"The cancer of the cardia and of the cardiac end of the stomach, and of the lower part of the esophagus, was in an ulcerated condition. The pericardium was found thickened, and the pleura contained recent lymph, and was full of fluid. The case was not correctly appreciated during life. There was intense emaciation, but no dysphagia or vomiting. The patient had little appetite and appeared to be phthisical. He suffered from cough, and had effusion into the pleura, which had been evacuated several times to the amount of one or two pints. The preparation showed that the ulcerated opening of the stomach was quite pervious, and thus the absence of dysphagia was explained. Diarrhea, resembling that found in phthisis, had been a prominent symptom; but though old tubercles were found in both lungs, and ulceration of the small and great intestines, the ulcers were rather of a dysenteric than of a phthisical character."

VII. Ferguson,⁷ reports the following case:

"The patient had suffered from pain in the epigastrium and back which was aggravated by the presence of food in the stomach. Subsequently there was vomiting. When admitted to the hospital, although fairly well nourished, she had lost flesh to a marked degree, her appearance was cachectic, and she suffered constant pain in the back and epigastrium. All solid food was rejected by the stomach. She had hematemesis at one period, recurring repeatedly every day for three weeks. Nourishment was given principally by the rectum. A diagnosis of cancer of the stomach was made. She died on the 29th of January, 1884. Full one-third of the cardiac portion of the stomach was found ulcerated, the ulceration also involving the lower end of the esophagus. There were no enlarged glands in the neighborhood of the growth, and no secondary deposits in other organs."

VIII. At a meeting of the Society for Medical Improvement, Dr. Jackson⁸ showed a specimen of cancer of the cardiac end of the stomach with the following history:

"Mrs. B., died February 27th, aged fifty-three. She was a small, spare, tough woman, and passed all her life in this region. At twenty-two she married, and had nine healthy children. Catamenia ceased at forty-four. She worked very hard; had always a good appetite; but her food often distressed her after meals, so that she 'had dyspepsia ever since she was a girl.' She was hardly ever known to vomit; and during her pregnancies she was well, and never had nausea. Until she became sick, could never relish acids — as vinegar, cider, or even an apple — then, these were particularly grateful to her. I can get no trace of cancer in her family. In August, 1859, she had so much distress in the region of the stomach and esophagus, that she commenced taking homeopathic remedies, which she continued till near the close of life. There was no improvement of her suffering, and in the spring of 1860 there was nausea and sometimes vomiting; and by July the vomiting was constant on taking food. In December she complained of no pain except a peculiar distress which came on a few minutes after taking food, and was generally relieved by its coming back again. There was not at this time any hardness to be felt in or around the stomach; nor was there any ever discovered; nor was there much tenderness at the epigastrium. The settled opinion seemed to be

when I first saw her in December that she had a stricture of the esophagus. This arose from the fact that she persistently felt and said that the food stopped a little more than half-way down the esophagus — putting her hand to mark the exact spot; so circumscribed was the pain, and so confident was she that the stoppage was there that it had to be believed. She was at this period taking liquids and pap, literally all the time, and vomiting nine-tenths of it again, within ten minutes, alleging that it had stopped half-way, 'just there.' Exploration of the esophagus with instruments of various kinds, discovered no resistance whatever. Still, the same experience went on to the last, and the patient was sure the food went only so far, and from that spot was thrown back. For the last two months she took large quantities of food, and her relish was keen, being nothing hurt by the constant ejection of what was taken. Five days before death she raised about a pint of dark, bloody, grumous mucus, somewhat, but not very offensive, and this was the only time anything of the kind appeared — or anything but food. Until a few days before the close, she kept about the house, and on the whole, I think suffered less pain than any other victim of this disease I have seen. Except the stomach, the organs of the body were found remarkably healthy. The cardiac portion of the stomach was in a state of open cancerous ulceration, to the extent of two and a half to three inches from the lower extremity of the esophagus, but the disease did not extend at all up the esophagus, and it was perfectly defined in the stomach, the rest of the organ being quite healthy. The general character of the structure was that of a firm encephaloid, and the surface of the ulcer uneven, and of a yellowish-white, opaque color; the edges were softer, raised somewhat, rounded and vascular. The esophagus throughout was quite healthy, being neither thickened nor dilated."

(To be continued.)

WHAT NUMBER OF CASES IS NECESSARY TO ELIMINATE THE EFFECT OF CHANCE IN MORTALITY STATISTICS, ESPECIALLY THOSE OF TYPHOID FEVER: A STATISTICAL STUDY.

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WITH a view to ascertaining to what extent chance may affect statistics gathered for the purpose of determining the mortality of any particular disease and incidentally the results of any special treatment as shown by such mortality, I have tabulated from the records of the Boston City Hospital, a long series of cases of typhoid fever — over 3,000 in number — this being a disease which hospital records render convenient for this purpose.

These cases have been divided into groups of different sizes — that is, into groups of fifties, hundreds, two-hundreds, etc., and the mortality computed for each group. In thus arranging them no selection, of course, has been made, but every case has been included, and the cases taken *chronologically* according to the time of entrance into the hospital. Thus each group represents a continuous sequence of cases.

According to the doctrine of chances, the larger the groups, the smaller the variations will be found to be between the rates of mortality of the individual groups. By increasing the size of the groups, other

⁷ New York Medical Journal, March 8, 1884, p. 277.

⁸ Boston Medical and Surgical Journal, June 20, 1861, p. 332.

things being equal—that is, the conditions remaining the same—we should expect to find that with groups of a sufficiently large size, the mortality would be practically constant, and we should have a standard mortality; but, of course, the conditions do not remain the same. Nevertheless, we should expect to find that in groups containing a sufficiently large number of cases, these fluctuations would be reduced to a relatively small figure. The question is, What number of cases is necessary to eliminate variations due to chance and thus reduce the fluctuations to this degree?

The results given in the following tables are only directly applicable to typhoid fever; to what extent they are true of other diseases can only be determined by a similar collection of statistics for each disease.

These tables do not take into consideration any variations that may possibly be due to different modes of treatment. It is assumed that the treatment or the effect of treatment upon the mortality has been essentially the same in all the series.

Between 1882 and 1893, 3,176 cases entered the hospital; of these, 412 died, a mortality of 12.66 per cent.

Arranging these cases chronologically by fifties, we have Table I. By this it will be seen that the highest mortality was 24 per cent. and the lowest two per cent., a difference of 22 per cent.

TABLE I.

TYPHOID FEVER IN BOSTON CITY HOSPITAL 1882-1893 INCLUSIVE.

By Fifties.							
Cases	Dths.	%		Cases	Dths.	%	
1882	50	10	20	1887-88	50	1	2
	50	7	14		50	9	18
	50	11	22	1888-89	50	8	16
	50	7	14		50	6	12
1882-83	50	9	18		50	8	16
	50	9	18	1889	50	4	8
	50	8	16		50	3	6
	50	7	14		50	7	14
1883-84	50	10	20		50	4	8
	50	9	18	1889-90	50	8	16
	50	3	6		50	5	10
	50	3	6		50	5	10
	50	5	10		50	2	4
	50	2	4		50	7	14
1884-85	50	12	24		50	5	10
	50	5	10	1890-91	50	8	16
	50	3	6		50	3	6
	50	9	18		50	8	16
1885-86	50	3	6		50	7	14
	50	9	18		50	4	8
	50	7	14		50	4	8
	50	6	12		60	5	10
	50	4	8		50	4	8
1886-87	50	7	14	1891-92	50	4	8
	50	7	14	1892	50	10	20
	50	8	16		50	8	16
	50	7	14	1892-93	50	7	14
	50	9	18		50	10	20
1887-88	50	9	18		50	4	8
	50	7	14		50	5	10
	50	6	12		26	5	19
	50	8	16				
	50	8	16				
Lowest mortality				3,176	412		
Highest "						24%	
Difference						22	

Table II shows the relative frequency of the various mortality rates from two to 24 per cent.

TABLE II.

Number of groups with mortality of	%	
"	2%	1
"	4%	2
"	6%	6
"	8%	8
"	10%	7
"	12%	3
"	14%	12
"	16%	10
"	18%	8
"	20%	4
"	22%	1
"	24%	1
		63

Number of groups with mortality of 19%+ (26 cases) . . . 1

As it might be thought that possibly these large variations might be due to a difference in the virulence of the disease in particular years, the highest and lowest mortality in each year is shown in Table III, the per cent. being as before for groups of fifty. It will be seen by this table that in no year was there a group which did not have a mortality of at least 16 per cent., and with the exception of three years there occurred yearly groups with as low a mortality as two, four, six, and eight per cent.

TABLE III.

HIGHEST AND LOWEST MORTALITY IN GROUPS OF FIFTY, BY YEARS.

	Highest.	Lowest.
	22%	14%
1882	18	14
1882-83	20	4
1883-84	24	6
1884-85	18	6
1885-86	18	14
1886-87	18	2
1887-88	16	6
1888-89	16	4
1889-90	16	6
1890-91	20	8
1891-92	20	8
1892-93	20	8
1893-94	..	..

In the same year (1884-1885) in which occurred the highest mortality, 24 per cent., there is found a series with only six per cent. In every year, with the exception of three (1882, 1882-83 and 1886-87), the variations are quite large. On the other hand, in these three exceptional years, although the highest mortality is not greater than that of other years, the average is much higher, owing to the fact that no group has a lower mortality than 14 per cent, and consequently the variations are comparatively small. The average high mortality of these years, affects the larger groups as will be seen by the following tables. But as most of the years with high mortalities show also low mortalities, the greatest variations in Tables I and II cannot be attributed to differences of virulence in different years.

TABLE IV.

By Hundreds.

	Cases	Dths.	%		Cases	Dths.	%
1882	100	17	17	1888-89	100	17	17
	100	18	18		100	14	14
1882-83	100	18	18		100	7	7
	100	15	15		100	11	11
1883-84	100	19	19	1899-90	100	13	13
	100	6	6		100	7	7
	100	7	7		100	12	12
1884-85	100	17	17	1890-91	100	11	11
	100	12	12		100	15	15
1885-86	100	12	12		100	8	8
	100	13	13		100	9	9
1886-87	100	11	11	1891-92	100	14	14
	100	15	15		100	15	15
	100	16	16	1892-93	100	14	14
1887-88	100	16	16		76	10	10
	100	14	14				
	100	9	9		3,176	412	
Highest mortality							19%
Lowest "							6
Difference							13

TABLE V.¹

By Two-Hundreds.

Cases Dths. %			Cases Dths. %				
1882	200	35	17.5	1888-89	200	26	13.0
1882-83	200	33	16.5		200	21	10.5
1883-84	200	25	12.5	1889-90	200	24	12.0
1884-85	200	24	12.0		200	19	9.5
1885-86	200	24	12.0	1890-91	200	26	13.0
1886-87	200	24	12.0		200	17	8.5
	200	31	15.5	1891-92	200	29	14.5
1887-88	200	30	15.0	1892-92	176	24	13.6
Highest mortality						17.5%	
Lowest "						8.5	
Difference						9.0	

¹ The division by years in this and the subsequent tables is only approximately exact.

TABLE VI.

By Three-Hundreds.

	Cases	Dths.	%		Cases	Dths.	%
1882-83	300	53	17.6	1887-88	300	40	13.3
1883-84	300	40	13.3	1888-89	300	32	10.6
1884-85	300	36	12.0	1889-90	300	32	10.6
1885-86	300	36	12.0	1890-91	300	34	11.3
1886-87	300	47	16.6	1891-92	300	38	12.6
Highest mortality						17.6%	
Lowest "						10.6	
Difference						7.0	

TABLE VII.

By Four-Hundreds.

	Cases	Dths.	%		Cases	Dths.	%
1882-83	400	68	17.0	1888-89	400	47	11.7
1883-85	400	49	12.2	1889-90	400	43	10.7
1886-86	400	48	12.0	1890-91	400	43	10.7
1887-88	400	61	15.2	1891-93	376	53	14.0
Highest mortality						17.0%	
Lowest "						10.7	
Difference						6.3	

TABLE VIII.

By Five-Hundreds.

	Cases	Dths.	%		Cases	Dths.	%
1882-84	500	87	17.4	1891-93	500	61	12.2
1884-86	500	64	10.8	1893	176	24	13.6
1886-88	500	71	14.2				
1888-89	500	61	12.2		3,176	412	12.66
1889-91	500	54	10.8				
Highest mortality						17.4%	
Lowest "						10.8	
Difference						6.6	

TABLE IX.

By Six-Hundreds.

	Cases	Dths.	%
Group 1	600	93	15.5
Group 2	600	72	12.0
Group 3	600	145	14.5
Group 4	600	64	10.6
Group 5	600	72	12.0
Group 6	146	24	16.5
Highest mortality			15.6
Lowest "			10.6
Difference			4.9

TABLE X.

By Seven-Hundreds.

	Cases	Dths.	%
Group 1	700	100	14.2
Group 2	700	96	13.7
Group 3	700	88	12.5
Group 4	700	75	10.7
Group 5	376	53	10.4
Highest mortality			14.2
Lowest "			10.7
Difference			3.5

TABLE XI.

By Eight-Hundreds.

	Cases	Dths.	%
Group 1	800	117	14.6
Group 2	800	109	13.6
Group 3	900	90	11.2
Group 4	776	96	12.0
Highest mortality			14.6
Lowest "			11.2
Difference			3.4

TABLE XII.

By Nine-Hundreds.

	Cases	Dths.	%
Group 1	900	129	14.3
Group 2	900	123	13.6
Group 3	900	98	10.8
Highest mortality			14.3
Lowest "			10.8
Difference			3.5

TABLE XIII.

By Thousands.

	Cases	Dths.	%
Group 1	1,000	141	14.1
Group 2	1,000	132	13.2
Group 3	1,000	115	11.5
Highest mortality			14.1
Lowest "			11.5
Difference			2.6

TABLE XIV.

By Fifteen-Hundreds.

	Cases	Dths.	%
Group 1	1,500	212	14.1
Group 2	1,500	176	11.7
Difference			2.4

Arranging the highest and lowest mortality in each of these groups in one table we have the following (Table XV). By this it will be seen that not till 1,000 cases are recorded are the variations between the different groups reduced below three per cent.

TABLE XV.

Groups of	Highest Mortality	Lowest Mortality	Difference	Difference, omitting first 400 Cases
Fifty	24.0	2.0	22.0	22.0
One-Hundred	19.0	6.0	13.0	13.0
Two-Hundred	17.5	8.5	9.0	7.5
Three-Hundred	17.6	10.6	7.0	5.3
Four-Hundred	17.0	10.7	6.3	4.5
Five-Hundred	17.4	10.8	6.6	4.0
Six-Hundred	15.5	10.6	4.9	3.8
Seven-Hundred	14.2	10.7	3.5	3.3
Eight-Hundred	14.6	11.2	3.4	2.7
Nine-Hundred	14.3	10.8	3.5	1.3
One-Thousand	14.1	11.5	2.6	.8
Fifteen-Hundred	14.1	11.7	2.4	

It was said at the beginning that the continuous high mortality through 1882 and 1883 made the variations in all the groups containing more than one hundred cases larger than would be the case if these exceptional years² were omitted. If the first 400 cases of these years be excluded, it will be seen by the fourth column of Table XV that the differences between the highest and lowest mortalities is less in all the groups containing two hundred or more cases. The smaller groups are not affected for reasons that will be obvious on studying the tables.

In groups of one thousand cases the variations are reduced to eight-tenths of one per cent., while in groups of eight hundred cases they are less than three per cent.

It would thus appear that, assuming the conditions to remain the same (as was done in these tables), it requires from 800 to 1,000 cases to eliminate the effect of chance upon statistics giving the mortality of typhoid fever. Likewise it would seem that if the results of one kind of treatment are to be compared with those of another, an equal number of cases is required to obtain a standard mortality for each. The error due to assuming the conditions to have been the same in the above tables must be appreciable, if not large but it is partially if not wholly allowed for in the persisting variation in the largest groups of cases. It stands to reason that the less the variations in the conditions the less the variations in the results. On the other hand, the condi-

² In 1886-87 was also continuously high.

tions will always vary more or less. The only condition we have control over is treatment. It is doubtful if this has practically varied in the above series—that is, so as to affect the results. It should be said that the average mortality of 12.6 per cent. does not correctly give the result of treatment in the Boston City Hospital, as the cases dying within a few days after admission have not been excluded.

May it not well be that similar variations from chance alone may occur in statistics of mortality or statistics of the effect of special modes of treatment, of other diseases, such as diphtheria, pneumonia, chorea, epilepsy, etc.? At any rate until the contrary has been shown to be the case, it would seem that it is not safe to accept such statistics as evidence of the efficacy of treatment unless based upon the results in a very large number of cases. That so large a number as 800 to 1,000 is required in typhoid fever at least, is, I think, generally overlooked.

CARDIAC STIMULANTS.¹

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THE condition of the heart is constantly watched by the medical man. From time immemorial all physicians have sought in the pulse as exemplifying the heart of their patients, important aid with regard to diagnosis and weighty suggestions as to treatment. To-day no practitioner is too wise and none too simple to regard it. Neither the gravest consultation nor the most hurried and perfunctory visit is ended before skilful fingers, watched with a mixture of awe and approval by the family, have dwelt upon the radial artery. In all diseases at all stages the behavior of the heart is considered both as an index of the bodily state and a guide for the management of the case.

Unfortunately, this singular unanimity of the profession scarcely extends to the interpretation of the silent message which the heart vouchsafes, and still less to the mode of treatment appropriate to the occasion.

It is the object of the present paper to lay down some general rules as to the choice of cardiac remedies.

As has already been intimated, such a subject touches upon or overlaps all therapeutic measures in all conditions, so that our present consideration will unavoidably be very limited in its scope and incomplete in its details. Yet it is hoped that some practical benefit may be obtained.

In a general way, the disorders of the heart may be divided into those in which it shares in a general weakness of the system and those in which the original trouble is circulatory, using the word in its broadest sense.

The term general weakness is meant to include nervous debility. It is an interesting fact that the great majority of patients who come voluntarily to a physician because they believe the heart to be diseased are happily mistaken, and are really either dyspeptics, hypochondriacs, sufferers from intercostal neuralgia or addicted to some excess which has occasioned palpitation. The hypochondriacs are many of them medical

students, some of whom come in anxiety each year to their instructors for examination. I can recall only one of all such whom I have happened to auscult who actually had an organic lesion. The cases of intercostal neuralgia are apt to be anemic and to have tender spots along the course of an intercostal nerve and the heart is found to be normal. The victims of excess (in tea, coffee, tobacco or venery) are numerous. Their general appearance betrays them; and their heart-sounds have a hurried, quick, sharp, and as it were impatient character at the apex, unassociated with enlargement or persistent murmur. There is little muscular element in the first sound. There may or may not be a slight basic systolic murmur, or at the apex a systolic whiff, once or twice during each respiratory cycle. The nervousness of the apex sounds is quite recognizable. The auscultatory signs are valuable in these functional cases, because the patient may not voluntarily confess his wrong-doing, and yet it is useless for him to swallow drugs without reforming his habits. It is better that for a time the special indulgence should be wholly stopped both because total abstinence is more likely to be attained than is temperance and because even a small amount of tobacco, for instance, will keep the already nicotized heart in its diseased state.

Alcoholic excess often affects the heart in the way just described, but the other bodily effects are usually too evident for one to need to auscult the heart in order to recognize the nature of the case, and besides arterial and myocardial degeneration may be present, so that the prognosis and treatment are not those of functional disturbance.

In the purely functional cases, bromide and a tonic usually bring immediate subjective improvement, and make it easier for the patient to abstain from the exciting cause. If there be anemia, iron is useful. Otherwise I am apt to prescribe compound tincture of cinchona. Nux vomica and strychnine are usually regarded as physiologically incompatible with the bromides, but in this class of cases ten or fifteen grains of bromide of sodium and five or ten minims of tincture of nux vomica seem to me an efficient combination. An analogous experience is the favorable effect upon some cases of enuresis when the belladonna which has been used in vain is combined with nux vomica and the enuresis ceases. Clinical facts are sometimes like Wilkie Collins's heroine, "superior to logic."

Tincture of strophanthus in a dose rarely exceeding five minims, three times a day, has a good effect upon nervous palpitation.

Cases of general and nervous debility sometimes have excessive cardiac weakness out of proportion to the other symptoms. The heart impresses one as thin and flabby. It may be somewhat dilated and there may be inconstant murmurs. The condition is not devoid of danger. There may be sudden collapse, with pulmonary congestion and death. At the same time the mind has considerable influence upon the disturbance, so that assurances that there is no valvular disease and that with returning bodily vigor the heart will become strong, contribute to the cure. About two years ago, a gentleman who had returned from a scientific expedition to Mexico with neurasthenia, and whose condition was causing his family much anxiety, allowed me to show him to a class of medical students as an unusually fine illustration of multiple inorganic murmurs. He recovered rather rapidly after a sea-

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