CHAPTER VIII.

CLINICAL STUDIES.

As has already been stated, the Reports which were issued from Parliamentary Road Hospital contain Clinical Studies of considerable interest, but few probably surpass in importance the observations made on the question of Stimulation in Fevers generally, but especially in Typhus Fever, and on the protective influence of vaccination in Small-pox.

At this period it was commonly held that alcohol served a double purpose in the treatment of fevers—it fed as well as stimulated the patient, and the first paper we have mentioned is a closely-reasoned appeal to the facts of clinical experience as showing that its function was one of stimulation only.

In the second paper the value of vaccination in Small-pox is considered in relation to severity of attack, and the theory is advanced and illustrated by a diagram which has formed the pattern for many subsequent illustrations that protection against the disease wanes with the length of the interval which elapses between vaccination and subsequent exposure to infection, and that the individual "drifts" towards recurring susceptibility to the disease in after years.—(ED.)

(1) *Stimulation in Typhus.*[1]

I propose to make a study of stimulation as exhibited in 1538 cases of typhus fever treated in the City of Glasgow Fever Hospital between 25th April, 1865, and 1st May, 1867. My object is to show the method and results of a course of practice in which alcohol has been employed as a stimulant.

Everybody knows that alcohol in all its relations is surrounded with doubt, and fruitful of disputation. Is it purely stimulant, or partly food? How does it leave the system, or does it leave the system at all? are all questions concerning the answer to which there are differences of opinion, unfortunately

[1] *Glasgow Medical Journal*, 1867.

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not unbiassed by social and moral considerations. I do not intend to discuss any of the chemical or physiological investigations to which those questions have given rise. It would not influence my practice in the least, although it could be demonstrated that every drop of alcohol is assimilated and detained in the tissues, or that none of it is assimilated and detained. All agree that alcohol is a stimulant, nay more, that its first and most evident action is that of a stimulant. It may or may not be food, but whatever may be the truth in that respect, if not stimulant it is nothing, if a food it is a highly stimulant food. It follows, therefore, that those who give alcohol as a stimulant have all the benefit of whatever nutritive value it may possess, if any, and avoid the evil of narcosis, or impairment of function into which stimulation soon passes, while those who give alcohol as a food are liable to all those evils. All food is stimulant in some degree, but not to a degree which makes this property the chief characteristic. Good beef-tea is decidedly stimulant, and were it so in the sense that alcohol is, then I should give it in fever with the same caution and under the same restrictions as alcohol. A sentence from the writings of Dr. Todd and of Dr. Gairdner will best show the bearing of opinion on this subject upon practice. "Alcohol," says Dr. Todd, "possesses its stimulating property because it is a form of aliment appropriate to the direct nourishment of the nervous system, and to its preservation; and its special adaptation to this system gives it an immediate exciting power superior to any other kind of food." . . .

Dr. Todd would rather over-stimulate than under-stimulate. "I am convinced that it is much better to err on the side of over-stimulation than not to give enough; for if we have over-stimulated a patient, it is very easy to pull him down again; there are plenty of appliances and means for this purpose; but if the patient sink too low nothing is more difficult than to restore him."

Turning to the cases of continued fever detailed by Dr. Todd, the following seem to be peculiarities, but still, such as flow naturally from the preceding. First. There is but a very rude attempt at graduation in the exhibition of stimulants. If any stimulant is given it is almost invariably brandy, and the amount is increased and diminished by gigantic strides, and is always high. Thus, a common procedure is to rise by twelves up to forty-eight ounces of brandy, often to double the amount all at once, one day twenty-four, the next forty-eight ounces. Age, sex, habits, &c., though noted, make really very little difference. The same circumstances arising in a number of patients varying in all their characteristics would meet the

same treatment. A girl of eighteen gets forty-eight ounces of brandy every twenty-four hours for days. So do men of fifty or sixty in similar symptoms. Second. As part of this rule differentiation of cases, there is but little explanation ever given of the circumstances supposed to indicate increase or diminution of stimulants. The date of the fever is not noted with care. Often no special reason whatever is given, but merely the statement that the brandy was doubled, or halved and so on.

We take Dr. Gairdner as representing those who use alcohol as what it is without dispute—a stimulant. He says—"I have been throughout guided in the use of alcoholic stimulants by the conviction that they are really *stimulants* and *tonics*— *i.e.* medicines, and not food properly so-called. The maintaining of the opposite view by so high an authority as the late Dr. Todd, and the practice founded upon it of giving these stimulants, as a general rule, at an early period of all acute diseases, and in very frequently repeated doses all through the day and night, I cannot but regard as a grave error, leading to the probability, almost the certainty, of an injurious excess in their use. My own habitual practice has been to give stimulants, if at all, only in very moderate quantities along with the food, and, in general, as an aid to the digestion of food,— the only exceptions being in the case of persons largely and habitually dependent upon stimulants from old and formed habits and in a comparatively small number of acute cases for a very few days, sometimes only a few hours, to help the system over a dangerous crisis, or to co-operate with other needful remedies, such as antimonials in pulmonary inflammation." And again speaking of pneumonia he says, "Stimulants . . . have been freely used in cases in which the vital powers seemed in danger of failing; and that, whatever the treatment in other respects may have been. But . . . I have never given stimulants very largely, or as a matter of routine, or of aliment; almost never in slight cases, or in the early stages of the disease; and very rarely indeed to young persons, or to those not habituated to the use of alcoholic drinks." The practical results of this principle will be best exhibited as the antitheses to those enumerated above as derived by Dr. Todd from his theory.

1. The system of regulated quantities is in the main a bad one. The giving of stimulants is quite a matter of momentary comparative consideration. There rarely are twenty-four continuous hours in which stimulants ought to be given throughout at the same ratio, rarely even six. Cases occur in which it is desirable to visit the patient again and again, and give or withhold according to present circumstances.

2. No rule of thumb of universal application can be given by which to describe cases which ought to be stimulated, much less by which to descry the need of stimulation in the distance. Stimulation is entirely *pro re nata*. The most severe cases may pass through the fever safely without such aid. Mild cases, so far as the absence of those signs of nervous exhaustion described, may require alcohol. I have made various attempts to formulate some phenomena or class of symptoms which demand stimulation, *e.g.* a pulse above 120, but have abandoned them all. The only circumstance which I still regard as a decided occasion for the use of stimulants is irregularity of pulse, and it is on the whole from the heart that nearly all true indications are to be derived, certainly not from functional nervous derangements.

3. Alcohol is, like all stimulants, a narcotic, when given to excess. As a general rule, the problem in fever is to employ the stimulating without eliciting the narcotic effects. Whatever benefit Dr. Todd claims for alcohol as an antidote to or preventive of delirium is to be ascribed to alcoholic narcosis, or, in plain words, the stupefaction of intoxication. I am convinced, from observation, that a fever patient is much more sensitive to both actions of alcohol than a person in health. Half an ounce of port-wine may cause flushing of the face, and general vascular excitement, and that so manifestly, that an intelligent nurse will draw attention to the fact. In other cases, especially children, so small a dose is a narcotic. It produces sleep. When along with a frequent pulse and a weakly acting heart, there is sleeplessness or delirium, alcohol may be employed as a soothing agent with more benefit and safety than opium. Occasionally in adults, under these circumstances, I have even administered as a draught two ounces of whisky made into toddy; with the effect of inducing a comfortable sleep after opiates had completely failed. From these facts I am certain that Dr. Todd's patients who were receiving "from two to twelve, or *even* sixteen drachms" of brandy every half hour, or hour, were in a state of continuous narcosis. This is the clinical fact expressed in the dogma, that alcohol is "the best preventive of and antidote to delirium in acute disease." I cannot believe that perpetual sleep, if artificially induced, is to be desired in fever. An alcoholic sleep prolonged from day to day in a healthy man would certainly injure him. . . . It is a common observation of mine that sleep artificially induced in a fever patient is characterised by a tendency to shallow respirations, congestion of the lungs, rapid feeble pulse, and general evidences of a loss of nervous energy. I believe this condition really is the impairment of nervous energy which accompanies narcosis, and

not the result of want of nourishment, whether alcoholic or food proper. We have the analogy in a case of opium poisoning; and the treatment appropriate to both cases is to rouse from the narcotic sleep, and in the act of rousing, without other aid, the respirations deepen, the pulse gains in strength, and diminishes in frequency and the impaired nervous power is restored.

4. In Dr. Todd's phraseology an alcoholic stimulant is a food. We believe that we cannot employ alcohol as a food without also developing its dangers as a narcotic, and consequently we must resort to those substances more commonly known as food—beef-tea, milk, arrowroot, &c. To these aliments, but not to alcohol, we may apply the proposition and prefer giving too freely to a system of depression. If I am convinced of having done good by giving alcohol as a stimulant, I am convinced of having done harm; and I am quite conscious of having benefited the patient by stopping stimulants, as by administering them even in the same case, when they had been too long continued.

5. In the practice of one who adopts Dr. Gairdner's principles, there will be no such rude gradations in the records of individual cases, no such uniformly high scale of stimulation over-riding all considerations of age, sex, habits, idiosyncrasy, day of fever, &c. Every single dose of alcohol will be regulated in amount and determined as to continuance by a careful study of all those facts. No conceivable circumstance will ever warrant the exhibition of such a quantity as 48 oz. or even 36 oz. of brandy per diem, and the aggregate statistics of such a practice will bear the most delicate traces of the characteristics of the individual cases. I have endeavoured, with increasing fidelity, to follow the indications of those characteristics throughout my practice : and this paper is intended to test by analysis to what extent I have been successful in my endeavour.

It seems to me that, in taking sides in the discussion of a broad question, such as is at issue between those who use alcohol in continued fever as a food, and those who use it as a stimulant, every one before taking up speech ought to show cause why he should be heard. The question is not one regarding minute points of practice, affecting complications or other accidental phenomena of the disease, but refers to its whole course, to the fever as fever. . . . There is hardly any novel practice which may not be pursued, and yet we may be able to quote a few cases as successful, inasmuch as they survived, or to point to moderation in certain symptoms—the fall of the pulse, the absence of delirium, &c—as truly following the practice. But such moderation may follow, and not

be an effect, or it may follow and really be an effect; and yet the aggregate result may be bad. Principles which will lead a practitioner to give one to two bottles of brandy, for days together, to lads and girls of seventeen, are not *prima facie* prepossessing. They must be scrutinised before they can be accepted, and nothing short of most decided success over a more innocent creed can warrant their adoption. . . . Of 1538 patients treated 645 were stimulated, and it is with these in their various relations I have to deal. The method pursued in the investigation was to prepare sheets ruled with columns for the following data—Number of cases in Hospital Register, result, day of fever when stimulation began, number of days stimulation continued, total quantity of wine and spirits given, in ounces ; and then a series of double columns numbered from the 5th to the 21st day, into which was extended the *daily* amount of wine and spirits given in such cases as the day of the fever had been ascertained. In these sheets every case which had received a drop of alcoholic stimulants in the whole course of treatment was entered, the males and females on separate sheets, each quinquennial period being distinguished. Thus the entire series of 645 cases which were stimulated was arranged in a form which admitted of their classification in all possible ways. The number actually stimulated, not the total number treated, is in all cases the basis of calculation. . . . From five years of age, the proportion stimulated increases gradually, but not steadily. Between 10 and 25 there is the most rapid increase. From 10 to 15, double the number at the preceding period require stimulants ; and at the age of puberty the rise is most marked of all periods, being no less than three times the proportion immediately preceding puberty. At 40 there is another sudden rise, with little variation at the ages of adult life between. Above 60 nearly every patient was stimulated. Below 4 the proportion is nearly as great as from 10 to 14, but on examining the individual cases it is obvious that hardly any but fatal cases were stimulated, a fact which gives rise to great doubt how far stimulation at that early age is ever useful, the immediate occasion being generally some complication whose fatal issue is certain. The total quantity administered is surprisingly uniform at all the ages, merely showing, however, that the time over which the stimulation extends is the important, because variable, element to be determined. . . . The doubtful part of treatment is when to begin, how much to give, and how long to continue. The average total quantity consumed by all cases is 22 oz. of wine and 9½ oz. of spirits ; the average total cost of this quantity is 2s. 10d. . . . In all inquiries intended to determine the natural course of a disease, we must look to the phenomena

observed in those who recovered apart from those who died. Death is an extraordinary event which cuts short the course of the disease, and spoils the fatal case for complete observation, merely leaving the mark of fatality at the particular period in the disease at which death occurred. This is about all the information conveyed by a death relative to the natural history of the disease. . . .

Mortality.—We may say in the most general terms that at all ages fever is more fatal to males than to females. During the reproductive period, from 15 to 40, when adult life is in full vigour, the difference is so marked as from 7 to 18 per cent. in favour of the female. At the beginning of life the risk is about equal to both sexes, between 40 and 54 also it is equal, while at the ages above it is more than twice as fatal to men as to women. The period of least danger may be said to be that immediately preceding puberty in both sexes. It is somewhat remarkable that out of 165 males between 10 and 14, not one should have died. The ages of the three females who died at that age were 12, 13, and 14, showing a tendency of the deaths to the higher parts of the period included. The prognosis, so far as it depends on age, will be with great safety uniformly favourable for patients at that period. The first years of manhood show an increase of danger far beyond the first years of womanhood. Indeed, above 19, her sex seems to advantage the female as much as from 5 to 10 years—*e.g.* a woman of 20-24 runs no more risk than a man of 15-19, and so on up to 40. As regards the male, his sex is in the same degree a disadvantage. However we put it, the importance of the mere fact of sex in prognosis is obvious.

The *percentage stimulated* of each sex gives more information than the mortality alone. It is a measure of the broad impression of the disease upon the general mass of the patients, of the general strain put upon the vitality of the system short of absolutely breaking it. Hence, from the relation of the mortality and the proportion stimulated, as well as from each considered by itself, certain lessons may be learned. Thus, a high mortality coinciding with a high point of stimulation indicates fatality and severity in the fever at that age, while a low mortality with a high point of stimulation means severe but not fatal. The rule is that the mortality and stimulation rise and fall together, both being governed by the same set of circumstances. . . .

Looking at the curves of stimulation for the two sexes first comparatively, it will be observed that while the general percentage is 43.7 for the females and only 36.6 for the males, the percentages at the different ages are decidedly greater among the males at all periods except these, 0-4, 10-14, and most

remarkably 20-24. The numbers at the earlier age being small may be neglected. At 10-14 barely four per cent. more females were stimulated than males, a proportion which is fully accounted for by the circumstance already noted, that there were no fatal male cases at that age. With one extraordinary exception, then, females at all ages suffered less from the fever than males. The maximum of stimulation is attained by males ten years before females, *i.e.* at 55. After that age every male was stimulated, but every female not until we reach the age of 65. Everything tends therefore to impart more interest to the fact that at the age of 20-24 no less than 20 per cent. more females required stimulants than males, and to tempt us to a special inquiry into the cause. In looking at the diagram the eye is at once caught by the sudden rise in the female curve, carrying it above the male, as if some aggravating circumstance struck in and at once raised the type of fever to a platform of severity in the females, to which the males do not attain for a period of five years, and which is hardly surpassed in the same sex by the addition of twenty years, for it is notable that the line passes with but little elevation from 20 to 40. The first question which suggests itself is, does the mortality coincide? While in general mortality and stimulation run parallel, there are also exceptions, showing that causes operate at certain ages which produce severity but not fatality. Such a cause marks the period of puberty in both sexes, when the ratio is 1 death to 6.1 stimulated. Passing above that, in the stimulation, we find a nearly doubled mortality, with a lower rate of stimulation, or one death in three stimulated, and this proportion does not vary much in after ages, tending on the whole to fall. I think we may fairly infer from this, that whatever the cause of the mortality, it was something individual rather than general, something which tended to the death of certain cases without being associated with severity affecting the general mass of male patients. Having pointed out that the mortality among females is less, and the stimulation also less than among males, we might suppose this to be an example of the general law of relationship pointed out above; but comparing the ratios in the two sexes, we find that the fall in mortality is in much larger proportion than the fall in stimulation, and that this disproportion is most marked between 20 and 40. Throwing the four periods together, one male died to 2.8 stimulated, but only one female to every 4.8 stimulated. We have here, therefore, evidence of some cause confined in its operation to the female sex, while acting widely makes the constitutional impact of the fever severe but not fatal. This much further is evident, that it is a cause which, while acting widely at

certain ages, is not equally active at all ages. Above 40 the ratio is much the same in both sexes and at all periods. At puberty also, as we have just seen, the sexes are alike; in childhood the statistics do not warrant any conclusion. The cause is therefore not in sex merely, though it may be in some passing attribute of sex. It is not equally active over all the periods between 20 and 40, but most active immediately after puberty, less so in the next period, and about equal in the two last. Prosecuting the inquiry it is forced upon our attention that the period between 20 and 40 embraces in the female the most active part of reproductive life. Typhus fever is a disease which invades every organ and function of the body. It takes the individual, as he or she is, and raises the whole system, with all its redundancies and defects, for the time being to a higher level; so that all is represented, but on an exaggerated scale. The pulse and the temperature vary in health during every twenty-four hours, so that a daily curve can be drawn representing their rise and fall. In fever the curve is reproduced with greater amplitude, but the same outline. A person whose brain in health is active will in fever be delirious, and the subjects of his daily thoughts will assert their old supremacy. The habits, occupations, and social circumstances of large masses of men put their mark on the phenomena of this disease with great distinctness, and it would indeed be surprising if the sexual functions did not leave clear traces of their influence on the general outline of the course of fever, especially at the period of life when those functions are established. On the male side we cannot expect more than indefinite traces of this influence, as the exercise of the function in the male does not necessarily affect the bodily condition. But in woman, menstruation, pregnancy, child-birth, and suckling, alternating throughout the greater part of her life, are all marked by deep constitutional sympathy; and each sets its mark upon the system much more distinctly than any natural process to which the male is exposed. My first step was to classify female patients into the married and the unmarried. At the first three periods the division was easily made, and the results are quite trustworthy; but from the terms of admission to the Hospital (which is chiefly intended for those whose legal support is able-bodied, or who are otherwise not paupers), a great majority of my female patients are married as we advance into the nubile years, and those who are not so are widows, single and not in the main to be selected as patterns of the virtues. Therefore I rely chiefly on those earlier periods. The following table gives a contrast of the married and the unmarried as to stimulation and mortality at four quinquennial periods.

Age.	Total Treated.	Married.					Unmarried.				
		Tr.	Died.	p.c.	Stim.	p.c.	Tr.	Died.	p.c.	Stim.	p.c.
15-19	140	14	...	...	6	42·8	126	8	6·3	48	38
20-24	73	44	4	9	30	68·4	29	2	6·9	17	58·6
25-29	64	47	4	8·5	27	57·4	17	3	17·6	11	64·7
30-34	78	71	11	15·5	47	66·2	7	2	28·6	3	42·8
Total.	335	176	19	10·8	110	62·5	179	15	8·3	79	44·1

The general conclusion of these data is to trace the chief demand for stimulants to the married portion of the female patients. At the age we are more especially investigating the percentage stimulated is 68.4 for married, 58.6 for unmarried. At 30.34 the difference is more marked still, and even among the few married at 15-19 there is a predominance of stimulation. At 25-29 the result tends to an opposite conclusion, though not so decidedly in that direction as at the other ages in the direction we have just pointed out; while, taking the general aggregate of cases, 18 per cent. more married than unmarried females were stimulated. Though a column of mortality has also been given, I do not think any safe use can be made of it at present. We shall be able shortly, after a further selection of cases, to proceed to some inference in this respect also.

Having got thus far in the inquiry, the reflection arose that it is not the mere fact of marriage, but consequent phenomena, which constitute the difference between the two classes of women. Therefore, still proceeding by the method of exclusion, I have carefully gone over my ward journals, and taken note of every case of pregnancy or suckling which has been recorded. I have arranged the result in the following table, in which those distinguished as married are sub-divided

Age.	Total Married.	Pregnant or Suckling.			Neither.		
		No.	Stim.	Per Cent.	No.	Stim.	Per Cent.
15-19	14	9	5	55·5	5	1	20
20-24	44	19	15	78·9	25	15	60
25-29	47	21	11	52·3	26	6	23
30-34	71	20	13	65	51	27	53
35-39	61	17	10	58·8	44	23	52·2
Totals,	237	86	54	62·5	151	72	47·6

into those who were either pregnant or suckling, and those who were neither. The percentage of each sub-division who were stimulated is added.

We thus prove conclusively that the activity of the reproductive function at the time of seizure causes the excess of stimulation which characterizes those periods of age. We prove, however, that whatever influence the fact of past maternity may have, it is the actual condition during the time of illness which gives the most decided bias to the fever. Nearly all those women were mothers of families; but it is not the deteriorating effect of rearing a family so much as the being actually pregnant or actually suckling which renders stimulation necessary. While the general tendency of the percentages at all periods is in this direction, it may be thought that the absolute difference is not so great as it ought to be; but I appeal to these figures more to prove the tendency than to measure the exact amount of its influence in these precise cases. No special care was taken to ascertain the condition of the female patients in this respect, as I had not theory on the subject until it grew out of the present statistical study. No inquiry was made either as to pregnancy or suckling, unless they forced themselves into notice from striking appearances. My conviction is that of the young married women by far the majority were actively productive; and though I desire to adhere entirely to recorded facts and to keep within the limits of my own cases, I may reasonably infer that the same laws were applicable to the married females admitted to this hospital as have been proved regarding the entire married female population. . . .

Having for the purpose of this inquiry tabulated every case of pregnancy and suckling admitted of which note was taken, it may be well to present the results, as tending to elucidate the entire relation of those conditions to typhus fever. They are probably unique in the practice of one hospital. From an examination of various fever-hospital reports, our experience seems much more extensive than usual in this respect.

With reference to this table, observe (1st) how closely the percentage of married females who were puerperal agrees with the tables given by Dr. Duncan in the chapters already quoted[1] for the aggregate of productive women. (2nd) Suckling women more uniformly required stimulation then pregnant women. This is evident at nearly all the ages, and when the totals are contrasted we find that 74 per cent. of the former were stimulated against 50 of the latter. Indeed the suckling woman who has typhus presents a perfectly distinctive appearance to the accustomed eye. Anaemia is a marked condition even in

[1] *Fecundity, Fertility, and Sterility,* by Dr. Matthews Duncan, Part I., c. 1-3.

the midst of the vascular activity of the fever. The cutaneous surface, especially as seen in the face, is not hyperaemic, but pale; the rash is not copious nor active; the pulse is feeble and frequent; the asthenia most marked throughout. Among the lower orders a habit of prolonged lactation is very common, frequently extending far into the second year of infant life, and caused partly by the apparent economy of this mode of sustenance, and partly also by certain Malthusian hopes of averting speedy pregnancy. (3rd) The fact of stimulation in pregnancy is chiefly associated with abortion and miscarriage. At the age 20-24 five aborted, and all the five were also

Age.	Total Married.	Pregnant or Suckling.		Pregnant.				Suckling.				Of Pregnant aborted.		
		No.	Per Cent.	No.	Died.	Stim.	Per Cent.	No.	Died.	Stim.	Per Cent.	No.	Died.	Stim.
15-19	14	9	6·4	4	...	2	50	5	...	3	60	2	1	...
20-24	44	19	26	8	...	6	75	11	1	9	81·8	5	5	...
25-29	47	21	32·8	7	...	1	14·2	14	1	10	71·4	1	...	...
30-34	71	20	25·6	12	1	8	66·6	8	...	5	62·5	3	2	1
35-39	61	17	27·	8	...	2	25	9	2	8	88·8	1	1	...
40-44	44	7	14·5	7	1	4	57	...	...	...	...	3	2	1
45-49	29	3	10·3	...	...	...	...	3	...	2	66·6	...	...	...
Totals,	310	96	31	46	2	23	50	50	4	37	74	15	11	2

stimulated. Of the 46 who were pregnant, 15 or 32.6 per cent. aborted, and of those who aborted 73.3 were stimulated as against 38.7 of those who carried the foetus safely through the fever. (4th) As regards fatality, suckling proved itself the more dangerous condition of the two, 8 per cent. of those who were suckling having died, and 4.3 per cent. of those who were pregnant. It is worthy of remark also that the only two pregnant women who died aborted, and I am inclined to think that the abortion was an accompaniment of the moribund process, and not at all the cause of it. On the other hand, the asthenia which is produced by suckling must be closely associated with the fatal issue as a remote or even a proximate cause. The general result of these two facts—the increased stimulation and the increased mortality—is to establish the proposition that suckling is uniformly an unfavourable element in the prognosis of typhus; while pregnancy does not add much to its dangers. (5th) As to the chances of the foetus in typhus, my experience is that they are most favourable in the intermediate months of pregnancy, between the 3rd and the

7th. Before the 3rd the mother generally aborts, after the 7th generally miscarries. (6th) The prospects of the child surviving in cases of miscarriage are almost nil. They are born with a stock of vitiated blood; and in my experience only one child, born between the 8th and 9th months, survived. Several survived a few days, but this one only—a female—left the hospital in vigorous health. (7th) A condition somewhat different from that of abortion or miscarriage arises when typhus seizes a female immediately after child-birth, at full time. Though a serious, this is not a very fatal complication, which is especially interesting as contrasted with the deadly nature of puerperal scarlatina. One common characteristic of these cases was very marked bronchial irritation. There is always more or less bronchitis in typhus, but in these particular cases it extended deeply into the tubes, and was accompanied by copious secretion. Probably the addition of the effete materials from the degenerating uterine tissue to the poisonous products of the fever imparted an unusually irritating property to the blood. (8th) To complete this summary of the bearing of the generative functions in the female on typhus, I may add that menstruation as a rule has little effect on the progress of the disease. The outset of the pyrexia, if it falls on a menstrual period, generally stops the discharge, if established; but seems not to defer its appearance if not established. The menses appear at all stages, being only influenced in amount. During the last week there is an evident tendency to menorrhagia, which is, however, the general character of all hemorrhages occurring then, and arises from the fluidity of the blood. During convalescence, and until health is established, there is suppression, as in all similar conditions of body, however caused. . . .

Observe (1st) among the recoveries there is a decided increase in the number of days over which stimulation was required, as the patients become older. From 10 to 14, an age which we have shown passes through fever with the greatest immunity, the duration is at a minimum in both sexes—four to five days. From 15 to 19 there is a sudden rise to from 7 to 8 days. Afterwards there is rather a decline until between 30 and 40, when we reach 9 days; and from 50 to 54 there is a maximum of from ten days to a fortnight. The average extent of stimulation over all cases is a week. (2nd) Among those who died there is a great diversity in the duration, a fact from which but little can be learned. It diminishes as the years advance. One remark is suggested by the short average of the fatal cases below ten years. It strengthens the doubt already expressed as to the utility of employing stimulants under such circumstances as are thus denoted. Indeed, I

confess for myself to the strength of the inclination to dose plainly moribund cases with spirits, which one does not overcome until experience has given confidence to the judgment. Having said so much for myself, I may venture to add that this is a too common resort of young practitioners, and especially of house surgeons, in emergencies. (3rd) Contrasting the sexes, it is evident that, while the proportion requiring stimulants is, as we saw, generally lower in females than in males, the length for which they require it is longer. At all periods save three this is so. The difference is merely fractional; but in an average of this sort a few decimal figures indicate considerable difference in the actual numbers. The practical effect is that, out of the same number of both sexes receiving stimulants, there will always be a greater number of females receiving them at one time. We shall come upon this fact subsequently.

Closely related to the duration is the amount of stimulants. . . . In order to ensure greater accuracy, I employed the whole number of days and the whole number of stimulants as divisor and dividend. Observe (1st) the relation of the wine and spirits, which will be apparent throughout our investigation. The stronger stimulants were appealed to, as the circumstances demanding their agency became more serious. As we rise in the ages the spirits take the place of the wine; among females wine predominates, to those who died spirits were much more largely given in both sexes than to those who recovered, and to males more largely than to females; all being facts which necessarily result from the administration of alcohol as a stimulant. (2nd) The average total amounts for all ages were about $23\frac{1}{2}$ oz. wine and 8 oz. spirits, to males who recovered; 27 oz., or rather more than one bottle, of wine and 6 oz. of spirits to females who recovered; above 11 oz. wine and $16\frac{1}{2}$ oz. of spirits to males who died; and about 14 oz. wine and 15 oz. spirits to females who died. Absolutely the largest quantity given during the course of the fever to recoveries was given to females between 50 and 54. It amounts to about 13 bottles wine, and $1\frac{1}{8}$ bottles whisky. (3rd) No such statements of total amounts are of any value as an index to the pitch of stimulation, unless taken along with the number of days over which they are spread. The columns showing the average daily dose there are therefore the most important. A general survey shows a steady increase in the amount of alchohol as we rise in age, obtained by the increased use of spirits. Running the eye down the column of male recoveries, the daily dose of wine rises from one to two glasses, with but a mere fraction of whisky, until we reach 20. After that age the wine falls again to one glass, while the whisky rises from

half a glass to rather more than a glass. Among female recoveries, the wine increases from one to two glasses, and then remains steady at rather less than two glasses, while the whisky does not reach half a glass until we come to 30, and not to a whole glass until we come to 50. The daily dose of alcohol is throughout much less to females than to males; and the females seem to follow the males in absolute amount about a period of five years in arrear, a fact which would correspond to the circumstance already noted regarding the percentage stimulated in each sex at the several periods.

The daily dose for all ages shows but slight traces of this difference, and is of no great value in presence of the detailed averages for the various periods. Taking all recoveries together, it is about 3½ oz. of wine and one of whisky. Turning to the fatal cases, the doses are much larger. The Maximum of all ages and both sexes is 8 oz. whisky per day to males between 30 and 34; but in general the dose was, to males, from one to two and two and a-half glasses of whisky, with one glass of wine; to females, from one to one and a half glasses of whisky, and one to two glasses of wine. Taking all deaths together, the daily dose was one and a quarter glasses of wine, and one and a half glasses of whisky.

Stimulation as related to Day of Fever.—A patient suffering from a specific fever (we might say a specific disease) may be likened to a traveller with a beaten path before him, over which he must toil, every mile of which has its own dangers and its own necessities. Relative to the progress of a case of typhus, each day may be regarded as a stage in the advance either to recovery or to death. There can be no delay, no resting by the way, and according to the traveller's condition as he passes each successive milestone, we judge of his chance of reaching the end in safety, and of the artificial aid he may require to help him on. Hence, to throw metaphor aside, it is of the greatest importance to ascertain the exact date of the commencement of the illness. This is the central fact to which all the phenomena of fever must be referred, that we may estimate correctly their value as a guide to prognosis and as indicative of treatment. There is hardly a symptom which can be interpreted absolutely. A condition which, at one day of the fever, is hopeless, may be quite consistent with recovery at another, and *vice versa*. So also the treatment varies. A matter of such primary importance as stimulation cannot therefore be satisfactorily treated without investigating its relation to the day of the fever. To the study of this relation we have now to address ourselves.

Of the 645 cases which were stimulated in 451 the day of the fever was ascertained, and it is with these 451 cases we

have now exclusively to deal. . . . It must be remembered that my chief object is to show the variations according to the day of fever, in the amount of alcoholic stimulants administered. Each day is therefore made the subject of a distinct calculation; the total number actually stimulated on the particular day being the divisor, and the total amount of wine and spirits given on that day to those patients being the dividend. The result is a perfectly accurate average of the dose from day to day. As formerly, the subject branches into three divisions—the number stimulated, the duration, and the quality of stimulants in relation to the day of fever.

Since the value of the actual dose of alcohol administered on any day of the fever, is derived entirely from the relation of the day of the fever to the phenomena of the fever, it will be necessary first to attempt to attach a value to each day in the gradual ascent through which fever tends to recovery or death. In the previous tables it has chiefly been by age and mortality that we have, so to speak, checked the stimulation. Now we have to distinguish nicer grades with less appreciable variations. The progress from day to day is marked less distinctly than that from age to age, and yet as far as this progress is accompanied by shades of severity, so far ought there to be corresponding variations in the degree of stimulation as we have endeavoured to employ it. . . .

The table just referred to (not included) determines the most important days in the course of the fever, those which bring to the patient either a favourable or fatal issue. Observe (1st) as regards the day of crisis, at the age 0-14 nearly half the cases had it on the 12th or 13th days, and a large proportion of the remainder on the 15th. At 15-19 the majority had the crisis on the 13th, and more than two-thirds on the 11th, 12th, 13th, or 14th days together. At 20-29 the crisis was most frequent on the 12th day, but between that and the 13th, and 14th, there is but little difference in frequency. At 30-39 the majority had the crisis on the 14th day, but with little difference between that and the 12th and 13th. At 40-49 a large majority got the crisis at the 11th day, but a considerable number also at the 13th and 14th. At the most advanced ages the crisis fell chiefly on the 14th day, but also in many cases on the two days immediately preceding. Taking all ages together, the most critical day was the 13th; the 12th and 14th approaching very closely, so that the 12th, 13th, and 14th days bring the crisis to nearly three-fourths of all cases. (2nd) There is a distinct postponement of the crisis as patients advance in age. As in all phenomena of fever, the age 15-19 is peculiar in this also that the crisis is on the whole later than at the period immediately following, and it is only then that we have instances of

a crisis so late as the 17th day. But the general tendency to delay of the crisis with advancing age, is evident both from the position of the maximum and also from the larger percentages at other later periods. (3rd) Turning to the fatal days, we find that from the smallness of the numbers we can hardly make any inference from the several ages. At 20-29 nearly one-fourth of the deaths occurred on the 11th day, the remaining three-fourths falling on the later days of fever. At 30-39 one-fifth occurred on the 14th day, the remainder being distributed pretty equally over the other days, starting from the tenth. At 40-49 the 10th and 12th are the most fatal days. At the older ages, the 14th is the fatal day, the 9th and 10th following hard after. Taking all ages together, the 15th was the most fatal day, the 10th, 11th, 12th, 14th, and 16th sharing the fatality pretty equally. (4th) A general view of the fatal and critical days suggests the observation that they concentrate towards the same days or groups of days, showing that the same period in the fever brings the crisis to some, and to others death, either closely before or closely after. Thus at 20-29 the maximum of fatality on the 11th immediately precedes the maximum of favourable crisis on the 12th. So also at 40-49 the fatal precedes the critical maximum, while at 30-39 and at the most advanced ages both maxima coincide on the same day. It is worthy of note, that while no deaths occurred at the youngest period after the 12th day, at the remaining ages there is a considerable proportion who, having passed the usual critical and fatal days, still died in the fourth week. These are cases carried off by various sequelae or complications, especially such as affect the chest—pneumonia, pleurisy, &c. To put it in the most general form, the great majority of cases find a crisis or death between the 10th and 16th days, and those who die subsequently are carried off by complications in the 4th week.

Next in importance to the days of crisis and of death stands the day on which the vital powers sink so low as to call for the first administration of stimulants. I have therefore constructed Table VI., showing for certain periods of age, the percentage of the total number stimulated at that age, who were so for the first time on each day of the fever. The percentage of deaths out of the number thus put upon stimulants is given, and will be remarked upon shortly. Meanwhile observe (1st) that at 0-14 the majority of those ultimately stimulated required it by the 9th day; at 15-19 the majority stimulated required it by the 9th day, the 8th not falling far short, so that 44 per cent. of all stimulated required it first on one or other of these days; at 20-29, the majority falls to the 10th; but the 9th approaches so nearly that, between the two 45 per cent. of the whole are

accounted for. At 30-39 the majority again falls to the 10th; but on the 8th, 9th, and 10th days together more than half of the whole number went upon stimulants. At 40-49 the majority began on the 9th, but only one per cent. less on the majority began on the 9th, but only one per cent. less on the 10th day. At the most advanced ages the majority falls to the 10th day; and, including the 8th and 9th days, nearly 60 per cent. of the entire number are accounted for. Taking all ages together, we find that in 41 per cent. of all cases stimulated, it is commenced on the 9th or 10th days; and, if we include the 8th and 11th days, 68 per cent. of all had within that space been actually put on stimulants. (2nd) Contrasting age with age, there is an earlier demand for stimulants as we near advanced ages. In this, as in other phenomena, the age 15-19 is older than its years indicate. By glancing down the percentages at the eighth day, it will be seen that a larger proportion was put on stimulants, so early as that day, at this period than at any age whatever.

In accordance with the principle enunciated that, to study completely the natural course of a disease, we must consider the recoveries and the deaths separately, I have compiled certain tables which I shall now explain. My first object is to ascertain the prognostic value of the fact of stimulation being required on certain days of fever. To return to the metaphor of a measured journey, if we liken those 451 patients who all received stimulants to a regiment on the march, what are the earliest signs of failure shown by those who will ultimately break down, at what stage is it most ominous for those signs of failure to appear? . . . The conclusion is very evident,— stimulation beginning very early or very late in the fever, is in both cases apt to prognosticate a fatal issue. The former class is composed of those whose strength fails before the journey is well begun, while the latter, few in number, however, comprises such as pass through the fatigues of the fever, but arrive at its close with some serious local lesion, such as pneumonia, pleurisy, gangrene, bedsores, &c. There is a peculiarity in the course of the black line (in a diagram not reproduced) which I cannot explain. Its highest points uniformly fall on even days, the 6th, 8th 10th, 12th, 14th, 16th, and 18th, meaning that it is of more serious import to require stimulants first on an even than on an odd day of the fever. This fact is rendered still more curious when we remark that it is more or less obvious even at the several periods of age, especially 20-29 and 40-49. . . . The result is to show more clearly the early failure of strength which distinguishes the fatal cases, and also to bring out in another way the fact elicited in our endeavour to fix the fatal and critical days—that there are certain points in the progress of the fever where

unusual danger awaits the patient, which he may encounter successfully, and so pass the crisis, or unsuccessfully, and so die. The particular result which suggests these remarks in this connection is . . . that the days on which the *largest number*, both of those who recovered and those who died, first showed signs of failure sufficient to require stimulation, are either the same or immediately consecutive. We have already remarked the coincidence of the critical and fatal days, and other illustrations of the same truth will present themselves. . . . It is less hopeful to require stimulants before the 9th day or after the 15th, less alarming at the 9th day, and least alarming of all from the 10th to 14th day.

In order to give expression to the fact of duration in reference to the days of the fever, it is necessary to treat the statistics in a different way. The fact of the commencement has been fully studied : but while some require the artificial support of alcohol for one or two days, others require it for a week or more. If we take note on each day how many men of our imaginary regiment are actually served with stimulants, distinguishing those who recover from those who die, we give expression to this variety of requirement in the aggregate. . . . The maximum of stimulation in recoveries is determined by favourable symptoms, while the maximum of deaths is determined by death, and this coincidence places in the clearest light the fact that death and the crisis are parallel events, the alternative conclusion presented at certain definite periods at each age. In general, the most critical day coincides with that in which the greatest number of individuals was receiving stimulants. The majority, at all ages together, get the crisis on the thirteenth day ; and the majority of those who recovered were receiving stimulants on the twelfth. This consists with my practice, which is, so soon as signs of a crisis appear, to diminish or withhold stimulants. The tendency to subsidence of the symptoms is resisted by the continued exhibition of alcohol, and it is from the beneficial effects of this practice that I state so strongly that I feel satisfied of having done as much good by withdrawing as by giving stimulants, even in the same cases.

In this investigation no account has hitherto been taken of sex. . . . I have already shown that, while, as a rule, of equal numbers of each sex a larger percentage is stimulated of males than of females at some part of the fever, the stimulation is more prolonged among the females than among the males. Hence there is no inconsistency in the two statements, that the fever presses more heavily on the females at the period of climax, and that the percentage of females stimulated is less than of males. The number of individuals stimulated

is smaller compared with the number treated, but within the number stimulated the necessity is more continued. . . .

Having now succeeded in obtaining a pretty clear idea of the relative necessities of each day of the fever, as determined by the tendencies to death or recovery, the days of the greatest need of stimulation, &c., all that remains to be done to complete an inquiry, which I fear must have seemed tedious even to the most enthusiastic, is to examine . . . the average dose of wine and whisky administered per day of the fever, *calculated from the number stimulated at each particular day.* My object being to determine the stimulant power employed to sustain the system and to discover how it has been proportioned to the demands of the fever, I have added . . . the value in alcohol of the average dose of wine and whisky as calculated from data furnished by the wine merchant. He informs me that there is 19 per cent. of alcohol in the wine, and 60 per cent. in the whisky. As my object is not to get an absolute but a relative measurement, it is of no importance whether or not these are rigidly accurate data. The same standard being always employed, the result must be correct, so far as the ratio goes. . . . In a general way, the dose expresses all the varying shades of importance which belong to those days. Let us go over the ages seriatim. 0-14, most critical day, the 12th ; maximum dose of alcohol also on the 12th. 15-19, most critical day, the 13th, maximum dose on the day preceding. 20-29, most fatal and critical days, 11th and 12th ; maximum of alcohol on 13th, with decided increase of power on 11th and 12th days. 30-39, most critical and fatal day, the 14th, maximum of alcohol, 11th, 12th, and 13th. 40-49, most fatal and critical days, 10th, 11th, and 12th ; maximum of alcohol, 12th, with great rise on 11th. 50-79, most critical and fatal day, the 14th, with maximum of alcohol on 13th. At all ages, most critical day, the 13th ; maximum of alcohol on the 12th. . . . The average dose increases and diminishes *pari passu* with the numbers who required it, the greatest number requiring stimulants on the 12th, the largest dose being on the 12th,—showing both in each individual, and in the grasp of the fever on the mass of patients, a climax of severity.

In writing this paper I have had a two-fold object, both to exhibit as minutely and faithfully as possible the practice pursued, and also to deduce from the statistics of stimulation such information regarding the natural course of Typhus as might be hoped for from the study of the impression left upon those statistics by the circumstances of each case. Although no such classification has been adopted, it may be observed that the various branches of this statistical study fall into two

groups. In one we seek for variations in the amount, duration, &c., of stimulation, due to causes which are well known to influence the course of the disease; while in the other we proceed in the opposite direction, and seek to explain certain variations by discovering influences sufficient to account for them. To the former class belong age and sex; to the latter suckling, pregnancy, &c., and partly to both classes our inquiry into the relations of the day of fever to stimulation. The common property through which these and all other circumstances are related to stimulation is in so far as they modify the vital force on the maintenance of which the patient depends for a safe transit along the beaten path of the fever. Alcoholic stimulants are a two-edged sword in the hands of the practitioner. If employed within the range of their stimulant action, *which is variable for every case*, they are helpful; if pushed beyond, into their narcotic action, they impair the vitality, which it is our aim to augment; even as pure stimulants, they may be used unnecessarily, so as to push and urge the labouring energies of the system, maintaining an unnatural excitement in a journey which would with leisure have been more easily accomplished. In any case this definite journey lies before the fever-patient. Whatever the advancement of knowledge may add to the power of the physician, certainly, at its present stage, treatment has no efficiency except as an ancillary to the vitality of the patient. The recognition of this as a fact in the natural history of fever seems to me to be the secret of its successful treatment. In the course of this paper, especially of the latter part, I have pointed out many facts, the tendency of which is to prove that there is a determined course and climax in the disease. Individual differences from age, sex, habits, social circumstances, &c., do not obliterate this periodicity, but at most exhibit it in some as death, in others as a crisis; or again, in a demand for stimulation, marked by intensity, as shown in the numbers requiring it, in the amount required, or in the duration of the requirement; there being always some shock to indicate the arrival at, if not the passage, over a period of natural and inevitable trial to the vitality. The action of the physician is thus limited purely to intelligent and minute observation; to the employment of every means to relieve the constitution of all *impedimenta*, and equip it for a journey which must be traversed; to the acquisition of an intimate acquaintance with every inch of the road, and to the judicious use of such means as are at his disposal to sustain the vitality of the individual until all the dangers are past. There is a certain perennial element of truth in this position. It is external to the system that we must look for the greatest prospective triumphs of

medicine over zymotic disease. Prevention will always be better than cure. What Lister seems to have accomplished in Surgery is the perfection of our hopes in Medicine. The poison of typhus has as definite an existence as the poison of the rattlesnake, or as arsenic. We may be able some day to isolate it, as well as them. If we have in carbolic acid, or sulphuric acid, an agent which will neutralize and destroy specific poisons, it still remains true that outside the body the work must be done, to be done effectually. The immediate result of the introduction of these poisons into the system is to set agoing a process of perverted nutrition. The administration of the sulphites, for example, may even destroy the active poison, and stop this process; but, for the completion of the work of cure we must still fall back upon the vitality of the system, and trust to the activity of its functions for the elimination of the morbid products. We may even, therefore, hold it impossible that any advance in the science of medicine can unseat this as the first principle in our treatment of specific disease—the support of the vital energies in their natural tendency through disease to health.

NOTE.—Since the publication of this paper it has occurred to me that the circumstance that few patients come under hospital treatment before the 6th to 8th day of the disease might be held to vitiate my conclusions as to the day of earliest need of stimulants. Though there is some force in the objection, still, as a fact, shown by the ward-journals, it is very rarely that I found it requisite to stimulate until some days after admission.

(2) *A Study of 972 Cases of Small-pox, with reference to the modifying influence of Vaccination.*

It is of great importance to keep clearly in mind that vaccination is a *process* and not merely an *operation*, as regards the individual. Though the operation may be performed to-day, the person operated upon is not really vaccinated until some days have elapsed. Hence it is *prima facie* absurd to propose vaccination as a mode of *treatment* of Small-pox, or to use vaccine lymph as a medicine or antidote to actual Small-pox. It would be equally reasonable to inoculate a person in whom natural Small-pox was already active. Vaccination and revaccination must be practised as a process through which the system must pass, requiring time for its completion, and therefore to be begun without a moment's hesitation where the system is unprotected, or where it is well to renew the protection.

After closely observing over 1000 cases of Small-pox in hospital, I have become deeply impressed with the helplessness of medicine when face to face with the unmodified disease. In this sense the only successful mode of treating Small-pox is by vaccination. To take firm hold of its efficacy and necessity, and enforce their convictions in practice without wavering, is the most useful, almost the only useful, action the medical profession can adopt against variola. When a case presents itself the first question in prognosis is regarding vaccination, although then the chief work of vaccination has been done, inasmuch as the only other circumstance in the patient's condition which is worth mentioning as affecting the prospects of recovery is the extent of the eruption, which I shall show is the direction in which post-vaccinal Small-pox is chiefly modified. If *vaccinated*, then the attitude is one of hope that the disease may be cut short, however bad present appearances are, though, in fact, the probability is that the symptoms are from the first trivial. If *unvaccinated*, then the attack will probably be severe, the eruption copious or confluent, and we recognise a virulence and deep constitutional disturbance against which the resources of medicine are powerless.

As regards the individual, the opportunity for medical interference is past, and we can only turn his case to profit by following on those about him the practice from the neglect of which he suffers.

I find that the mortality among my unvaccinated cases was 30 per cent., among my vaccinated cases 9 per cent. (1) Therefore by vaccination in childhood the lives of the unvaccinated would have been transferred from a risk of 30 per cent. to one of 9 per cent. (2) But from the statements of the patients or their friends I found that about 60 per cent. of the unvaccinated, and 50 per cent. of the vaccinated knew that they were exposed to the contagion of Small-pox. Therefore, exactly that proportion had, on their own showing, had a clear chance of obtaining protection by primary and secondary vaccination. (3) Above a half of these cases of Small-pox were avoidable: but when we consider that every case had a good lineage of cases derived from it, we may safely say that, mild as the epidemic was in Glasgow, it might with ease have been reduced to a third of its extent, and by a much larger proportion of its mortality, by the prompt use of demonstrated means of prevention. And when we speak of *Small-pox as preventible*, we must remember that we use the word in a much more exact sense than when, in the present state of our knowledge, we speak of *Typhus or Cholera being preventible*. The latter are preventible as the ignition of a dress is preventible by caution, while Small-pox is preventible as the

ignition is preventible, by making the fabric of the dress non-combustible.

Being convinced, then, that recent Small-pox experience can be turned to a public advantage only in so far as it can be made to teach the public the benefits of vaccination, and knowing also that, in reference to the phenomena of Small-pox after vaccination, the profession are still necessarily only collecting facts, I have made a special study of the statistics of 972 cases of Small-pox so as to forward those ends. This number includes all the cases admitted to the City of Glasgow Fever (Small-pox) Hospital, Parliamentary Road, from 1st January, 1871, to 30th April, 1872. Previous to the former date, only 11 cases were admitted, and, excepting a few treated at Barnhill Poorhouse, my remarks embrace the entire hospital experience of Small-pox in Glasgow up to the latter date.

TABLE I.

Age.	Total Treated.		Vaccinated.				Unvaccinated.				Odd Cases.	
			V. M. visible.		Said to be but no V.M.		Admitted to be.		No information and no V. M.			
	T.	D.	T.	D.	T.	D.	T.	D.	T.	D.	T.	D.
0-4	39	11	6	...	1	...	30	11	...	...	2	...
5-9	142	21	71	1	4	2	50	15	13	3	4	...
10-19	343	30	228	10	15	1	95	19	3	...	2	...
20-29	337	53	233	20	16	3	76	29	7	...	5	1
30-39	78	22	59	9	5	4	14	9	...	...	...	...
40-49	20	9	15	6	4	3	...	...	...	...	1	...
50-59	8	1	6	1	1	...	1	...	...	...	...	...
60	5	3	5	3	...	...	...	...	...	...	...	...
All Ages,	972	150	623	50	46	13	266	83	23	3	14	1
Percent's,	...	15·4	...	8	...	28·2	...	31·2	...	13	...	...

METHOD OF RECORDING AND CLASSIFYING CASES.

This Table shows those 972 cases as primarily classified with reference to vaccination, and distributed in decennial periods of age. Under this head I shall explain the principle of classification of the cases which form the subject of my remarks, and the precautions taken to insure the accuracy of my facts.

(1) *As to Vaccination.*—If the vaccination marks were visible then their *number* and *quality* were noted. The quality was determined according to the standard described in my paper on " Revaccination," in *Glasgow Medical Journal*,

May, 1871. In the ward journals the quality is described as "very good," "good," "indifferent," "bad," "very bad"; but in my tables I have reduced those degrees to two, viz., "good" and "bad." Sometimes persons were said to be vaccinated, but no marks could be seen, very frequently because of the abundance of the eruption. In some of those cases which recovered an inspection before dismission discovered vaccine marks, sometimes "very good." Those who died, or who were not so examined, are placed in a separate column as "said to be vaccinated, but v.m. not visible." I do not observe in the Reports on Small-pox, as observed in London and Dublin, any allusion to this difficulty. Even the best vaccine mark is readily obscured, or even hidden by a copious eruption, and unless such special means as I have described are adopted, it is impossible accurately to ascertain the facts of Small-pox in the vaccinated. Under "unvaccinated" also there is a separate column in this Table, containing those regarding whom no information could be got, but on whose persons no marks were visible, usually not because of the abundant eruption, but because there was really none. These were no doubt unvaccinated, and are so reckoned for the objects of this paper. A few cases of second attack of Small-pox, also of Small-pox modified by recent primary vaccination, are classified simply as "odd cases."

(2) *The extent of eruption* formed another object of methodical observation. The descriptive terms employed in the ward journals were "rare," "sparse," "copious," "semi-confluent," "confluent," "haemorrhagic." These are all reduced to three categories in this paper, viz.—the "rare," "copious," and "confluent."

INFLUENCE OF VACCINATION ON MORTALITY.

General Mortality.—Of the 972 cases under review, 150 or 15.4 per cent. died. Of these, 669 were vaccinated, and 63 of that number died, or 9.4 per cent., 289 were unvaccinated, and 86 of that number died, or 29.75 per cent. The remainder are classified as "odd cases," 14 in number, with one death. As already stated, therefore, the fact of vaccination without further refinement, reduced the mortality to less than a third.

Influence of Age and Sex on Mortality.—It is obviously well to gauge the amount of other influence which may interfere with our conclusions as to the influence of vaccination. The only ones which seem to demand special inquiry are age and sex, the effects of which are exhibited in the following Table.

The facts of the Table are so obvious as to require but little elucidation. The relative fatality in the sexes is striking,

especially among the vaccinated, and at all the ages. These figures are too limited to admit of generalization; but, from the immense field of induction afforded by the statistics of the "Metropolitan Asylum District," which show the same contrast, but in a much less marked degree, I believe it merely to be an illustration of the common law of all epidemic diseases,

TABLE II.

Age.	Vaccinated.								
	Male.			Female.			Total.		
	T.	D.	Per Cent.	T.	D.	Per Cent	T.	D.	Per Cent.
0-4	5	...	...	2	...	...	7	...	...
5-9	36	3	8·2	39	...	...	75	3	4·
10-19	123	6	4·8	120	5	4·1	243	11	4·5
20-29	173	18	10·4	76	5	6·6	249	23	9·2
30-39	42	12	28·5	22	1	4·5	64	13	20·3
40-	19	9	47·3	12	4	33·3	31	13	42
Totals,	398	48	12	271	15	5·5	669	63	9·4

Age.	Unvaccinated.								
	Male.			Female.			Total.		
	T.	D.	Per Cent.	T.	D.	Per Cent.	T.	D.	Per Cent.
0-4	15	4	26·6	15	7	46·6	30	11	36·6
5-9	39	12	30·7	24	6	25	63	18	28·5
10-19	57	10	17·5	41	9	22	98	19	19·4
20-29	69	28	40·6	14	1	7·1	83	29	35
30-39	11	7	63·6	3	2	66·6	14	9	64.3
40-	1	...	...	...	...	...	1	...	...
Totals,	192	61	31·7	97	25	25·7	289	86	29·75

and that the explanation simply is, that men are more weighted in the race than women through more rapid deterioration of staying power, partly from necessary toils and anxieties, and partly from more irregular habits.

Quality and Number of Vaccine Marks in relation to Mortality.—It is evident that, in so far as the success of the operation of vaccination is indicated by the *quality* of the vaccine mark—i.e. of the local traces left upon the skin—we should

expect to find some relation between the quality of the vaccine mark and the protective influence, as tested by subsequent events. If the operation has been successful, and if we can decide, long after its performance, that it has been so from the local traces left, then we ought to find that in a vaccinated local community uniformly exposed to variolous contagion the proportion of those with good marks of vaccination who are attacked is much less than the proportion of those having bad. From the nature of the case there are insuperable practical difficulties in the way of proving this, except very indirectly; but the *protecting* influence of vaccination becomes, in those who do take Small-pox, a *modifying* influence, and can thus be submitted to various methods of measurement as to nature and duration. We have the unmodified disease as found in those who have never been vaccinated, as a standard, and the extent to which the phenomena of Small-pox, after vaccination, deviate from this standard may be made the subject of exact investigation.[1]

Vaccine marks may be considered as to quality or number simply, or as to number and quality combined, and the modifying influence may be exhibited and estimated in the mortality, or in the extent of the eruption. We are at present looking for it in the *mortality*.

As to *Quality* simply, the following table shows that of 335 persons having " good " marks, 13 or 3.8 per cent. died; while of 156 persons having " bad " marks, 33, or 21 per cent., died. The contrast is apparent at all periods of life, but rises steadily from a minimum in the earliest to a maximum at the latest periods. The mortality of our 289 unvaccinated having been 29.75 per cent., it is evident that badly vaccinated persons are in the aggregate not much better protected from a fatal result than unvaccinated; and looking to the age, the badly vaccinated approach the unprotected condition more and more nearly as they become older.

As to *Number* simply, 491 cases were observed, of whom 46 had died, and it was found that of 313 persons who had only 1 mark, 32 died, or 10 per cent., of 161 persons who had 2 marks, 14 died, or 8.7 per cent., while of 14 persons who had 3 marks, of 2 who had 4 marks, and of 1 who had 8 marks, none died.

As to *Number and Quality combined* when so far subdivided, the data at my disposal are insufficient to warrant any

[1] Those who are acquainted with the literature of vaccination will not require to be told that all I aim at in this paper is to confirm, and perhaps more vividly illustrate Marson's paper originally published in the *Med-Chirurgical Transactions*, vol. xxxvi. I am not aware of any previous systematic confirmation of his results; and I have elaborated the relation of vaccination to extent of eruption more than Mr. Marson.

conclusion. The preceding facts as to number of vaccine marks, *without regard to quality*, point to no practical conclusion excepting this, that by introducing vaccine matter into several places on the child's arm, you are more likely to be successful than by introducing it at one only, on the principle which leads a bad marksman to throw a handful of stones instead of one. There can be no doubt that quality is of more importance than number, that it is better to have one really good mark than several bad ones, and that the vaccinator should endeavour to succeed in one or two spots rather than carelessly to insert his lymph in half-a-dozen.

TABLE III.

Age.	Total.		"Good" V. M.			"Bad" V. M.			Quality of V.M. not noted	
	T.	D.	T.	D.	Per Cent.	T.	D.	Per Cent.	T.	D.
0-4	6	...	1	...	...	2	...	...	3	...
5-9	71	1	34	...	...	11	...	...	26	1
10-19	228	10	134	5	3·7	50	4	8	44	1
20-29	233	20	123	5	4	64	13	20·3	46	2
30-39	59	9	32	2	6·2	17	7	41	10	..
40-	26	10	11	1	9	12	9	75	3	...
All Ages,	623	50	335	13	3·81	156	33	21·1	132	4

I must confess that, led by the analogy of fevers and other infectious diseases, in which a mild attack, so far as we know, is as protective as a severe one, and on the general principle that the production of a constitutional effect, and not the amount of the specific poison which produces that effect, is the important factor in conferring constitutional immunity. I made my observations with the expectation that quality of mark alone would prove to be of importance. That is to say, I thought that one good mark must be as protective as several. While, undoubtedly, quality is of much greater value than mere number; while a person with one good mark and two bad marks cannot be supposed to be better off than one with one good mark only, nor can any number of bad marks give better ground for confidence than one, except on the rough principle already alluded to, still there are evidences that, in producing the constitutional effect of vaccination, the quantity of the specific poison introduced does bear some relation to the extent of immunity conferred. In coming to this conclusion I have in my mind the elaborate observations made by Mr.

Marson, on numbers sufficient to make his result worthy of notice, and the confirmation of those results, furnished by the experience of the Homerton and Stockwell Hospitals by the Metropolitan Asylum Board, during the recent epidemic of Small-pox. These latter are, that of 632 persons having one good mark 5.3 per cent. died; of 674 persons having two good marks 4.1 died; of 301 having three good marks 2.3 died; and of 259 having four or more good marks only 1.1 died. My own cases showed that of 191 persons having one good mark 8 died, or 4.2 per cent., while of 130 having two good marks 5 died, or 3.8 per cent., and of 13 persons having three good marks, and one having four, none died. My observations therefore coincide with those quoted.

The real meaning of these facts seems to me to be, that *the quantity of a specific poison has something to do with the immunity conferred by the constitutional infection.* The number of vaccine marks can have no meaning excepting in so far as they indicate in a general way the quantity of lymph introduced into the system. It cannot be that the *same quantity of lymph,* introduced into four spots successfully confers more immunity than if introduced into one spot successfully, or that, by dividing a cicatrix into four, its protective value is increased. Hence I am inclined to think that the local and permanent phenomenon which would best indicate the quantity of lymph introduced, and consequently show even more striking relations to the mortality, would be the *superficial area* of good vaccine cicatrices. It seems evident, from Marson's description of his mode of vaccination, that he would produce five good vaccine marks, whose united area would probably little exceed that of one vaccine mark such as is left by the operation as practised at our public vaccine stations in Glasgow. The data for establishing my conjecture as to the area could not be obtained without immense trouble. Still I think the residuum of these observations is this—that it is of great importance in relation to the general etiology of diseases propagated by specific poisons—that *the quantity of vaccine virus absorbed regulates the duration and thoroughness of the constitutional immunity from Small-pox conferred.*

INFLUENCE OF EXTENT OF ERUPTION ON MORTALITY.

A rate of mortality indicates not only the fact of the death of certain individuals, but also the fact of the risk run by those who did not die. A greater percentage of mortality therefore indicates that the persons making up the centum ran a greater risk of death. To measure and exhibit this risk is of importance, but cannot always be done. In Typhus I have employed,

as a general indication of the fact as well as a means of estimating it, the proportion of patients stimulated, which rises and falls with the mortality. In Small-pox we obtain a better measurement of risk by classifying patients according to the extent of the eruption. The risk of life is almost absolutely in proportion to the extent of the eruption. By testing the effects of vaccination as shown in the proportion of persons having a certain extent of eruption we shall not only demonstrate a very important clinical fact, but, by appealing to a much wider basis of induction than mere mortality affords, we shall lessen the risk of error, and also bring out in greater relief what may be only faintly shown in the preceding pages.

Mortality from Small-pox directly proportioned to the extent of the Eruption.—In the following table the vaccinated and unvaccinated cases are arranged in three categories, according as the eruption was "rare," "copious," or "confluent":—

TABLE IV. a.

Age.	Vaccinated.						Unvaccinated.					
	Rare.		Copious.		Confluent.		Rare.		Copious.		Confluent.	
	T.	D.	T.	D.	T.	D.	T.	D.	T.	D.	T.	D.
0-9	44	...	12	2	1	...	12	...	35	6	29	19
10-19	133	1	54	...	17	9	12	...	34	3	39	13
20-29	125	...	67	5	29	17	8	...	31	3	40	25
30-39	22	...	20	...	14	13	1	...	4	1	8	7
40-	11	...	7	3	10	10	1	...	...	...	...	...
All ages,	335	1	160	10	71	49	34	...	104	13	116	64
Percentage				6·25		69				12·5		55

The result is that only one death took place among those having a "rare" eruption, whether vaccinated or unvaccinated. On referring to the Journal of the Ward, I find that this death was not in any way connected with Small-pox. The patient had chronic cardiac disease, and, after having been walking about for above a week, died suddenly. We may therefore say that *no person having a "rare" eruption dies from Small-pox whether vaccinated or unvaccinated.*

Of those having a "copious" eruption, among the vaccinated 6 per cent., among the unvaccinated 12 per cent. died. Of those having a "confluent" eruption, among the vaccinated 69 per cent., among the unvaccinated 55 per cent. died.[1]

[1] This predominance of fatality among the *vaccinated* "confluent" does not affect our present line of inquiry, but it evidently arises, at any rate in part, from the average age of the vaccinated being much higher.

No remarks are required to prove from these statistics that the gravity of a case of Small-pox depends very directly on the extent of the eruption.

INFLUENCE OF VACCINATION ON EXTENT OF ERUPTION.

Vaccination influences the fatality of Small-pox by diminishing the original extent, as well as occasionally checking the subsequent course of the eruption (see Diagram).—The relative proportion per centum of the three degrees of eruption in natural Small-pox, *i.e.* in the unvaccinated, was this :—

Of 254 unvaccinated persons
13 per cent. had a "rare" eruption.
41 do. do. "copious" do.
46 do. do. "confluent" do.

On the other hand, the proportion per centum of the three degrees of eruption in modified Small-pox, *i.e.* in vaccinated cases, as shown in the last table, is this :—

Of 566 vaccinated persons
59 per cent. had a "rare" eruption.
29 do. do. "copious" do.
12 do. do. "confluent" do.

So that the proportions are more than reversed. While *unvaccinated* people are liable to "confluent" or fatal Small-pox, in the proportion of 46 per cent. of those attacked, 59 per cent., of the *vaccinated* who are attacked, take the "rare," or non-fatal form of the disease.

We have spoken of "good" and "bad" vaccination. Any effect which we suppose vaccination to have, ought to be very decidedly influenced by its quality. That such is the case is shown in this table :—

TABLE V. *a.*

Age.	Good.			Bad.			Quality not noted.	Total Observed.
	Rare.	Copious.	Confl'nt.	Rare.	Copious.	Confl'nt.		
0-9	30	5	...	10	1	1	1	48
10-19	103	24	5	21	20	7	4	184
20-29	87	29	5	21	25	17	3	187
30-39	17	13	2	3	6	8	...	49
40-	8	1	1	1	4	7	1	23
Total, -	245	72	13	56	56	40	9	491

The relative proportion per centum of the three degrees of eruption in Small-pox found in persons who had "good" and "bad" vaccine marks was this, therefore :—

Of 330 persons having good marks
74 per cent. had a "rare" eruption.
22 do. do. "copious" do.
4 do. do. "confluent" do.

While *of 152 persons having "bad" marks*
37 per cent. had a "rare" eruption.
37 do. do. "copious" do.
26 do. do. "confluent" do.

We may bring the three gradations of proportions of eruption together as follows, so that at a glance it may be seen how vaccination tends, by reducing the original amount of eruption, to render Small-pox innocuous to life :—

	"Rare."	"Copious."	"Confluent."
Good V.M., -	74 per cent.	22 per cent.	4 per cent.
Bad V.M., -	37 do.	37 do.	26 do.
Unvaccinated, -	13 do.	41 do.	46 do.

The influence of Vaccination on the extent of the eruption diminishes as the age increases (see Diagram). It is necessary first to determine *what is the influence of age on the extent of eruption in the natural disease?* This is shown in the following table, in which the actual numbers given in Table IV. (*a*) are reduced to percentages of the whole number treated at each decennial period of age : —

TABLE IV. *b.*

Age.	Unvaccinated.			Vaccinated.		
	Rare.	Copious.	Confluent.	Rare.	Copious.	Confluent.
0-9	16	46	38	77	21	2
10-19	14	40	46	65	27	8
20-29	10	39	51	57	30	13
30-39	8	31	61	39	36	25
40-	...	...	...	39	25	36
All Ages,	13	41	46	59	29	12

From this Table it is evident that age alone, or age with the usual average deteriorating influence of vice, hardship, &c., has a decided influence even in the natural disease on the extent of the eruption, and that influence is in the direction of increasing the tendency to confluence. In other words, the older an unvaccinated person is the more risk he runs of having

the confluent or fatal form of the disease. Thus, while the proportions per cent. of "rare," "copious," and "confluent" cases are, during the first ten years of life, respectively 16, 46, and 38; during the ten years between thirty and forty, they are 8, 31, and 61, with an intervening gradation. The question therefore is, whether vaccinated persons show a *greater* "drift" than unvaccinated in the direction of confluence.

That in the vaccinated there is very decided "drift" in this direction is evident from the second half of the last Table, in which decennial percentages of the vaccinated also are given. Starting with a proportion of "rare," "copious," and "confluent" cases during the first ten years of life of 77, 21, and 2 per cent. respectively, we reach between thirty and forty years a proportion of 39, 36, and 25 per cent., with intervening gradations. That in the vaccinated there is also a very much greater "drift" towards confluence than in the unvaccinated will be manifest from the following Table, in which I have taken the percentages of the first decennial period as the standard, and have entered at each subsequent period the difference between its percentages and those of the preceding, using a *plus* or a *minus* sign, according as the difference is an increase or a diminution. In this way, at each decennial period after the first, we can see the exact amount of change or "drift" as I have called it, in the distribution of the percentages as compared with the previous period.

TABLE IV. c.

Age.	Unvaccinated.			Vaccinated.		
	Rare.	Copious.	Confluent.	Rare.	Copious.	Confluent.
0-9	16	46	38	77	21	2
10-19	− 2	− 6	+ 8	− 12	+ 6	+ 6
20-29	− 4	− 1	+ 5	− 8	+ 3	+ 5
30-39	− 2	− 8	+ 10	− 18	+ 6	+ 12

So that while in the successive decennial periods after the first "drift" towards confluence in the *unvaccinated* shows itself in a falling off of 2, 4, and 2 from the percentage of "rare" eruption, in the *vaccinated* the falling off is 12, 8, and 18. Still it will be noticed that the "drift" for the most part only goes the length of transferring the "rare" into the "copious" in the vaccinated, while in the unvaccinated it ends entirely in an addition to the "confluent."

The *quality* of the vaccine mark may be here again employed as a test of the accuracy of those conclusions. If the modifying

influence of vaccination diminishes as the age increases, then it ought to diminish more rapidly in those who are badly vaccinated than in those who are well vaccinated. The following Table is made up on the principle already described of percentages derived from the actual numbers in Table V. (*a*) :—

TABLE V. b.

Age.	"Good."			"Bad."		
	Rare.	Copious.	Confluent.	Rare.	Copious.	Confluent.
0-9	86	14	...	84	8	8
10-19	78	18	4	44	42	14
20-29	72	24	4	33	40	27
30-39	53	41	6	18	35	47
40-	80	10	10	9	33	58
All Ages,	74	22	4	37	37	26

During the first decennial period the percentages of the three degrees of eruption are much alike both in the well and in the badly vaccinated, being 84, 8, 8 in the badly, as against 86, 14, 0 in the well vaccinated; but while between 30 and 40 years of age the badly vaccinated have reverted so nearly to the condition of the unvaccinated as to present a percentage proportion of 18, 35, and 47, the well vaccinated still maintain the proportion of 53, 41, and 6 of "rare," "copious," and "confluent" cases respectively.

It is scarcely necessary to gauge the comparative amount of this "drift," except to contrast and exhibit to the eye *the stability of effect of a good vaccination and the rapidly fading effect of a bad one* (see Diagram). This the following Table, constructed from the preceding manner already described, does very clearly :—

TABLE V. c.

Age.	"Good."			"Bad."		
	Rare.	Copious.	Confluent.	Rare.	Copious.	Confluent.
0-9	86	14	...	84	8	8
10-19	− 8	+ 4	+ 4	− 40	+ 34	+ 6
20-29	− 6	+ 6	...	− 11	− 2	+ 13
30-39	− 19	+ 17	+ 2	− 15	− 5	+ 20

It may be said that in well vaccinated persons the amount of the "drift" towards confluence is not greater than age alone would explain until we get above 30 years of age. The badly vaccinated, on the other hand, show excessive instability, and the "drift" above 20 years tends to increase the "confluent" cases at the expense both of the "rare" and the "copious." There are therefore three degrees of "drift" increasing with age—

　1st. The *natural "drift"* as seen in the unvaccinated, which is least.

　2nd. *The "drift" as seen in the well vaccinated*, which is not greater than the natural drift until we pass the age of 20.

　3rd. *The "drift" as seen in the badly vaccinated*, which is greater than the natural drift at all ages.
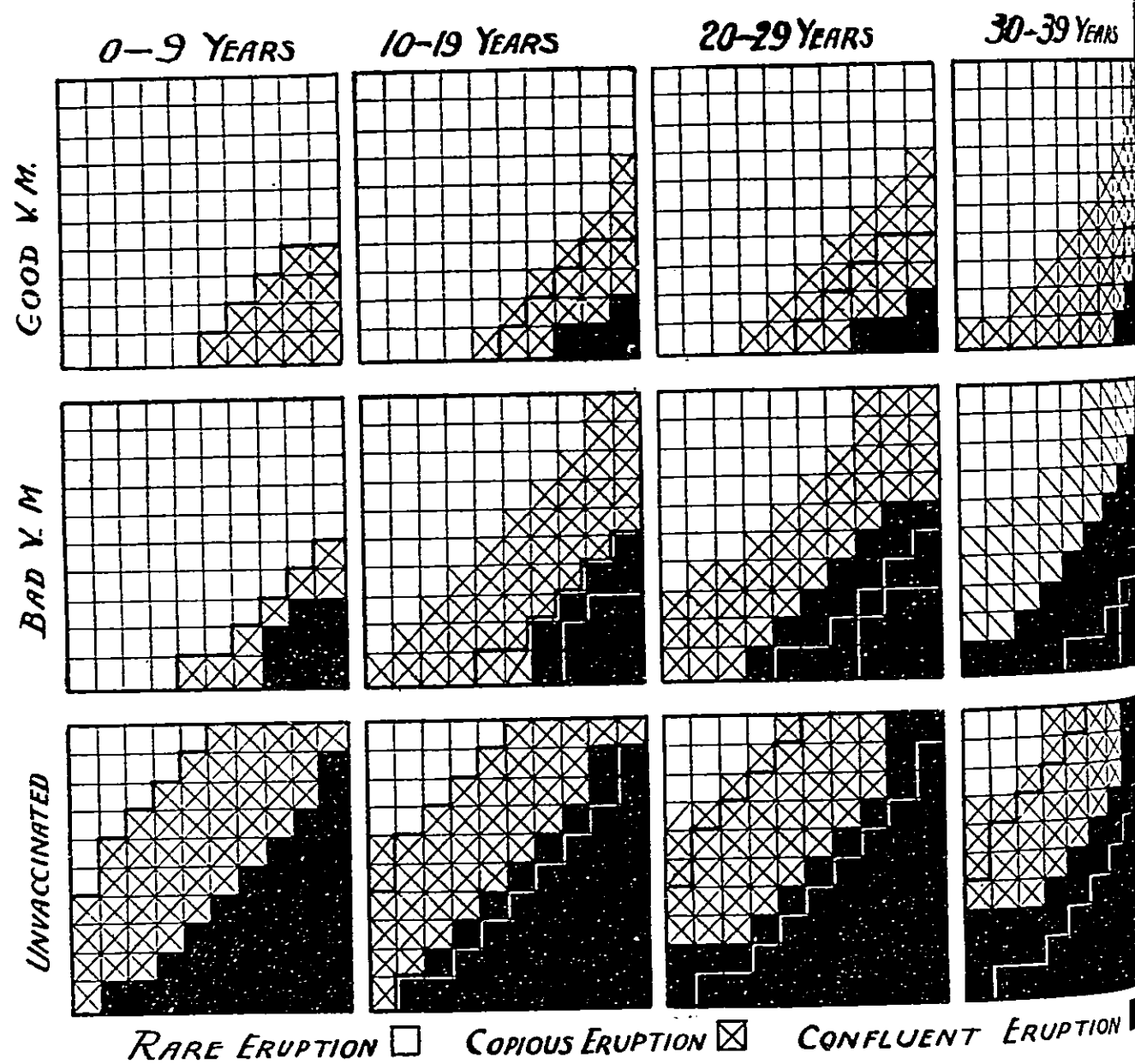
The large squares contain 100 smaller ones, so that the varieties of the smaller squares represent percentages.

DIAGRAM ILLUSTRATIVE OF REMARKS.

The general design of this Diagram is to exhibit to the eye the variable percentages of " rare," " copious," and " confluent " eruption found at different decades of life, in the *unvaccinated*, those who have a *bad vaccine mark*, and those who have a *good vaccine mark*. The following are the principal points which this Diagram illustrates :—

I. *Vaccination diminishes the original extent of the eruption* (p. 474).—This will be evident to any one who contrasts the squares *vertically*, passing from below upwards, especially in the column " 0-9 years."

II. *Age has a slight influence in increasing the tendency to confluence in the natural disease* (p. 475).—The lowest *horizontal* series of squares marked " unvaccinated " shows this. The outline of the original percentages with which we start at " 0-9 years " is retained in the subsequent squares by a black line for the " copious " and a white line for the " confluent." In the same way the " drift " of the disease with age is made apparent in all the Diagrams.

III. *The influence of vaccination on the extent of the eruption diminishes as the age increases* (p. 475).

IV. *The influence of a " good " vaccination is very stable, and of a " bad " very unstable.*—Indeed, until we get above 30, the " drift " of those having a " good v.m." does not exceed in amount what is due to age as seen in the unvaccinated ; but then those having a " bad v.m." have almost reverted to the proportions of the unvaccinated (p. 477).

The two upper series of squares display all this. Taking those under " 30-39 years," it is evident, in the first place, looking to the white and black lines, which represent the percentages at 0-9 years " that the " drift " in the unvaccinated is least, and in those with a " bad v.m." greatest. In the latter the black squares have swallowed up even those which were simply crossed, and have invaded the blank or " rare " squares. The eye at once recognises the gradual assimilation of the squares representing the "bad v.m." to the squares representing the " unvaccinated." Equally readily will a glance show the extreme stability of a " good v.m."

It must be remembered, when we speak of the tendency towards confluence increasing with age in the vaccinated in greater proportion than in those who have the natural disease, that in the vaccinated we set out so to speak from a higher level, and therefore have farther to decline. The proportions of " rare," " copious," and " confluent " cases seen in the natural disease, in the first decennial period of age are exactly reversed in the vaccinated. Therefore this greater " drift " in the vaccinated is in reality the tendency of Small-pox to revert to its natural type. In short, the ultimate issue of this inquiry is to demonstrate, almost to express in exact terms, what I believe to be the fact, that *in the aggregate* the influence of vaccination is unstable. We cannot prove this by finding the proportion of the vaccinated living at each decennial period who, being equally exposed, will take Small-pox; but in those at each decennial period who have taken Small-pox we can find evidence that, as you recede from the point of vaccination, the disease tends to emancipate itself from the modifying power of the vaccination, and to revert to its original type. In other words, the constitutional susceptibility gradually fades. At the same time, it is of the greatest practical importance to remember *how very stable in its effects vaccination may be made by care in the performance of it.* While variola very speedily throws off the modifying influence of a " bad " vaccination, it remains subject to the influence of a " good " vaccination to the latest periods of life. We may be sure that the protective follows the same law as the modifying power. Still these facts, derived from averages, furnish no argument against the revaccination especially in the face of known exposure to contagion, even of those persons who present evidences of perfect primary vaccination. " It is very well for us to know that one person, under inspection, of a certain age, with certain marks, runs so much less risk of proving to be susceptible when exposed to Small-pox than this other person. But so long as we cannot say, you are the individual who will escape, we have no right to leave him even to this diminished risk."

CHAPTER IX.

STUDIES IN VITAL STATISTICS.

WITHOUT some method of measuring results progress in Science is impossible, and the elementary requirements of the science of Vital Statistics are a knowledge of the number of deaths occurring in a given period, and of the population among which they occur.

At an early period the Municipal authorities of Glasgow were keenly alive to the advantages of accurate records of the movements of its population, and there is an echo of still earlier efforts in this direction in Dr. Clelland's report on the plan of Enumeration of the inhabitants of the City and its connected suburbs, which was approved by the Magistrates and Council in 1819.

From this report some extracts may be taken, if only for the interest of the historical associations which they recall.

"There was no enumeration of the inhabitants of Glasgow, that can be relied upon, before the year 1610; but there are grounds for supposing, that, about the time of the Reformation, in 1560, the population might amount to 4500. This estimate of the number is rendered probable from the circumstance that, in 1581, during the ministry of the first Presbyterian clergyman who officiated in Glasgow, the Confession of Faith was subscribed by 2250 individuals; although at that time there were certainly not so many persons in the city who could write, yet they might assent, and even include their children in the number : and the struggle between the professors of the Roman Catholic and Reformed Religion was then so warmly contested that it is probable their numbers were nearly equal.

In 1610, the Episcopal mode of government having been resumed in the Church, Archbishop Spottiswoode directed the population of the city to be ascertained, when it was found to amount to 7644; although, during the plague which raged