophied prostate and complete and permanent restoration of the lost function of micturition followed, the patient living and being in good health to the age of 90.

Further, as bearing upon the point under consideration, I would make reference to what has, not very infrequently, been observed in connection with the operation of lithotomy, where long continued atony or paralysis of the bladder had previously existed. In the instance of a patient (H. G.), 69 years of age, who is now alive with complete power over micturition, I opened his bladder from the perineum, and divided the floor of a greatly enlarged prostate, at the same time removing some phosphatic stones which were probably connected with the long continuing inflammation. After the prostate had thus been divided, a drainage tube was used as I have described. Previous to this operation, which was performed in 1887, the patient had been entirely dependent on the catheter for four years, during two years of which time he had worn the instrument continuously both by day and night. Had I in this instance contented myself by removing these phosphatic concretions, as I could easily have done with the lithotrite, the patient, I have not the least doubt, would never have recovered his bladder power, and in all probability have spent the remainder of his existence in the twofold employment of making stones and having them removed.

¹ Read in the Section of Surgery at the Annual Meeting of the British Medical Association held at Nottingham, July, 1892.

² *Trans. International Congress.*

³ *Surgical Disorders of the Urinary Organs.* 3rd Edition.