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THE EPIDEMIOLOGY OF BUBONIC PLAGUE IN HONG KONG

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HISTORICAL.

The present bubonic plague cycle which is widely spread over many tropical countries is popularly supposed to have started in Hong Kong in the year 1894. It started very much earlier, and most probably in Central Asia. As far as I am aware, the first authentic description was by Rocher (1878) who met with it in the province of Yunnan, which is near the Thibetan border. He stated that it had been known there for at least 30 years, and had broken out in epidemic form in 1855 during the Mohammedan Rebellion in that province, and again in 1866-7. It was believed by his informants to have come from further West in the first instance. Yunnan is a mountainous province and communications in those days were poor and travel was slow, hence the spread of the disease was slow. What traffic there was was Eastwards down two routes, one being due East to the neighbouring province of Kwangsi, the other being South-east to the port of Pakhoi on the south coast of China. There was an epidemic of plague in that town in 1867. Another severe one broke out in Yunnan Fu, the provincial capital of Yunnan in 1871, and a further one in Mongtse near the French Indo-Chinese border in 1871-2. When Rocher was in Yunnan in 1880 he encountered a severe epidemic, and in his later writings he mentions subsequent outbreaks, which he states showed a tendency to become less virulent as time went on. He also made the important observation that he noticed no connection between the incidence of plague and climatic conditions, and that the disease recurred regularly each May.

Lowry (1882) gave the first medical description of the disease in South China, having observed it in Pakhoi, and he compared the epidemic with those of Yunnan. He noted an unusual mortality

among the rat population immediately before each epidemic. He did not consider plague to be an old disease in those parts, because he could find no record of the disease previous to 1867 in Pakhoi. There is little information about the spread of plague in the interior, because there were few if any informed European residents or travelers in either Yunnan, Kwangsi or Kwangtung in those early years, but it undoubtedly existed in Kwangsi in the eighties. A feature of these epidemics was their severity. Lowry states that the mortality in Pakhoi, a city of 25,000 inhabitants, was between four and five thousand in the outbreak of 1882. He noted its recurrence in epidemic form every spring, and states that it was endemic during the rest of the year. This is of interest, for it will be seen that the same fact was true of Hong Kong. The disease died out in Pakhoi in 1884 for 10 years, when there occurred another epidemic. Throughout the eighties the disease was slowly travelling Eastwards through Yunnan, Kweichow and Kwangsi to the Kwangtung border. A severe outbreak occurred in Lungchow in 1890, (Sharpe 1894) and at Taiping and Nanning, all of them cities in Kwangsi. The disease was met with in epidemic form throughout Kwangsi for the next four years, and in the winter of 1894 it probably came down the West River to Canton, though some maintain that it came by sea from Pakhoi to the provincial capital. Canton, with a population of more than a million, is much the largest city of South China. It is the meeting place and trading centre of the two provinces of Kwangtung and Kwangsi, and a number of rivers and roads converge on to it. The first case recorded was by Dr. Niles (1894) who saw it in January. From that date the disease spread with great rapidity through the city, to reach its maximum in May. By July it had nearly died out. The mortality was far greater than in any epidemic in Hong Kong, being estimated to have been between 70,000 and 100,000 (Wu L. T. 1935, p. 739). People fled from the city to the country and neighbouring towns for safety, many coming to Hong Kong. In May a serious outbreak occurred in the latter city, which is only 90 miles from Canton. The first deaths were recorded on May 11th, but a considerable number of deaths must have occurred for many days previously, not being diagnosed as plague. The early epidemics in Hong Kong were well described at the time, whereas little or nothing was written about the outbreaks in South China or Yunnan. In addition to this, the first epidemic in Hong Kong is famous in that Yersin and Kitasato while working in that city, almost simultaneously discovered the plague bacillus, so that the impression was created that Hong Kong and not the interior was the place where plague first began.

The neighbouring ports soon became infected, Swatow and Amoy in the same year, Macao in 1895 and Fuchow in 1901. From these places the disease spread slowly inland, to reappear with diminishing severity in succeeding years. Details are very scanty about the interior,

but of the seaports there is better information. The last outbreak in Pakhoi and in Swatow was in 1916. Canton suffered in that year and in 1923 and 1925. Macao had an outbreak in 1912, since when records are incomplete. There is still a focus of infection in the hinterland of Amoy, where an outbreak occurred in the spring of 1937, and another one exists in one or two of the small coast towns between Hong Kong and Pakhoi and in Hai Nan Island. When I was in Kwangsi in the spring of 1937 I was informed by a Government medical officer there that an endemic focus still exists in the centre of the province, where an epidemic occurs every few years, necessitating the sending of doctors and supplies to the affected area. It is however safe to say that after the first decade of this century the disease steadily lost its virulence everywhere in South China.

PLAGUE IN HONG KONG.

As already stated, the first cases occurred in May 1894, being found in the more overcrowded parts of the town. Sanitary conditions at that time were very bad indeed. Owing to the lack of space for building purposes, houses were huddled together, usually of two or three storeys in height, built back to back, with dark cellars and beaten earth floors. The rooms were long and narrow with windows usually only at one end. The very narrowest of streets separated the rows of houses, so that ventillation was very poor. Several families lived in each dwelling room, the rooms being separated from each other sometimes by partitions and sometimes by curtains.

Slopwater pipes in the majority of buildings ran from the kitchens down the inside or outside of the houses to an open gutter used to carry away the slopwater from the ground floor, overflowing in many cases on to the ground. These open gutters discharged into channels below the level of the road, eventually to end in the Harbour. The pipes were described by Wilm (1897) in his report to the Government as "a system of drains (consisting) of small earthenware pipes, which frequently became stopped up, and, being leaky, allowed filthy water to escape into the houses."

The water supply of the town consisted partly of a supply from two reservoirs, but so far as the poorer parts of the town were concerned, very largely from surface wells. As a result of recommendations made to the Government, the use of certain of the wells and cellars was forbidden. The latter were then used as warehouses, thus being more than ever infested with rats, Simpson (1903). Conditions in Hong Kong have improved since then, but change was very slow, and even to-day in certain parts of the town there are over 1,700 persons to the acre. In fact there is more overcrowding to-day than at any time during the plague years. Streets are now much broader and more stringent building laws are enforced, but the 1931

death rate of 36.7 per 1,000 (Uttley 1938a) and a tuberculosis death rate of 4.2 per 1,000 living (both being standardised death rates) are an index of the state of local affairs.

Plague having broken out in the city, it did not die out for 30 years. It was soon made a compulsorily notifiable disease, but notification was always very widely ignored. Consequently any attempt to estimate the incidence or the fatality rate of the disease is pure guess work; the only reliable information about its severity is to be obtained from its death rate per 1,000 living. Official statistics, hitherto the only ones available, deal with the crude death rate of the Colony. These figures are often very wide of the mark, for plague rates in the city and in the country were probably very different, because housing and living conditions were and still are very different from each other, to say nothing about the differences in the rates for Europeans, Eurasians and the considerable population living in boats on the Harbour.

I have therefore restricted my survey to the urban Chinese population, and have personally investigated each death return for the years 1894 to 1923, the last year when an epidemic occurred*, and classified each one occurring in the urban Chinese resident population according to age and sex. All other deaths, such as those occurring among foreigners, Eurasians, the temporary or Harbour populations have been excluded. The result is that it has been possible to calculate the crude death rate for each year, and the standardised rate for the census years, of the plague cycle as it occurred in the cities of Victoria and Kowloon, which together constitute the urban areas of the Colony, and for the purposes of this paper may be considered to form one city, separated by the Harbour. For information as to the degree of the accuracy of these data, and for details about the structure and changes that have taken place in the urban population of the Colony, reference must be made to my paper (Uttley 1938b) on standardised death rates for tuberculosis in Hong Kong, where all relevant data are given in full and need not now be repeated.

Table I. shows the standardised death rates for each census year throughout the period. Crude death rates are given also. The epidemic of 1894 was much the worst of the whole series. The figure given does not register the true state of affairs, for according to Severn (1925) the rate was approximately twice this value, which records only those deaths occurring in the Colony. A large number of people fled from Hong Kong during the epidemic, many of them when they first noticed the dread disease on themselves, and a considerable number died on board the steamers while traveling up to Canton, which is only eight hours' journey away. I do not consider that in

* One death occurred in 1928 and two in 1929, otherwise the Colony has been free from plague since 1923.

subsequent epidemics there was an exodus of people on anything like the scale of that occurring in 1894. Rates for males and females separately are given only for census years, because it is only in those years that the sex and age distribution of the population is accurately known. Standardisation for the census years is against the England and Wales population of 1901. It is necessary to emphasise, as I have done in my previously mentioned paper, where I have given my reasons, that standardised death rates and epidemiological data dealing with Hong Kong are only approximations. It is quite impossible to obtain the accuracy of Western European or of North American figures, but the material herein published is the first dealing with Chinese in Asia where an attempt has been made to get nearer to the truth than by ascertaining crude rates. Elsewhere in China even crude rates, when given, are surmises, because nowhere outside of Hong Kong are there enough Western-trained physicians to be able to certify the cause of death in any but the smallest minority of all deaths.

In order to show the age incidence of plague deaths in Hong Kong I have chosen the year 1901, because it was a census year, and the age and sex grouping of the population was therefore accurately known, and because there was a severe epidemic (though not the worst one) and the errors due to the chance distribution of deaths were therefore reduced to a minimum. The results are seen in Table II. in which it will be seen that plague attacked all ages alike throughout adult life, except possibly in old age, (there were however, only 2,501 persons of 65 years of age or over in the whole population, so it is necessary to allow for the smallness of these figures in estimating the mortality at these ages.) The rate was higher in infancy and childhood, probably because children are about the home for longer periods of time than their elders, (who have to go out to earn a living), and are therefore more likely to be bitten by any fleas in the house.

In comparing the plague death rate with that from all causes, as in Table III, I recognise that falacies are introduced, but they are not sufficiently serious, I believe, to prevent the conclusion being drawn that plague did not attack the extremes of life to anything like the same extent that other diseases did. The table shows that in a severe plague year, more deaths in the second decade of life were due to that disease than to all other causes combined.

Table IV shows the seasonal distribution of the disease. Of the total of 16,693 deaths from the disease recorded in the 30 years under discussion, nearly two thirds occurred in May or June. Autumn showed the lowest rate, followed by winter. Spring saw the major parts of the epidemics, but once the half year was over the rate fell rapidly. All the epidemics lasted from 12 to 21 weeks. If they began early they finished early, if they began late they finished late. Of 14

severe epidemics, four began in March, seven in April, two in May and one in June. It therefore appears that in Hong Kong epidemics of plague began about a month later than in India. c.p. Russell (1935).

TABLE I.

Plague in Hong Kong, 1894-1923
Standardised death rates for census years, crude death rates for all years, with populations at census years.

Year.	Standardised death rate per 1,000 living.			Crude death rate per 1,000 living.	Population, (persons).
	Persons.	Males.	Females.	Persons.	
1894	—	—	—	16.70	—
1895	—	—	—	0.20	—
1896	—	—	—	6.20	—
1897	0.14	0.15	0.13	0.12	163,075
1898	—	—	—	5.42	—
1899	—	—	—	7.05	—
1900	—	—	—	4.44	—
1901	6.94	5.98	7.88	5.59	220,319
1902	—	—	—	1.91	—
1903	—	—	—	4.34	—
1904	—	—	—	1.44	—
1905	—	—	—	0.85	—
1906	—	—	—	2.69	—
1907	—	—	—	0.51	—
1908	—	—	—	3.07	—
1909	—	—	—	0.15	—
1910	—	—	—	0.08	—
1911	0.86	0.73	0.99	0.77	286,118
1912	—	—	—	2.09	—
1913	—	—	—	1.45	—
1914	—	—	—	5.93	—
1915	—	—	—	0.38	—
1916	—	—	—	0.09	—
1917	—	—	—	0.08	—
1918	—	—	—	0.63	—
1919	—	—	—	1.04	—
1920	—	—	—	0.27	—
1921	0.30	0.24	0.33	0.29	434,724
1922	—	—	—	2.28	—
1923	—	—	—	0.28	—

TABLE II.

Deaths from plague and deaths from all causes, with their age incidences, 1901.

Age.	% of total population in each age group.	Deaths from plague.		Deaths from all causes.	
		% occurring in each age group.	Death rate per 1,000 living.	% occurring in each age group.	Death rate per 1,000 living.
0—	3.94	4.71	7.34	31.60	209
5—	4.81	8.68	8.48	4.42	25
10—	6.16	13.15	8.63	4.05	17
15—	11.91	13.31	5.67	5.64	12
20—	15.56	11.60	3.76	6.88	11.5
25—	26.92	22.81	4.54	16.47	16
35—	16.58	11.60	3.83	11.22	17.5
45—	9.07	8.36	4.86	7.76	22
55—	3.84	3.57	4.76	6.20	42
65—	0.90	1.38	9.74	3.70	108
75—	0.24	0.81	18.90	2.04	221
Total.	220,319	1,232		5,724	

TABLE III.

Deaths from plague at ages, expressed as a percentage of deaths from all causes at ages, 1901.

Age group.	% of deaths from all causes.	Standard deviation of the %
0—	3.21	0.41
5—	42.29	3.11
10—	69.83	3.01
15—	50.77	2.78
20—	36.29	2.42
25—	29.80	1.49
35—	22.27	1.64
45—	23.20	2.00
55—	12.39	1.75
65—	8.02	1.87
75—	8.55	2.58
Total	21.52	0.54

TABLE IV.

Seasonal distribution
of plague.
1894-1923.

Month.	Total number of cases, 1894-1923.	Percentage of grand total.
January	155	0.9
February	298	1.8
March	735	4.4
April	2,249	13.5
May	5,021	30.1
June	5,131	30.7
July	2,063	12.4
August	663	4.0
September	185	1.1
October	73	0.4
November	51	0.3
December	69	0.4
Total number of plague deaths...	16,693	

TABLE V.

Monthly mean temperature.
Monthly relative humidity.
Monthly number of plague deaths.
1894 to 1923.

	Jan.	Feb.	Mar.	Apl.	May.	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Total.
1894.—M. M. Temp...	59.6	60.0	63.3	71.2	76.8	79.8	81.1	80.9	81.0	74.5	70.0	62.4	
Rel. hum.	76	76	78	88	85	86	83	85	80	69	63	67	
Plague	—	—	—	—	529	1,657	256	62	3	1	—	—	2,508
1895.—M. M. Temp...	56.5	60.2	63.1	72.3	77.2	81.2	82.1	81.4	80.1	74.8	67.6	63.2	
Rel. hum.	77	81	79	85	83	81	82	82	72	76	66	66	
Plague	—	—	—	—	3	12	2	4	2	—	4	4	31
1896.—M. M. Temp...	62.0	56.0	59.3	70.8	76.0	80.7	82.9	82.4	81.5	77.9	71.7	62.2	
Rel. hum.	79	86	89	88	80	85	83	81	81	75	77	68	
Plague	42	88	140	253	276	121	42	8	6	3	—	1	980
1897.—M. M. Temp...	63.1	54.2	63.3	68.4	79.1	81.5	82.1	80.8	81.2	76.8	69.8	60.6	
Rel. hum.	82	82	90	82	85	85	80	86	80	78	67	70	
Plague	—	—	—	—	3	1	10	1	1	—	2	2	20
1898.—M. M. Temp...	60.1	62.7	64.3	69.2	78.4	81.6	81.7	81.5	80.9	74.9	69.4	62.1	
Rel. hum.	68	80	82	82	84	84	81	83	81	70	63	56	
Plague	7	40	91	379	333	46	4	1	1	1	—	—	903
1899.—M. M. Temp...	59.0	59.6	64.9	69.9	77.6	79.7	82.9	80.9	80.3	74.8	67.8	66.2	
Rel. hum.	64	72	75	85	81	83	83	85	76	68	64	80	
Plague	1	1	22	87	350	416	206	62	44	2	2	8	1,201
1900.—M. M. Temp...	55.6	56.9	61.7	72.5	78.1	79.3	81.4	83.1	81.1	76.7	68.8	64.4	
Rel. hum.	78	76	87	85	83	83	84	79	73	74	70	68	
Plague	7	6	4	57	196	259	175	60	9	11	2	1	787

TABLE V. (*Continued*).

	Jan.	Feb.	Mar.	Apl.	May.	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Total.
1901.—M. M. Temp...	64.9	54.8	63.7	71.9	77.1	81.5	82.2	80.6	80.3	77.4	69.5	61.6	
Rel. hum.	84	52	79	87	86	81	82	84	78	70	66	68	
Plague	6	14	40	108	476	426	128	24	8	—	1	1	1,232
1902.—M. M. Temp...	63.1	59.5	68.1	73.1	79.4	80.3	81.8	81.8	80.8	76.7	71.5	64.6	
Rel. hum.	69	63	83	84	85	84	83	84	66	71	75	77	
Plague	—	—	1	16	92	113	154	44	4	2	1	4	431
1903.—M. M. Temp...	58.3	58.4	66.3	72.4	75.4	82.0	81.7	80.9	78.6	76.1	67.2	61.1	
Rel. hum.	70	75	90	84	88	83	85	85	85	71	65	59	
Plague	2	15	96	266	291	247	56	21	7	5	2	—	1,008
1904.—M. M. Temp...	59.5	62.6	63.2	70.7	75.6	79.8	81.1	80.8	80.2	76.5	68.8	60.7	
Rel. hum.	74	71	88	86	83	83	82	84	82	75	64	65	
Plague	—	2	6	22	81	140	68	13	9	—	—	1	342
1905.—M. M. Temp...	64.3	55.3	58.9	67.8	78.1	81.1	82.3	81.2	80.1	75.9	69.2	65.3	
Rel. hum.	80	85	88	85	83	83	81	84	82	72	68	81	
Plague	4	5	1	5	45	68	49	17	2	3	2	7	208
1906.—M. M. Temp...	58.4	60.4	61.6	69.0	76.5	82.4	82.9	83.2	81.0	75.6	67.4	63.5	
Rel. hum.	81	88	81	89	87	80	81	80	81	64	64	72	
Plague	2	25	57	123	332	114	17	5	—	1	—	—	676
1907....M. M. Temp...	61.4	58.7	63.8	69.2	76.2	79.9	82.5	81.9	80.6	79.0	71.5	61.9	
Rel. hum.	71	77	82	84	82	81	81	83	79	81	75	66	
Plague	—	—	2	1	19	37	42	16	3	5	3	3	131
1908.—M. M. Temp...	62.0	58.3	61.2	68.5	76.1	80.2	82.3	82.1	80.9	76.8	70.2	63.3	
Rel. hum.	79	77	78	89	80	85	83	84	84	79	65	78	
Plague	8	4	9	65	299	336	76	13	2	—	—	1	813
1909.—M. M. Temp...	60.6	60.4	64.1	71.1	74.9	82.1	82.2	82.8	82.2	77.8	70.4	63.6	
Rel. hum.	82	83	82	80	83	81	82	82	81	97	65	61	
Plague	—	—	1	3	13	18	3	1	—	—	1	—	40
1910.—M. M. Temp...	61.8	60.0	63.3	69.6	78.9	82.3	82.3	82.2	79.7	75.3	68.7	59.7	deaths.
Rel. hum.	78	80	85	83	78	80	82	84	83	73	72	67	
Plague	—	—	—	4	5	5	5	1	—	—	—	—	20
1911.—M. M. Temp...	58.9	60.2	65.5	69.7	75.5	82.9	82.0	81.9	81.1	74.3	69.1	64.3	
Rel. hum.	76	73	84	83	90	83	82	83	79	76	77	78	
Plague	—	—	—	3	51	81	55	22	—	1	2	4	219
1912.—M. M. Temp...	57.3	59.9	64.3	69.9	78.9	81.6	83.0	81.8	79.6	76.1	69.3	61.4	
Rel. hum.	81	77	87	82	85	86	81	84	72	69	67	76	
Plague	10	14	7	27	202	197	143	20	5	—	—	—	625
1913.—M. M. Temp...	59.2	60.5	61.7	71.2	77.2	81.2	82.8	81.6	80.4	76.1	70.0	61.0	
Rel. hum.	71	83	81	86	83	83	83	85	82	66	74	70	
Plague	1	3	6	23	49	66	78	50	30	16	9	21	352
1914.—M. M. Temp...	62.8	63.1	67.2	71.5	78.5	82.0	81.9	82.3	80.4	77.5	69.9	64.0	
Rel. hum.	71	81	85	85	81	80	84	80	75	78	75	74	
Plague	44	42	184	561	763	241	55	23	9	—	—	—	1,922
1915.—M. M. Temp...	60.1	63.6	64.9	74.6	75.5	81.6	83.2	83.5	80.9	78.9	70.9	63.4	
Rel. hum.	74	82	79	85	84	84	82	83	77	76	72	65	
Plague	—	3	—	3	34	20	33	20	5	6	4	—	128
1916.—M. M. Temp...	60.7	59.6	60.2	70.6	78.1	79.6	82.7	82.6	80.5	75.9	67.8	62.8	
Rel. hum.	74	81	81	83	84	86	80	83	79	72	66	63	
Plague	2	1	1	8	5	5	2	2	3	1	—	—	30
1917.—M. M. Temp...	55.8	59.4	61.6	69.4	74.8	81.8	81.1	82.0	82.0	77.0	68.2	59.2	
Rel. hum.	66	74	79	87	83	84	84	84	78	75	63	63	
Plague	—	2	—	—	11	6	7	2	—	—	—	—	28
1918.—M. M. Temp...	54.0	59.2	64.0	70.4	76.2	79.5	81.8	79.5	79.6	76.4	69.2	65.2	
Rel. hum.	51	73	82	84	85	86	85	86	82	67	78	81	
Plague	—	—	—	2	44	71	101	16	4	2	1	1	242
1919.—M. M. Temp...	61.5	58.0	66.7	72.5	76.6	82.6	81.8	82.8	80.1	74.2	68.1	61.0	
Rel. hum.	82	80	90	85	83	84	83	83	74	74	68	68	
Plague	4	4	5	1	30	90	151	111	16	1	1	—	414
1920.—M. M. Temp...	59.1	58.8	62.4	69.3	76.1	81.0	82.6	81.7	81.2	76.1	70.9	64.8	
Rel. hum.	58	85	85	85	89	83	84	86	82	71	77	75	
Plague	—	1	—	8	26	46	18	5	—	3	4	1	112

TABLE V. (*Continued*).

1921.—M. M. Temp...	58.8	59.7	03.9	71.9	77.1	81.0	81.6	82.2	80.0	75.8	69.8	64.5	
Rel. hum.	68	70	80	82	89	84	82	83	77	70	60	72	
Plague	2	5	1	5	24	48	26	5	3	—	4	5	128
1922.—M. M. Temp...	60.5	61.3	64.1	71.0	78.6	81.9	82.5	82.4	80.4	75.5	68.4	61.7	
Rel. hum.	83	85	82	82	85	83	82	83	79	75	62	67	
Plague	12	21	58	212	396	202	77	26	6	9	6	4	1,029
1923.—M. M. Temp...	60.0	58.8	65.2	71.5	77.8	80.6	82.0	81.2	81.1	76.0	71.6	64.3	
Rel. hum.	68	74	80	86	81	82	82	84	75	73	74	73	
Plague	1	2	3	7	43	42	24	8	3	—	—	—	133

TABLE VI.

Hong Kong 1894-1923.

Monthly number of plague deaths.
Monthly relative humidity.
Monthly mean temperature.
Monthly mean tension of aqueous vapour.

Month.	Mean number of plague deaths.	Monthly relative humidity.	Monthly mean temperature.	Monthly mean tension of aqueous vapour
January	5.2	74.6	59.8	0.393
February	9.9	78.6	58.9	0.400
March	24.5	82.9	63.1	0.488
April	76.5	84.9	70.3	0.638
May	167.4	84.1	77.1	0.786
June	171.0	83.1	81.0	0.880
July	68.8	82.8	82.0	0.903
August	22.1	83.4	81.7	0.899
September	6.2	78.5	80.6	0.818
October	2.4	72.2	76.2	0.657
November	1.7	68.2	69.4	0.500
December	2.3	69.5	62.9	0.410

I do not propose to publish the official data relating to the incidence of the disease, because as already stated, they do not show what was the true incidence. A large number of people who had plague in a mild enough form to recover were never heard of, and were therefore not included in the statistics.

THE CLIMATOLOGY OF PLAGUE IN HONG KONG.

Table V. shows the relation between the monthly number of plague deaths, the relative humidity and the monthly mean temperature throughout the thirty years. Table VI. is a condensed summary of the previous table.

It was considered by the earlier writers on plague in South China, e.g. Lowry (1882) and (1884) and Abbatucci (1911) that a severe epidemic of plague was usually preceeded by an exceptionally dry winter and spring. As it happens one or two of the winters in the early years of plague were dry, but taking the whole period together there is no statistical evidence for their statements. I have calculated the coefficient of correlation between the average monthly rainfall for the five months November to March and the number of plague deaths in the following season for the thirty years in which plague occurred; the figure is 0.06 (Probable error 0.18), so it is clear that there is no significant association between them. On the other hand I have calculated the correlation coefficients between various climatic factors and plague mortality, the results being shown in Table VII.

TABLE VII.

Correlation coefficients between various climatic factors and the mortality from plague in Hong Kong, 1894-1923.

	Relative humidity.	Monthly mean temperature.	Rainfall	Barometric pressure.	Absolute humidity.
Lag_0	0.31409	0.23509	0.22004	—0.27064	0.27528
Lag_1	0.24594	0.02928	0.04263	—0.09434	0.02783
Lag_2	0.22600	—0.19974	—0.14351	0.11395	—0.13690

The standard error in each case, assuming S.E. $= \frac{1}{\sqrt{n-1}}$, where n = 356, is 0.05308.

The mortality returns for the urban areas of the Colony have been accurate enough to permit of Table VII. being drawn up, and for the material shown there to be comparable with similar data published elsewhere. Because of occasional very wide fluctuations in the recorded figures, the actual monthly statistics have been converted into moving deviations, that is, deviations from a moving average, before being brought into use, I have based this work on Russell and Sundararajan's (1928) paper on cholera, and I quote from them to show how the moving average is obtained. "The 'moving average' is obtained in the following way. The total . . . mortality for a given 12-month period from January to December is taken, divided by 12, and the average figure obtained entered under 'June.' Next, the total deaths for the 12-month period from February to the following January are divided by 12 and the figure entered under 'July' and so on. The first figure being entered under 'June' places the average for the year a fortnight earlier than its actual position, because, of course, it really lies between the 30th June and 1st July. This is a matter of convenience, however, and, as the same method has been adopted throughout, it does not affect comparison of the final results. The points of

the moving average when plotted on the same graph as the actual monthly mortality figures, give a comparatively smooth curve, in striking contrast to the irregular peaks of the latter. After completing the moving average for the whole period of years under examination, the plus or minus deviations of the actual monthly mortality figures above or below the corresponding monthly value in the moving average curve were obtained. These monthly deviations were then correlated in the usual way with the actual rainfall (or other climatic) figures for the corresponding months."

In order to test whether the maximum mortality from plague coincided with the peaks of the various climatic factors under discussion, or whether there was a lag or delay in the relationship between them, I have worked out the mathematical values for these variations. I again quote from Russell and Sundararajan's paper to explain how these values are obtained. "In order to estimate this lag mathematically, the monthly rainfall (or other climatic) figures after being set up with (I) the (plague) deviation figures for the same month (lag_0), were successively correlated with (II) those of the following month (lag_1), and (III) with those two months later (lag_2)".

For example, in the first row of figures in Table VII, the climatic data are correlated with the mortality figures for the same months, January with January, February with February for each year, and so on. In the case of lag_1, January climatic factors were correlated with February plague mortality figures, February data with March mortality figures, and so on. In the case of lag_2, January climatic data were correlated with March plague mortality figures, February data with April deaths, and so on throughout the years covered by this survey.

Relative Humidity. All three figures in the column headed "Relative humidity" are statistically significant, with each lag being a smaller figure than the one before, indicating, that though there is a close relationship between the relative humidity value for one month and the plague deaths for that month, the value falls as the lag in time increases to one or to two months. Maximum relative humidity values tend to occur with a high plague mortality in Hong Kong.

Monthly Mean Temperature. The correlation coefficient for lag_0 is lower than in the case of relative humidity, and that for lag_2 is a statistically significant negative figure. There is little doubt that a high monthly mean temperature is associated with a high plague mortality, and that there is little or no lag between the one and the other.

Rainfall. Here again, the relationship, though a definite one, is rather less than the one before. The maximum is also in lag_0, indicating that outbreaks of plague accompany or follow on closely the beginning of the rainy season. The figure for lag_1 is not significant, and that for lag_2 barely so.

Pressure. There is a definite negative correlation between atmospheric pressure and plague in the case of lag_{11}; the other values are not statistically significant.

Absolute Humidity. The degree of correlation in lag_{11} between plague and absolute humility is not quite so great as with relative humidity. The value for lag_1 is not significant, and that for lag_2 is definitely a negative one.

It may be argued that these data do not shed any fresh light on plague mortality, but I maintain that they give definite mathematical values to the relationship between plague and certain climatic factors in Hong Kong, which all over the world are known to exercise a strong influence on plague mortality, and that they do so to an extent that will enable epidemiologists elsewhere to compare them statistically with corresponding values for their own countries.

The publication of this information is of interest in that to the best of my knowledge it is the first of its kind for bubonic plague in China.

ANTI-PLAGUE MEASURES IN HONG KONG.

When the relationship between bad housing conditions and plague was realised by the Government, a medical officer of health was appointed, new building ordinances were introduced which by the passage of time resulted in a certain standard type of house and tenement being erected as and when the older ones were pulled down in certain areas of the town, though not as yet where plague was worst. Alleyways were widened, wells abolished, drainage generally improved, most of the rat-infested ground surfaces replaced by concrete floors, and a better water supply introduced. These changes took a considerable time to come about, and they coincided with a general diminution in the severity and mortality from plague in the Far East. It is therefore difficult to assess the value of these changes so far as Hong Kong is concerned: they also coincided with a rapid increase in the population of the city, so that although hygienic conditions undoubtedly did improve considerably, yet the density per acre also increased. So far as the rest of China is concerned, during the period under discussion there was no change in the general sanitary conditions of the towns and countryside, which remained much as they had been for centuries.

I am inclined to think that the conclusions of workers in India apply to Hong Kong, namely that in the case of plague, as with some other zymotic diseases, there is a rise and fall in the conditions favouring the disease, and that this in the case of plague is likely to be due to an acquired immunity in the rat population, or that it may be due to other factors acting which are detrimental to the flea carrier. There is as yet very little evidence from China on this subject, but

it is to be noticed that climatic conditions have not changed in Hong Kong, either during or since the plague years, and that the rat population has certainly not diminished in numbers with the passage of time. No work has been done in Hong Kong to determine the immunity of the rat population, and according to Wu L.T. (1935) p. 775. no similar work has yet been done in South China.

RATS.

Rat catching in Hong Kong was instituted in 1901, and for many years the annual numbers caught have exceeded 100,000, with a steady tendency to rise. Table VIII shows the monthly mortality from human and rat plague, while Table No. IX shows the crude death rate for plague with the number of rats caught and the rate infected per 1,000 for the plague years for which there are records. There is usually a high infection rate among the rat population in those years when there is a high human rate, as would be expected.

The three species found in the Colony are:—

R. decumanus, constituting 41% of those caught.

R. rattus, constituting 32% of those caught.

R. musculus, constituting 27% of those caught.

Below are shown the total number of the three species found infected during the years 1909 to 1923, with the monthly percentages of their respective totals in brackets:—

	Jan.	Feb.	Mar.	Apl.
R. rattus	9 (1.4)	11 (1.7)	38 (5.9)	39 (6.1)
R. decumanus	47 (2.0)	89 (3.7)	212 (8.9)	347 (14.5)
R. musculus	—	—	—	1 (5.6)
	May	**June**	**July**	**Aug.**
R. rattus	156 (24.2)	149 (23.1)	133 (20.7)	57 (8.8)
R. decumanus	632 (26.4)	501 (20.9)	298 (12.5)	123 (5.1)
R. musculus	1 (5.6)	1 (5.6)	1 (5.6)	6 (33.3)
	Sep.	**Oct.**	**Nov.**	**Dec.**
R. rattus	25 (3.9)	13 (2.0)	7 (1.1)	7 (1.1)
R. decumanus	49 (2.0)	39 (1.6)	25 (1.5)	21 (0.9)
R. musculus	8 (44.4)	—	—	—

Total:	R. rattus	644
	R. decumanus	2,393
	R. musculus	18

FLEAS.

No flea surveys were carried out during the plague years. The only ones done were in 1928-1931. The results were as follows:—

X. cheopis	4,704
Leptopsylla	186
Ctenopsylla...	60
Ctenocephalus	44
Pulex	4
Ceratophylus	1
X. astia	—
X. braziliensis	—
Total	4,999
Number of rats examined alive	791
Flea index	6.32
Cheopis index	5.95

These figures are much too small to draw any definite conclusions from them, especially as the surveys were not carried out during an epidemic, but they are the only material available about the rat fleas of Hong Kong.

TABLE No. VIII.

Monthly mortality from Human Plague.
Monthly mortality from rat plague.
1909-1923.

Month.	Human plague monthly mortality.	R. rattus monthly mortality.	R. decumanus monthly mortality.
January	1.4	1.4	2.0
February	1.8	1.7	3.7
March	4.9	5.9	8.9
April	16.0	6.1	14.5
May	31.2	24.2	26.4
June	21.0	23.1	20.9
July	14.3	20.7	12.5
August	5.8	8.8	5.1
September	1.6	3.9	2.0
October	0.7	2.0	1.6
November	0.6	1.1	1.5
December	0.7	1.1	0.9
Total human plague deaths: 5,424.			

TABLE No. IX.

Hong Kong 1907-1923.

Number of rats caught. The number infected.
The infection rate per 1,000 caught.
The crude death rate of human plague.

Year.	Number caught.	Number infected.	Rate per 1,000 caught.	Crude death rate from plague.
1907	38,520	28	0.74	0.51
1908	27,244	157	6.75	3.07
1909	76,135	507	6.66	0.15
1910	77,755	120	1.54	0.08
1911	87,238	269	3.08	0.77
1912	89,970	492	5.74	2.09
1913	108,507	294	2.71	1.45
1914	101,658	651	6.41	5.93
1915	109,909	98	0.89	0.38
1916	111,629	76	0.68	0.09
1917	106,522	31	0.29	0.08
1918	103,641	203	1.96	0.63
1919	104,104	252	2.42	1.04
1920	107,267	19	0.18	0.27
1921	112,702	7	0.06	0.29
1922	109,296	25	0.23	2.28
1923	94,071	11	0.12	0.28
	1,566,168	3,241	2.07	

DISCUSSION AND CONCLUSIONS.

I have calculated the standardised death rates for census years, and crude rates for each year from 1894 to 1923 for plague occurring among the urban Chinese population in Hong Kong. The observed decrease in the mortality from its initial maximum, although it coincided with an improvement in the general hygienic and housing conditions of the Colony, probably occurred independently of these factors because of a coincident diminution in the severity of plague everywhere in South China, in which area there were no similar changes during the period under discussion.

Climatic conditions favour the spread of plague in Hong Kong in the spring and early summer. When the mean temperature rises to 63° the relative humidity to 83°, and the tension of aqueous vapour

to 0.500, epidemics are likely to occur. When these factors approach respectively the values of 82°, 83° or more for three to four months, and 0.900 the disease tends to die out. Inasmuch as these factors have often prevailed in non-epidemic years, and indeed when there has been no case of plague, as in the years following 1923, it is necessary to look for other causes which may govern the appearance of plague, either in epidemic or sporadic form in Hong Kong. These factors presumably may concern the bionomics of the flea, about which I am not competent to write.

I have calculated the coefficients of correlation between the five main climatic factors, relative and absolute humidity, monthly mean temperature, rainfall, and barometric pressure and plague, and also the 'lag' values for delays of one month and two months between plague and these climatic factors. In the case of the first four, relative humidity shows the largest coefficient for each of the 'lags' that is, it is the most important single factor of those under consideration, whereas barometric pressure has a high negative correlation, indicating that plague prevails when the pressure is low.

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CORRELATION TABLES.

A full set of correlation tables would involve five for each of lag_0, lag_1 and lag_2; as, however, it is lag_0 which is of the greatest interest, I merely give a set of five of lag_0.

Lag_0 Plague deviations.

Relative humidity	—200 and more	—150 to —199	—100 to —149	—50 to —99	0 to —49	0 to 49	50 to 99	—100 to 149	150 to 199	200 to 249	250 to 299	300 to 349	350 to 399	400 to 449	600 to 649	1,400 to 1,449	Totals
50°—53°	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	2
54°—57°	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1
58°—61°	0	0	0	1	3	0	0	0	0	0	0	0	0	0	0	0	4
62°—65°	0	1	0	2	14	0	0	0	0	0	0	0	0	0	0	0	17
66°—69°	1	0	1	10	15	0	0	0	0	0	0	0	0	0	0	0	27
70°—73°	0	0	2	9	19	0	0	0	0	0	0	0	0	0	0	0	30
74°—77°	0	0	2	8	30	0	0	0	0	0	0	0	0	0	0	0	40
78°—81°	1	0	2	16	34	8	3	0	1	1	1	1	0	0	1	0	69
82°—85°	0	0	3	9	56	41	7	8	4	0	2	3	1	1	0	0	135
86°—89°	0	0	0	2	11	5	3	1	1	1	1	0	1	0	0	1	27
90°—93°	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0	4
Totals:	2	1	10	59	185	56	13	9	6	2	4	4	2	1	1	1	356

Lag_0 Plague deviations.

Monthly mean temperature.	—200 and more	—150 to —199	—100 to —149	—50 to —99	0 to —49	0 to 49	50 to 99	—100 to 149	150 to 199	200 to 249	250 to 299	300 to 349	350 to 399	400 to 449	600 to 649	1,400 to 1,449	Totals
54°—56°	0	0	0	3	3	1	0	0	0	0	0	0	0	0	0	0	7
57°—59°	0	0	0	6	19	0	1	1	0	0	0	0	0	0	0	0	27
60°—62°	0	0	2	9	34	0	0	0	0	0	0	0	0	0	0	0	45
63°—65°	0	0	3	7	22	1	0	0	0	0	0	0	0	0	0	0	33
66°—68°	0	0	0	5	15	1	0	0	0	0	0	0	0	0	0	0	21
69°—71°	0	1	1	4	23	3	1	0	0	0	0	1	1	0	0	0	35
72°—74°	1	0	0	1	11	2	0	0	1	0	0	0	0	0	0	0	16
75°—77°	0	0	0	9	13	10	1	0	1	2	2	0	1	1	0	0	40
78°—80°	0	0	2	8	15	9	2	2	3	0	2	2	0	0	1	1	47
81°—83°	1	0	2	7	30	29	8	6	1	0	0	1	0	0	0	0	85
Totals:	2	1	10	59	185	56	13	9	6	2	4	4	2	1	1	1	356

Lag_0 Plague deviations.

Rainfall in inches	—200 and more	—150 to —199	—100 to —149	—50 to —99	0 to —49	0 to 49	50 to 99	—100 to 149	150 to 199	200 to 249	250 to 299	300 to 349	350 to 399	400 to 449	600 to 649	1,400 to 1,449	Totals
0—	0	1	5	34	105	7	2	1	2	1	0	1	0	0	0	0	159
3—	0	0	2	12	26	6	1	0	2	0	1	2	1	0	0	0	53
6—	0	0	0	4	22	6	2	1	0	0	1	0	0	0	0	0	36
9—	0	0	0	3	12	12	3	3	0	0	1	0	0	0	0	0	34
12—	0	0	0	4	7	7	1	1	0	1	0	0	1	0	1	0	23
15—	1	0	1	2	4	5	1	1	0	0	1	0	0	0	0	1	17
18—	1	0	1	0	3	5	1	2	0	0	0	1	0	1	0	0	15
21—	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0	4
24—	0	0	1	0	1	2	1	0	2	0	0	0	0	0	0	0	7
27—	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1
30—	0	0	0	0	1	3	1	0	0	0	0	0	0	0	0	0	5
33—	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	2
Totals:	2	1	10	59	185	56	13	9	6	2	4	4	2	1	1	1	356

Lag_0 Plague deviations.

Barometric pressure in inches.	—200 and more	—150 to —199	—100 to —149	—50 to —99	0 to —49	0 to 49	50 to 99	—100 to 149	150 to 199	200 to 249	250 to 299	300 to 349	350 to 399	400 to 449	600 to 649	1,400 to 1,449	Totals
29·500	0	0	0	1	1	2	2	1	0	0	0	0	0	0	0	0	7
·550	0	0	2	1	8	9	0	0	0	0	0	0	0	0	0	0	20
.600	0	0	1	1	10	12	4	5	0	0	0	1	0	0	0	0	34
.650	1	0	1	4	11	14	3	1	2	0	2	1	0	0	0	1	41
.700	0	0	0	3	7	7	1	0	1	0	2	0	0	1	0	0	22
·750	0	0	0	4	12	3	1	1	1	2	0	0	1	0	1	0	26
.800	0	0	0	4	16	3	1	1	2	0	0	0	0	0	0	0	27
.850	1	0	0	1	18	2	0	0	0	0	0	1	1	0	0	0	24
.900	0	0	0	10	23	3	0	0	0	0	0	1	0	0	0	0	37
·950	0	1	0	9	28	0	1	0	0	0	0	0	0	0	0	0	39
30.000	0	0	3	8	29	1	0	0	0	0	0	0	0	0	0	0	41
.050	0	0	1	11	17	0	0	0	0	0	0	0	0	0	0	0	29
.100	0	0	2	1	3	0	0	0	0	0	0	0	0	0	0	0	6
.150	0	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	3
Totals:	2	1	10	59	185	56	13	9	6	2	4	4	2	1	1	1	356

Lag_0 Plague deviations.

Tension of aqueous vapour.	—200 and more	—150 to —199	—100 to —149	—50 to —99	0 to —49	0 to 49	50 to 99	—100 to 149	150 to 199	200 to 249	250 to 299	300 to 349	350 to 399	400 to 449	600 to 649	1,400 to 1,449	Totals
0·200	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	2
·250	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.300	0	0	0	2	5	0	0	0	0	0	0	0	0	0	0	0	5
.350	0	0	1	8	28	1	0	0	0	0	0	0	0	0	0	0	38
.400	0	0	2	6	22	0	0	0	0	0	0	0	0	0	0	0	30
.450	0	1	1	11	23	0	1	0	0	0	0	0	0	0	0	0	37
.500	0	0	1	5	11	1	0	0	0	0	0	0	0	0	0	0	18
.550	0	0	1	1	11	2	0	0	0	0	0	1	0	0	0	0	16
.600	1	0	0	2	19	2	1	1	0	0	0	0	0	0	0	0	26
.650	0	0	0	5	13	1	0	0	2	1	0	0	1	0	0	0	22
.700	0	0	0	2	7	2	1	0	1	1	0	0	0	0	0	0	14
.750	0	0	1	3	6	7	0	0	0	1	2	0	0	1	0	0	21
.800	1	0	0	2	8	7	0	1	2	0	1	1	1	0	1	0	25
.850	0	0	1	7	12	19	5	3	0	0	1	2	0	0	0	1	51
.900	0	0	2	4	19	13	5	4	1	0	0	0	0	0	0	0	48
.950	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1
Totals:	2	1	10	59	185	56	13	9	6	2	4	4	2	1	1	1	356

BERIBERI IN ST. HELENA
A CLINICAL STUDY

by

P. B. Wilkinson,

Government Medical Department, Hong Kong.

"Say not the struggle naught availeth,
The labour and the wounds are vain,
The enemy faints not nor faileth,
And as things have been they remain."

HISTORICAL.

Since its discovery in 1502, the Island of St. Helena has never been self supporting; that is to say, it has never grown sufficient food for the needs of its inhabitants. One of the earliest references to this deficiency is to be found in the following letter, written in 1684:—

> "The greatest defect we know of in the Island is the want of grain. We are at length in hopes that you may produce very good rice upon your highlands. Captain Knox that lived 20 years in Ceylone informed us that there is a peculiar sort of rice that groweth best on high and dry land, the seed and cultivation of which he knoweth very well. He and one Ralph Knight that is on board his ship having wrought many years upon it with their own hands in Ceylone we wish he could stay 12 months that he might show the manner of 'inning' as well as sowing. The planters upon the Island are so loose and neglect a people that you are not to depend upon them for making of this or any new experiment but begin everything that is new upon the Company's ground with the Company's own negroes."
>
> (The Chairman and Court of Directors of the East India Company to Governor John Blackmore, 25th April, 1684.)

It is much to be regretted that Captain Knox was never able to start the cultivation of this "peculiar sort of rice." But the fact remains that rice has never been grown in the Island, and it has had to be imported from the earliest times.

The earliest statistics available on the subject were first compiled in 1810, when a distinction was made between rice and "paddy." The "paddy" of 1810 was certainly unhusked rice, but whether the "rice" which appears in the import tables of that date was polished or not, it is impossible to say. When the Crown took over the Government of the island from the East India Company in 1836, this important distinction was no longer made, and since 1836, all types of rice have been included under the generic name "rice." Up to the year 1885 the rice supplies of the island were imported for

all practical purposes direct from the East Indies. About this date the change in trade routes that resulted from the opening of the Suez Canal first began to manifest itself. The result was that the source of supply was diverted to London. Since 1910 all the rice imported, with the exception of a few war-time importations, has been a re-export from London. The histograms in Figure 1 have been plotted from the figures as they are given in the records. The abscissa shows the date, the ordinate the number of hundredweights of rice imported in that year, and also the population of the island.

It seems fair to assume that the bulk, at any rate, of the rice imported from the East Indies was unmilled. This assumption is supported by the testimony of old Islanders now living. Many people now in the sixties state definitely that the bulk of the rice eaten on the Island in their childhood was "brown" rice, and some of them also state that the long grained white rice, which was known as "fine" rice was considered a luxury in the eighties and nineties of last century and was only used as food by the upper classes. Nearly all these witnesses date the supersession of grown rice by white rice to the first decade of this century. Many of them say that "brown rice disappeared when the Boer prisoners left the Island."

The curves made from the import figures corroborate both my assumption and the testimony afforded by the older generation of Islanders. They show very clearly how the imports of rice from the East Indies declined in the decade following the opening of the Suez Canal, and how this declension reached the zero point in 1910. One can also see how the imports from England rose as the East Indian ones fell.

The assumption is also borne out by the facts relating to the first appearance of beriberi in the Island. Most unfortunately the records of disease in St. Helena are meagre in the extreme, and again one is compelled to have recourse to assumption and hypothesis.

The first mention of the disease in the records of the Island is found in the Death Register for the year 1854. Three seamen died of beriberi in St. Helena in 1854. The next mention of the disease is found in the Blue Book for 1886. Four cases, one of which died, were recorded in that year, and it is of importance to note that the man who died was a seaman. Deaths from the disease are also recorded in 1887, 1898 and 1900, and again all the cases which died were seamen. Unfortunately the Blue Books do not say whether the cases they record were seamen or islanders, but an examination of the Death Registers have made it possible to say that all the deaths from beriberi which occurred in St. Helena before 1901 were cases of the disease landed from ships. The following table shows the deaths from the disease and the years in which they occurred, from 1854 up to the present day.

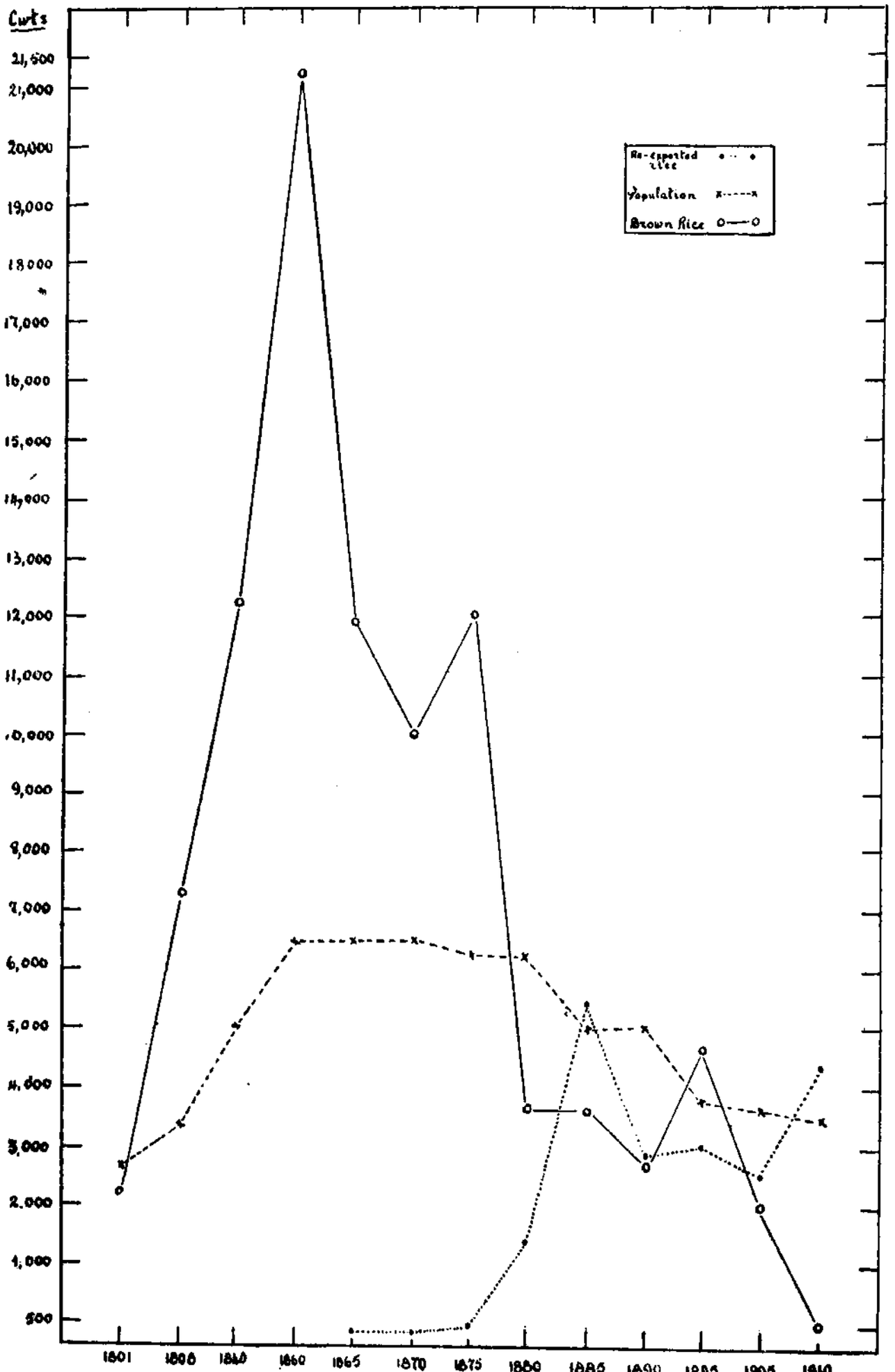


Figure 1. Frequency polygons showing rice importations and population levels from 1801 to 1910.

DEATHS FROM BERIBERI.

1854.	3.	Seamen.
1886.	1.	,,
1887.	1.	,,
1898.	2.	Norwegian seamen.
1900.	1.	Seaman.
1902.	12.	1 Seaman, 11 prisoners, Boers.
1903.	1.	Seaman.
1907.	1.	,,
1926.	2.	Seamen. Both lascars.
1934.	1.	Islander.
1935.	1.	Islander.

It is well known that ship-beriberi was a common type of the disease during the last 2 decades of last century, and the older Islanders give vivid descriptions of these dropsical men being brought ashore to be taken to the Hospital. Some of them also state that in the eighties and nineties of last century the disease did not occur among the Islanders themselves. The credibility of their accounts is strengthened by a detail remembered by many of them, that the disease was commonest in the crews of Norwegian ships. It is matter of common knowledge that in 1894 the crews of Norwegian ships were compelled by statute to use bread baked from white flour, or a mixture of wheat and rye, so that their diet became deficient in supplies of vitamin B_1. This accounts for the fact that beriberi was seen far more frequently in Norwegian than in English ships, though the sanitary condition of the English ships was much inferior to that of the Scandinavian.

It is, then, justifiable to assume that most, if not all, of the cases seen in St. Helena from 1886 down to at any rate 1900, were cases of ship-beriberi which had been landed at the Island.

There was an outbreak of the disease among the Boer prisoners of war, and in 1902 eleven of the prisoners are recorded to have died of beriberi. It is difficult to ascertain at the present day why this outbreak occurred. No record of the diet allowed to the prisoners is extant, and such remarks as occur in the Annual Reports of the period would almost lead one to believe that they were kept in the lap of luxury. In the Annual Report of 1903 the Colonial Surgeon observed that the disease had appeared for the first time among the Islanders, and he inclined to regard it as a legacy left by the prisoners. One can only adopt an attitude of suspended judgment towards this observation. The Colonial Surgeon had only been a few months in the island when he made it, and it is known from a letter written by him in 1907 that even at that date he still clung to the belief that the disease was an infectious one. Doubt must, therefore, still exist as to whether any of the earlier recorded cases were indigenous or not.

From 1904 onwards the disease has appeared regularly in the returns. It ceased to appear in them from 1915 to 1926, two seamen who were landed suffering from beriberi died here of the disease. It seems that the disease next attracted attention in 1934, in which year 75 cases of varying degrees of severity were recorded. Since that date investigations into the clinical manifestations and aetiology of the disease in St. Helena have been pursued with energy.

One more set of curves is appended here to show the relation between shipping calling at the island and seamen admitted to Hospital. The histograms in Figure 2 show the incidence of beriberi from its earliest recorded appearance in St. Helena to the present day.

The histograms show how commonly the disease was seen in St. Helena towards the end of the last century, and most of these cases were probably ship-beriberi. The disease then began to appear in the island itself. A scrutiny of the death registers for the early part of this century leaves one with the impression that it is possible that some of the early cases were not recognised as such. During the period 1900 to 1910 inclusive, there were 25 deaths from Bright's disease, 14 from Nephritis and 2 from unqualified dropsy. Bright actually described an acute inflammation of the kidney accompanied by dropsy and albuminuria and a chronic form in which dropsy is absent. What is and what is not Bright's disease is a most controversial subject. In any case, neither the acute nor the chronic forms of Bright's disease are common. One is left to choose between the two horns of a dilemma. Either the island experienced an unprecedented outbreak of various kidney diseases in this decade, or some of the cases were not nephritic in origin at all. The latter supposition seems to accord better with the results of 2 years of clinical observation. These results show that beriberi is common, nephritis quite uncommon. The only kidney lesions noted at autopsy have been those co-existing with hyperpiesis or gross cardio-vascular disease. It is, therefore, justifiable to conjecture that some, at least, of these cases may have died of beriberi, but unfortunately it does not appear to have been the practice to make postmortem examinations in St. Helena. It is amusing to note that O'Meara in 1816 gave the island a bad name for causing "hepatitis." Were a twentieth century O'Meara minded to substitute "nephritis" for "hepatitis" he could obtain abundant support for his allegations from the records of the first decade of his century.

From the evidence afforded by the records, such as they are, it seems clear that there is a definite correlation between the importation of polished rice and the appearance of beriberi. It is indisputable that no case of the disease appears in the medical records until 21 years after rice began to be re-exported from Great Britain to St. Helena, and it is unlikely that the 19th century cases which are on

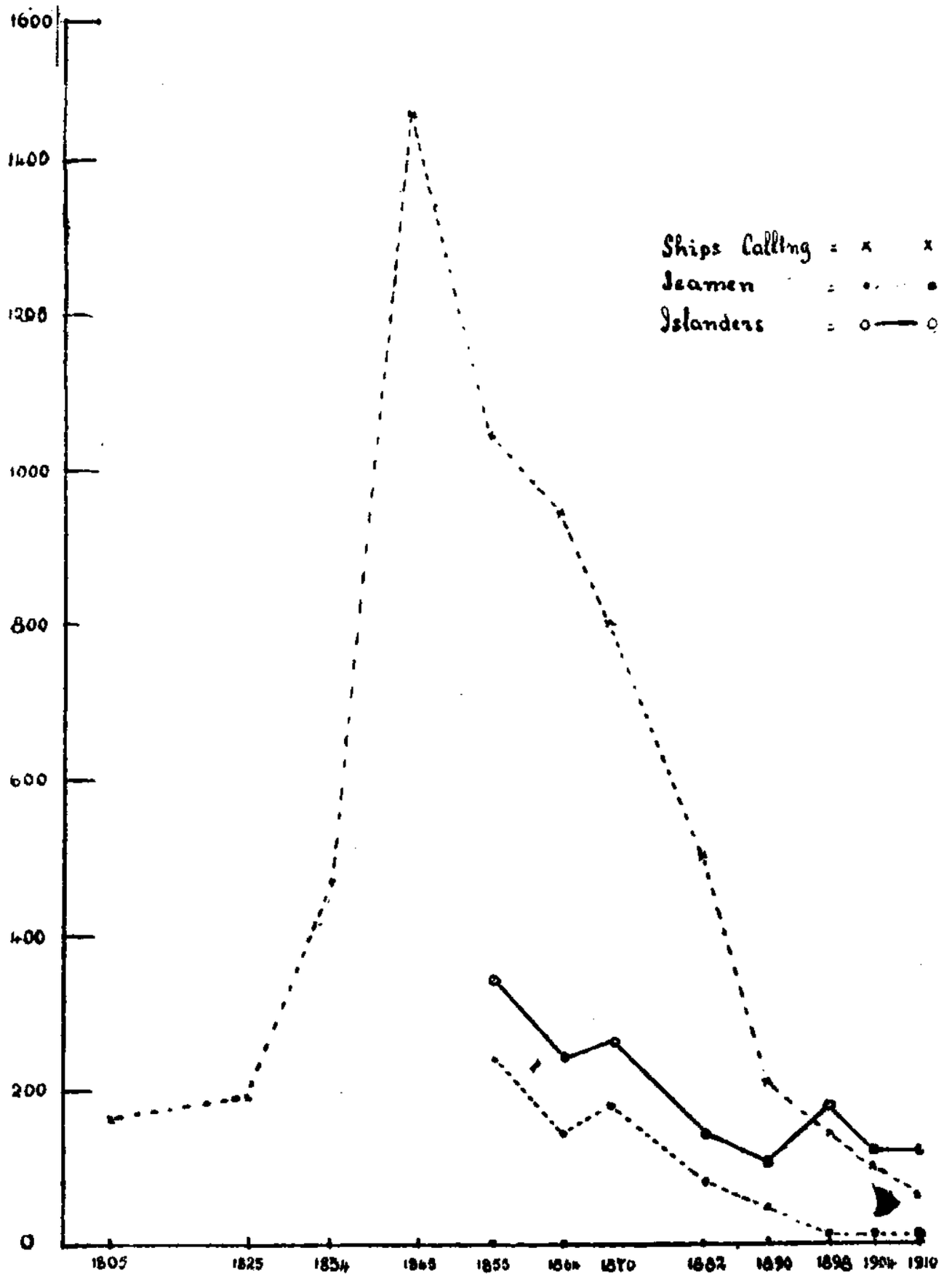


Figure 2. Frequency polygons showing the relation between shipping calling at the island of St. Helena, and admissions, both seamen and islanders, to hospital.

record were indigenous for the reasons already given. A dispassionate study of the historical data leaves one with no other conclusion but that the disease has appeared, and is maintaining itself in St. Helena, because the staple food of the Islanders has become polished rice.

EPIDEMIOLOGICAL.

It is scarcely possible, as yet, to say what is the average number of cases of the disease seen each year. After the end of February 1934, it became abundantly clear that beriberi existed on the Island, and during the remaining months of 1934, all cases of the disease which were met with in the course of daily practice were noted and written up. It would, therefore, obviously be unfair to draw any conclusions for the year 1934: first, the work was not carried on for the whole year; second, because a number of the cases noted and written up in the early part of the year had obviously developed the disease months before they came under observation.

In 1935 a total of 21 cases came under observation. It will be seen from the appended curves in Figure 3 that there was a sharp rise in the incidence of the disease from September to the end of the year. In fact, 16 out of the total of 21 cases for 1935 were observed during the last four months of the year. There are three factors which probably helped to produce this rise. First, the Island had had much less than the usual amount of rain during the winter months and this caused root crops to be later than usual; second, the fishing which usually becomes good in September, when the hot season is beginning, was exceptionally poor in 1935. In one or two of the cases, the onset of the disease was specificially related to the shortage of normal food supplies and the necessity of amplifying them by tinned salt beef. And third, it is, of course, well known that beriberi tends to disappear during the winter months only to reappear again with the onset of the hot season. Whether such a seasonal variation in incidence is a constant feature of the disease in St. Helena can only be determined by further careful investigation. It is quite possible that such a variation does exist, but it is only fair to point out that 12 cases have already been observed during the first quarter of 1936.

Certain interesting points emerge from the geographical study of the disease as it exists in the island. The majority of the cases which have been studied live in Jamestown, Longwood or Half Tree Hollow. There is also a relatively large number of cases in the Sandy Bay area, and a sprinkling of cases in the Blue Hill district. No cases have occurred in the Horse Ridge, Lot's Wife Wood or Wild Cattle Pound areas.

It is notorious that the worst housing conditions in the island are to be found in Jamestown, Longwood and Half Tree Hollow.

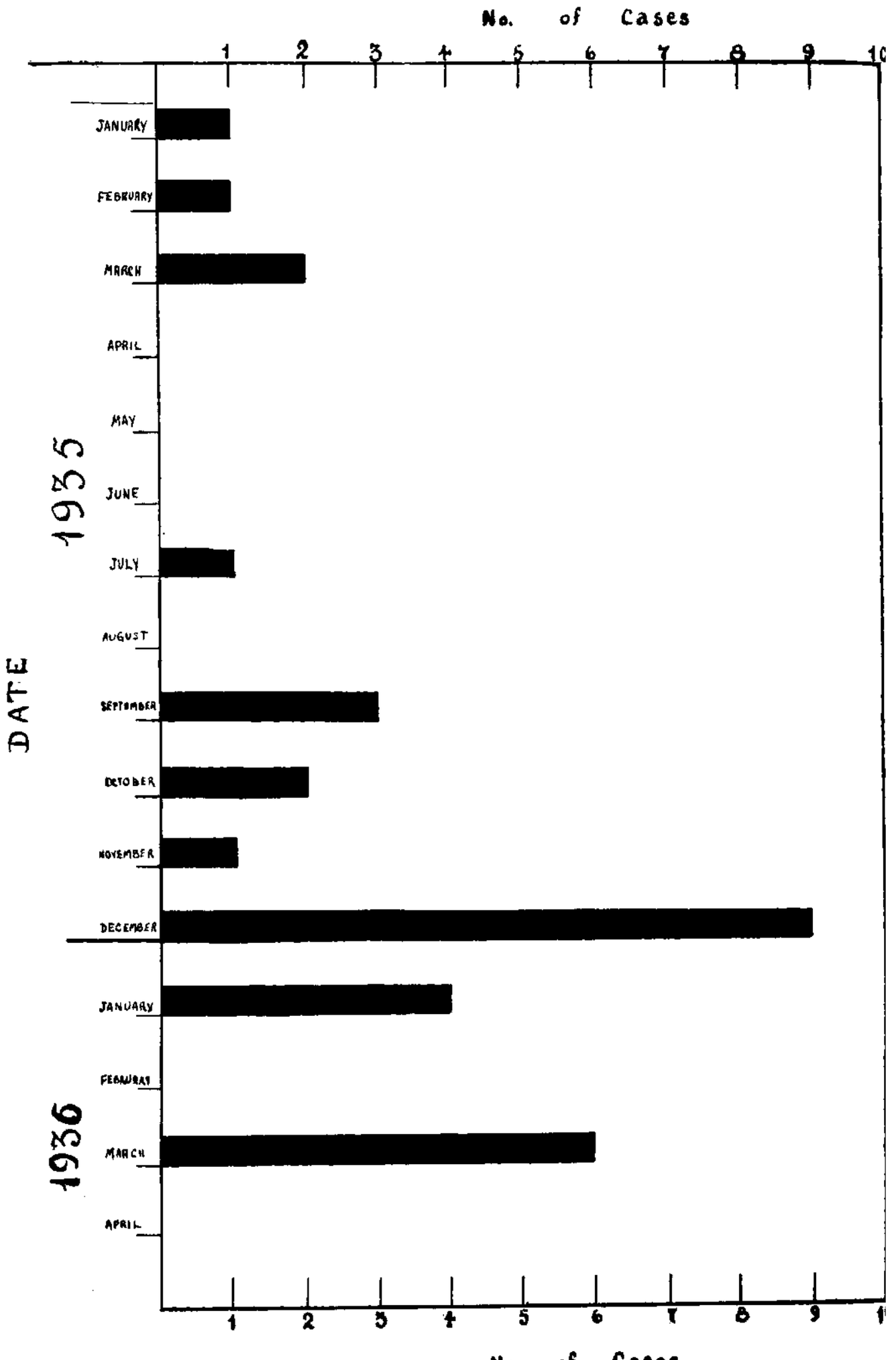


Figure 3. Histograms showing the seasonal variations of beri-beri from January, 1935 to April, 1936, and the rise in numbers during the hot season, September-March.

It would be unjustifiable to infer that any relationship existed between housing conditions and the incidence of the disease, but it is evident that there is an indisputable correlation between the economic status of the people and their liability to contract the disease. The poorer the people are, the more likely they are to develop beriberi. In this context it is of interest to note that, speaking generally, the inhabitants of Jamestown and Half Tree Hollow have no gardens and no access to cultivable land. It must be noted, on the other hand, that most if not all of the cases occurring in the Sandy Bay area occur in families who possess gardens of some sort or another.

The following list shows the geographical distribution of the cases hitherto observed :—

Jamestown	22
Longwood	19
Sandy Bay	20
Half Tree Hollow	26
Blue Hill	2
Horse Pasture, etc	3
White Gate	
Bluemans Hill	12
Unlocated	3
Total	107

When a disease is caused by a fault in diet, one naturally expects to find it sometimes affecting more than one member of a family. Such a familial incidence has been noted in this series, and further investigation would almost certainly show that this incidence is more frequent than appears from the figures about to be given.

In four families both husband and wife were found to be suffering from the disease, and in one of these households a cousin was also found to be affected. In one family three brothers, in two others two brothers, and in one two sisters were found to be affected. In two cases the adult son of a woman patient was found to have beriberi and in both cases the son lived at home. And in one case the middle aged son of a beriberic father aged 70 also had beriberi. In this family, so the father told me, the mother died of beriberi. Three of the women who developed the disease during pregnancy brought their babies for treatment during the first few months of their existence. They had attempted, contrary to advice, to breast feed the infants, while they themselves were still suffering from the disease, and the results were disastrous.

One pair of brothers and one brother and sister, who do not live under the same roof have also been treated for beriberi. One family

showed in an interesting way that the occurrence of the disease in several members of one household is due rather to some factor affecting all the inmates of the house than to any familial tendency to the disease. In this household, the grandfather aged 76, his son-in-law aged 30 and his grandson aged 24, all suffered from the disease. The grandson unfortunately died in one of the cardiac crises incident to the disease. Although it is true to say that there is no familial tendency to the disease, in the usually accepted sense, there is some evidence to show that members of one family tend to develop the same clinical picture if the family is living on a beriberi producing diet. In a family now under observation the mother, one grown up son and one grown up daughter all suffer from the dry type of the disease. In all three cases the onset was comparatively sudden, and within less than a week walking had become impossible. Two of the three cases developed the disease before 1934, and have now progressed to a stage of permanent atrophy. The son has responded well to treatment and is now walking normally.

It is, of course, obvious in all these cases that the disease occurs in different members of the same family because all members of one family eat the same food, and if that food is deficient in vitamin B_1, then all members of the family tend to suffer from B_1 deficiency. The generalisation that all members of the same family eat the same food is not strictly true, and this may help to account for the fact that some of the people in these households had escaped the disease.

As regards sex incidence, the figures in this series of 107 cases are as follows—males 78, females 29. This striking disparity is not to be interpreted unhesitatingly as meaning that females are less prone to the disease than males. Women are more capable of enduring, and are certainly much readier to endure chronic ill-health, than men. They are also less ready to come forward and present themselves as patients. These factors alone would do much to annul this apparent inequality, but even so there would doubtless be some preponderance of males. That this preponderance is to be attributed solely to factors incidental to employment, such as fatigue, over-exposure, chill, is unlikely, for were these factors operative to any extent, then one would expect to find some occupational incidence of the disease. A careful scrutiny of the series fails to reveal any striking connection between occupation and liability to beriberi and it is scarcely justifiable to infer from observations made in St. Helena that men who are doing heavy work have a greater tendency to show neuritic signs than those who are engaged on sedentary jobs.

There is no question at all that pregnancy and the act of childbirth predispose very strongly to the onset of the disease in women, but this point is of such importance and interest that a separate section will be allotted to it.

It is worthy of remark that many of these patients have obviously been ill for some months and are suffering from a considerable degree of physical disability before they think it necessary to consult a doctor and it is astonishing to note how advanced the neuritis may be, judged purely by physical signs, in cases who are still at work.

The duration of the disease can only be estimated from the histories given by the patients. For the most part they appear to be reliable witnesses whose statements are worthy of credence. The average duration (mode), assuming this to be the period from the onset of the symptoms to the date of coming under observation, appears to be about three weeks, but the periods given range from 2 days to 7 years. In assessing the value of these statements it must be remembered that the disease is one which shows a marked tendency to relapse. Twenty cases, or 18.6% of the whole series give a history of previous attacks of 'swelling,' and in most of the cases giving a duration of years, cross-examintaion reveals that the history of the disease has shown an intermittent course. This is due to the fact that many of the Islanders have to lead a hand to mouth existence. A transient spell of work enables them to improve their economic status and diet, and any member of the family suffering from beriberi naturally tends to recover during this period. The work comes to an end and the case relapses.

The actual relapse rate in the series is 7.4%. That is to say, eight cases have returned with obvious beriberi, evidenced by oedema, pain, weakness and reflex disturbance of some sort. The rapidity with which cases relapse depends almost entirely on the economic standing of the home from which the patient comes. The interval is usually one of months and in some of the cases has been well over a year. Clinical observations made on these cases lead one to the conclusion that the power of the human body to store vitamin B_1 in any quantity is either negligible or non-existent.

Four cases in this series have died. It must be admitted that two of these deaths were directly due, not to beriberi, but to co-existent cardio-vascular conditions. Two of the deaths, however, were due directly to beriberi. One of them was a child of three, the other a young man of 24. In both a post-mortem examination was made, and marked dilatation of the right ventricle coupled with pulmonary congeston and oedema was demonstrated in each case. This gives a mortality rate of 1.8% calculated on the basis of two deaths attributable directly to beriberi, or a rate of 3.7%, calculated on the total of four deaths.

Beriberi attacks all ages. This is clearly shown by the histograms in Figure 4. It will be seen from these histograms that the age of election appears to be from 20 to 45. It is a curious fact that the

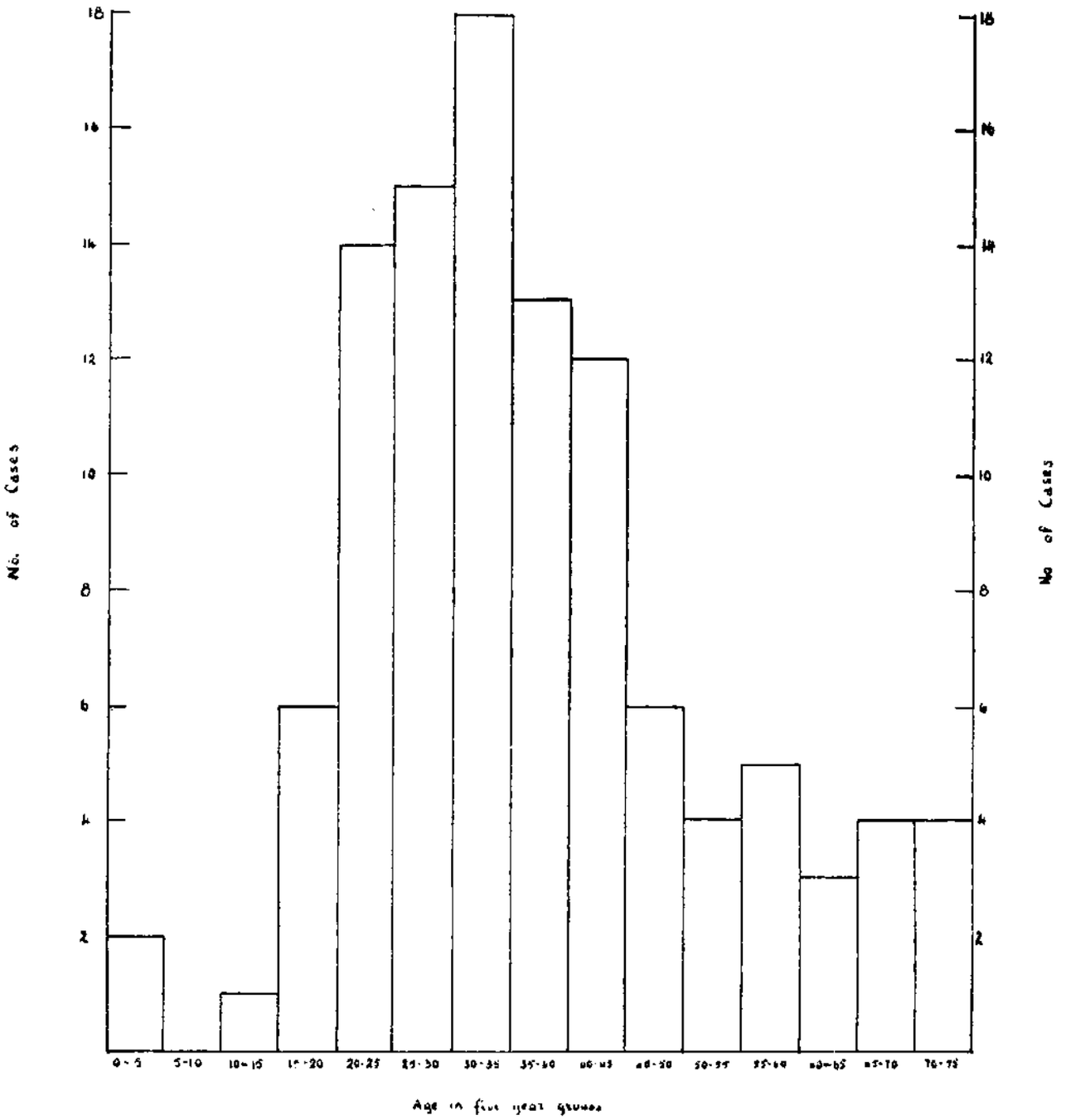


Figure 4. Histograms showing age incidence of 107 cases of beri-beri.

disease seems to be rare during the age period 5-15. It is by no means uncommon to see infants suffering and suffering severely from the disease, but once the children begin to walk and run they appear to become less liable to attack. The histograms show that no case has been noted in the age group 5-10, and only one in the age group 10-15. Investigations made on the knee and ankle-jerks of the school children bear out this observation. Why this should be so is as yet unexplained. On the other hand, the disease is just as common in old age as in infancy, if not commoner. It is probable that the disease has been more readily diagnosed in elderly people than in infants as it was not routine practice to test the tendon-jerks of babies.

CLINICAL FEATURES.

Before embarking on a detailed discussion of the clinical features of the disease, it may be well to state that all forms of the disease—that is to say rudimentary, wet and dry—have been noted in this series. Most of the cases observed belong, fortunately, to the rudimentary group; fortunately, because they respond most readily and rapidly to treatment.

The mode of onset is usually gradual. The first symptoms complained of are usually 'cramps' or a 'feeling of tightness' in the calves and thigh muscles. These dysaesthesiae are usually associated with or followed by a mild degree of dyspnoea on exertion and possibly some palpitation. Many of the cases come under observation at this stage of the disease, and at this stage a careful physical examination usually elicits an abundance of physical signs, slight maybe but none the less definite. As has already been pointed out, the patient has usually complained of these symptoms for about three weeks before coming to the doctor. This is the type of case most commonly seen on the island.

Occasionally the onset is much more sudden. One woman in this series gave this history. "One afternoon her gait became 'staggery.' By next morning she was unable to stand without help, her fingers and toes had become 'dead' and her arms were weak and 'unsteady.'" A few other cases with an onset of this sort have been seen, but they are much rarer than the cases with a gradual onset.

The search for factors which predispose to the onset of the neuritis has revealed some interesting facts. It is well known that parturition causes a sudden and rapid depletion of the mother's vitamin B_1 reserve. 41.3% of the women in this series show a definite connection between pregnancy or childbirth or both, and the onset of beriberi.

The twelve women who showed this association can be roughly classified in two clinical groups. In one group the disease appears to be precipitated by the act of childbirth; in the other group symptoms have become apparent during the later months of pregnancy, but the

act of childbirth though intensifying the existent symptoms does not do so to such an extent as to incapacitate the woman completely.

Five cases were noted in the first group, seven in the second. The history of a case occurring in the first group is given here.

Mrs. R. J. O'D. aet 35.

She has borne 7 children of whom 2 are now dead. She has always had good health. The youngest child was born on 22.12.34. For one week before the birth of this child she had complained of pain in the soles of the feet, numbness in the finger tips and dyspnoea on exertion. She had no oedema but had complained of palpitation on exertion. She states that the arms and legs did not become weak at this time, and says that she could walk normally up to the time of her delivery. She had had no symptoms of this kind during her earlier pregnancies.

On December 29th she tried to stand up but found her legs "gave way under her." She was seen on the 2nd January, 1935. On examination she showed a symmetrical and peripheral paresis of arms and legs, accompanied with pain, tenderness and gross sensory impairment. She was unable to stand unless supported on both sides. There was a slight degree of foot drop, and some atrophy of pherpheral muscles in both legs. No atrophy was noted in forearms or hands. Both the left arm and left leg were slightly more involved than the right. She showed no abnormality of the cranial nerves. Arm reflexes were present and equal on both sides. Both knee and ankle-jerks were absent, even with reinforcement. Plantars were flexor and there was no abnormality of sphincters. Abdominals were absent, but this was to be expected.

There was a marked degree of ataxy in performing all tests in both arms and legs. The left leg could scarcely be raised sufficiently from the bed to allow the heel knee test to be performed.

On sensory testing there was complete glove-stocking to all forms of stimulus. Postural sensibility and appreciation loss of passive movement were completely lost in the fingers and toes and were impaired in the wrists and ankles. A vibrating tuning fork was not perceived below the iliac crests and the elbow joints. The calves were intensely tender on deep pressure, and scratching the soles quite lightly evoked a moderate degree of pain. There was a very slight degree of pitting over both tibiae, but the urine showed no abnormality. The other systems were normal.

The woman's diet consisted of rice, fish, salt, bread, tea, margarine and tinned milk. She had cabbage and beans once a week, and occasionally a banana. She rarely if ever obtained eggs, fresh milk, fresh meat, fruit or butter, nor did she have vegetables other than her weekly cabbage. She was told that she would be able to walk unaided in three months.

The baby was removed from the breast, the feet were kept at a right angle to the legs and the diet was corrected as far as her means would allow. She was given grs. XV of dry yeast daily. Subjective improvement was marked within one week. By the beginning of April she was walking quite well without a stick and could dress herself unaided, though threading a needle was still a little difficult. Her knee-jerks did not return until August, by which date the only symptom she complained of was numbness in the extreme tips of the fingers and toes.

This case is typical of the group now under discussion. The first symptoms usually appear from a week to a fortnight before delivery and are taken little notice of. The woman then has her child, she lies in for the routine period, and finds when she gets out of bed that her legs collapse under her. Pain is not usually a prominent feature in these cases, but the dysaesthesiae, especially 'burning of the soles,' are frequently a source of intense discomfort to the patients.

The prognosis appears to be uniformly good if treatment is begun directly the diagnosis is made. Recession of the area of sensory loss is a much more satisfactory criterion of the progress of recovery than reappearance of the reflexes. Some of the patients report spontaneously that the numbness has "gone down so much this week," and these subjective reports are generally reliable. The reflexes not infrequently take months to reappear. In one case in this group of 5, the knee-jerks took twenty-one months to reappear and the ankle-jerks are still absent. The woman is and has been free from symptoms for twelve months. In the case which has just been described, although the knee-jerks had reappeared after eight months' treatment, the ankle-jerks were still absent.

With one exception all five of the women in this group have had large families—two have had seven children, one five, one four and the fifth one. It is curious to note that they had none of them complained of symptoms suggestive of peripheral neuritis in any of their previous pregnancies.

In the second group, which contains seven cases, the symptoms usually appeared earlier in the pregnancy at about the 6th or 7th month, and they exemplify perfectly the general description already given of the onset in a typical case of beriberi. When cases come under observation at this stage, it appears to be quite possible to save them from the catastrophe of becoming bedridden for weeks, by instituting treatment designed to increase the amount of vitamin B_1 in their diet.

It is also not uncommon to see patients who complain of the onset of milder symptoms immediately after childbirth, and it must be stressed here that this division into groups has been made solely for the purpose of descriptive convenience. These cases are all cases of beriberi; they differ merely in degree, not in kind, and the so-called "first group" has been dealt with at considerable length simply because it affords one of the most striking clinical pictures presented by this protean disease. One further case history is given here to illustrate the milder type of case.

Mrs. A.F. aet 28.

Apart from a quinsy in 1935 she has had no past illnesses. She has had seven previous pregnancies and has remained well throughout and after them. Her last child was born on March 4th, 1936. She was seen on the 13th of May, 1936, and stated that throughout the last two months of her pregnancy she noticed that her legs "felt heavy," but there was no loss of feeling in fingers or toes. She also complained of breathlessness on exertion, and noticed that her ankles had become a little swollen. She lay in for 11 days, and when she got up she found her soles were tender. Two weeks later the skin of her feet and legs began to feel "drawn tight," and at the beginning of May her hands became painful, her finger tips numb and her insteps "dead." Her right hand has become weaker and she has dropped things. She complains now of a constant "burning pain" in the inner three fingers and inner half of the palm of the right hand. The left hand and the legs have

shown no weakness. She now has no dyspnoea on exertion, oedema or palpitation. Her menses are regular and she is breast feeding her child.

On examination the heart, lungs and abdomen showed no abnormality. Teeth were horribly carious and she complained of anorexia but no dyspepsia. The bowels were not constipated.

The cranial nerves showed no abnormality. The knee and ankle-jerks were slightly increased on both sides, the arm jekrs were normal. Plantars were flexor, and the sphincters normal.

There was slight weakness of the right interossei and some flattening of the right hypothenar eminence.

There was no demonstrable atrophy elsewhere; no fibrillation was noted. The motor power of trunk and legs was normal. On sensory testing a patchy hypaesthesia and hypalgesia could be demonstrated in the fingers and toes of both sides. There was no loss of postural sensibility and a vibrating tuning fork was well perceived everywhere. There was no pain or deep pressure over any muscle masses. Slight ataxy was noticed in the right arm in performing the F.N. F.N.F. and F.F. tests.

The woman's diet consisted of rice, fish, salt, white bread, tea, margarine and occasionally some fresh milk. She obtained some kind of fresh vegetable three or four times a week. She never had butter of fresh meat. Her symptoms cleared up rapidly on treatment with dry yeast and correction of her diet.

One factor which appears to predispose to the onset of beriberi in males is arteriosclerosis. In most of the males in this series who were over 50, co-existing arteriosclerosis of greater or less degree was noted. It is also an interesting clinical observation that those cases of beriberi which show the most marked arteriosclerosis are those who respond least well to the specific treatment with B_1.

Another factor which appears to be of importance in this connexion is the presence of persistent low-grade infection. 56 cases in this series showed a degree of oral sepsis so marked as to be disgusting. Many of these cases instead of possessing teeth had merely a collection of blackened stumps more or less loosely imbedded in inflamed and infected gums. It was, naturally, not unusual to find that many of these patients had a coexistent infection of the tonsils. It appears to be justifiable to infer that marked oral sepsis predisposes to the onset of the disease, as the condition was noted in 52.3% of the cases in this series.

It also seems probable that a serious illness of any sort may predispose to the onset of the disease. One man who had had a liver abscess treated in hospital by aspiration and a course of emetine, developed an attack of beriberi within one week of leaving hospital and returning to his ordinary home diet. No definite connection has been noted between exposure or fatigue and the onset of the disease, but one highly intelligent man definitely attributed the onset of his attack to the fact that he had just had to assume extra responsibilities owing to the illness of one of his mates. There is also other evidence to show that emotional factors may exercise a predisposing influence.

In only one case in the series has fever been noted during the course of uncomplicated beriberi. This was in a young man of 23 who suffered severely from the wet variety of the disease. He was admitted to hospital critically ill with a pulse rate of 140, and on admission he had a temperature of 100°. This fell to normal within 24 hours of admission and remained normal. It is true that the vast majority of the cases have been treated at home, but even so it is safe to say the disease is almost always afebrile.

The bar diagrams in Figure 5 show graphically the percentage manifesting the signs and symptoms enumerated.

Taking the symptoms first, it is clear that the weakness of the limbs is one of the most frequently occurring. 86% of the patients in this series complained of some degree of weakness. The weakness is most commonly noted in the legs, and the usual complaint is that the legs 'feel heavy' after mild exertion. Weakness of the arms and hands is very much rarer; only 8.4% of the whole series complained of this symptom. In the majority of the rudimentary cases no perceptible degree of muscular atrophy can be made out. In the dry cases of long standing there is invariably some degree of atrophy and this may be quite pronounced. In the wet cases atrophy is not infrequently masked by oedema. In only three cases in the series was fibrillation noted. Two of these cases were examples of the wet type, and both made apparently complete recoveries. The third case was of the dry type, and gave a 3 year history. She now has a permanent foot drop and marked wasting of the arms and legs. Genu recurvatum has been observed in seven cases only in this series.

Dyspnoea on exertion is an exceedingly common symptom. The complaint usually made is of a "feeling of tightness in the chest" and "panting" when going up hill. Most, but not all, of the cases which complained of this symptom show some degree of cardiac involvement. The symptom was noted in 95.7% of the cases. Palpitation is a fairly common symptom and has been noted in about 50% of the cases in this series. It is most commonly complained of by those patients who on examination show some degree of cardiac involvement.

Acroparaesthesiae are also very common as would naturally be expected, but other dysaesthesiae are almost as common. Many of the cases who complain of numbness of fingers and toes, also complain bitterly of 'burning' in the soles of the feet and this is most troublesome when they are in bed. Another common perversion of sensation is the feeling of "cold water trickling" down the outer side of the thighs and legs. Several cases have stated that on occasion they have actually felt their trousers to see if they had got splashed with water, so vivid has this sensation been. Only two cases have complained of a girdle sensation. Numbness of the lips, tongue and face is distinctly

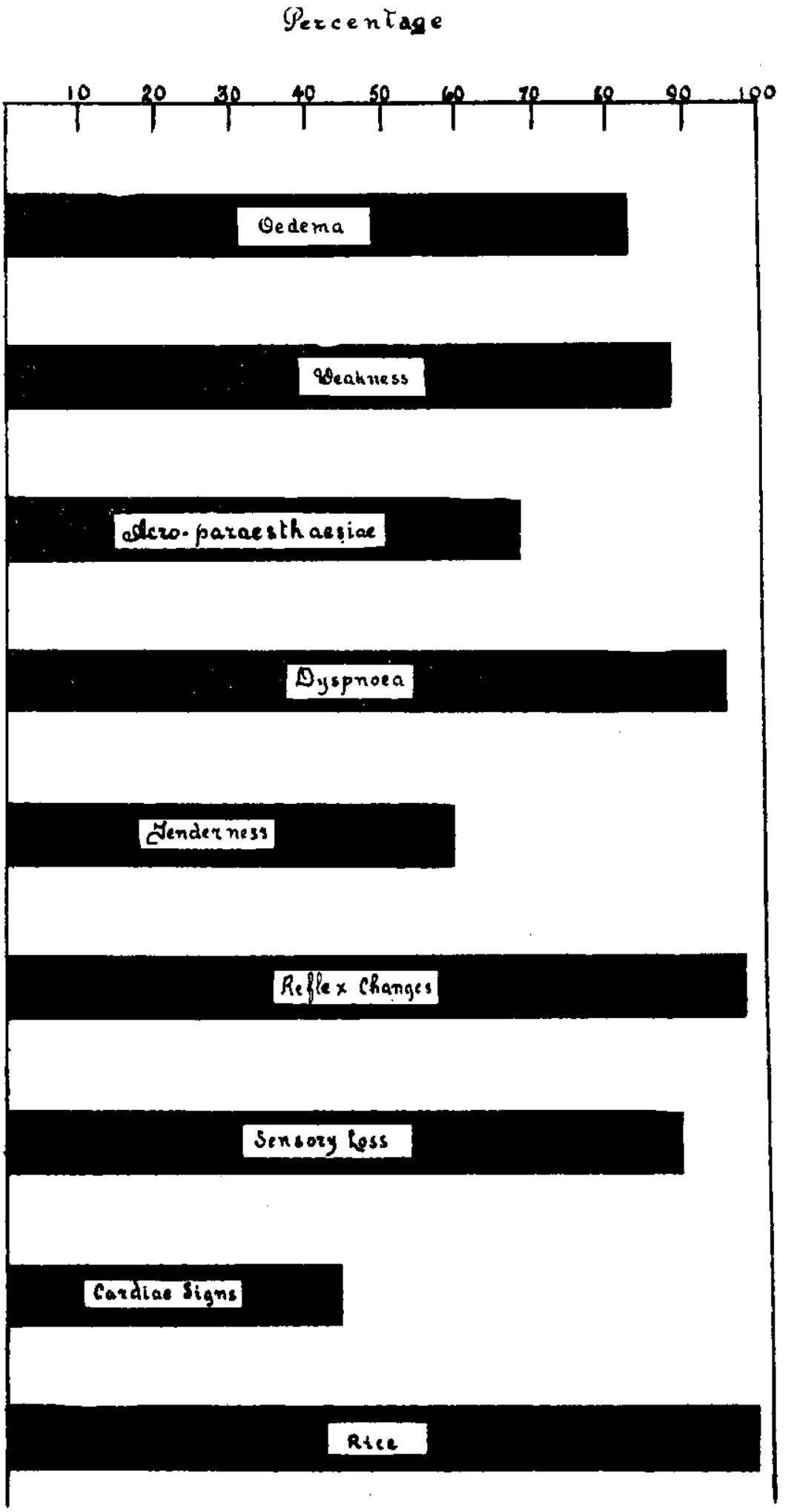


Figure 5. Bar diagrams showing the comparative frequencies of various signs and symptoms in 107 beri-beri cases.

rare. When the 5th cranial nerve is involved, the commonest symptom is a feeling of numbness in the lips; tongue and face. In one case who showed a well marked diplegia, there was loss of sensibility to cotton wool and pin prick in both halves of the face, and both corneal reflexes were diminished. As a rule the dysaesthesiae appear early in the disease, and frequently they are the first symptom which causes the patient to seek advice. It is usual to find that both sides of the body are equally affected, but one or two cases have complained of a more or less hemiplegic distribution of numbness. In these cases it has always been possible to demonstrate an objective loss on both sides of the body, though sometimes this has been more marked on one side than the other. Trophic changes have been neither frequent nor marked in this series. In the cases showing a considerable degree of atrophy and sensory loss, the skin of the hands and feet is usually thin and glossy, and the extremities are cold. No changes in the nails have been observed.

Tenderness on pressure of muscle masses can be elicited in about 60% of the cases. It is not as a rule a prominent symptom, but one woman suffered so severely from it that she had to protect her legs from the pressure of bed clothes by a cradle. Another fairly common statement is that leather soled shoes have been found unbearable owing to tenderness of the soles. The calves and thighs are the sites in which tenderness is most frequently found on pressure. It has been distinctly rare to find tenderness on pressure of the arm muscles; in fact this has only been the case in two patients.

Turning now to the signs which are found on physical examination, great importance is to be attached to the existence of demonstrable oedema. It is one of the commonest and one of the earliest signs in the rudimentary cases, and has been noted in 68% of the whole series. The most frequent finding is some degree of pitting on pressure over the tibiae. In the frank wet cases the legs may present the picture of a solid oedema so marked as to be reminiscent of the last stages of cardiac dropsy. In such cases there is invariably oedema of the arms and face, and in two cases there was oedema of the abdominal wall also. The rapid loss of weight observed when these cases are vigorously treated is very striking. One of the wet cases lost 10lbs. in one month while in hospital. In two of the most severe wet cases huskiness was noted on admission to hospital, and in one of these cases oedema of the larynx was observed.

The changes due solely to the neuritis are as a rule, readily demonstrable on examination of the central nervous system. Perhaps most important in this category of signs are the changes found on examining the reflexes. In 97.0% of the cases in this series some abnormality in the reflexes was noted, in the sense of exaggeration, diminution, inequality on the two sides or complete loss.

An analysis of the results of examinations in this series shows that in 34 cases both knee and ankle-jerks were completely lost. In 19 cases the knee-jerks were present while the ankle-jerks were lost; in 44 cases there was some inequality between knee and ankle-jerks; in 6 cases all the tendon jerks were equally exaggerated ,while in only one case were they all equally diminished. Three of the cases showed no abnormality of reflexes. These results are appreciated more readily in tabular form :—

	Cases	*% of total*
Loss of knee and ankle jerks	34	31.7
Knee jerks retained, ankle jerks lost	19	17.7
All equally exaggerated	6	5.6
„ „ diminished	1	.93
Some inequality between AJ and KJ	44	41.1
Normal reflexes	3	2.8

In no case has any swelling or enlargement of nerve trunks been detected on clinical examination. The tenderness of calves and thighs on deep pressure has already been dealt with, and mention has also been made of the dysaesthesiae and the objective findings usually correlated with them. Although 12% of the cases in the series are noted as having no objective sensory loss, it is safe to say that a more careful examination would have demonstrated some such loss. The commonest objective finding is a glove-stocking loss to pin prick and cotton wool. In slighter cases of the disease one may only be able to demonstrate a patchy hypalgesia and hypaesthesia over the shins and forearms, and rarely one finds the sensory loss limited to the extreme tips of the fingers and toes. The glove-stocking loss is usually coupled with loss of joint sense in the toes and fingers and inability to appreciate the vibration of a sounding tuning fork placed on the styloid processes and malleoli. There is also, as a rule, a dissociated anaesthesia. In two cases a hyperaesthesia to heat was noted in the area of sensory loss. The tenderness on pressure of the calves forms a very striking contrast to the complete loss of response to other sensory stimuli.

The cranial nerves are very rarely involved. In only one case in this series was any involvement noted. These photographs show well the marked degree of bilateral facial weakness displayed by this case. She was admitted to hospital with gross weakness of all limbs —she was unable to stand or feed herself—and with acute dilatation of the right side of the heart. For ten days her systolic blood pressure ranged from 96-100 and her condition was critical. She made an excellent recovery, and has now resumed her normal activities.

The cardio vascular system is frequently involved. In only 47 or 43.8% were the findings normal, the other cases all showing some

abnormality. In those cases with marked dilatation of the right side of the heart, epigastric pulsation and pulsation of the veins in the root of the neck are noted on inspection. On percussion the area of cardiac dulness is usually enlarged to the right, and on auscultation the heart sounds are usually faint, and evenly spaced. It may be impossible to tell first from second sound, anl the rhythm is typically tictac. In this condition of the heart it is common to find murmurs, usually systolic in time, due to relative insufficiency, and reduplication of the second sound, particularly the triscupid second, is also a common finding.

Systolic bruits and reduplication of the second sound are the most usual findings in those cases who are not critically ill, but caution is required in giving a prognosis in any case showing cardiac involvement, for acute dilatation of the right side of the heart may supervene without warning and with alarming rapidity. Extra-systoles are by no means uncommon, and were a marked feature in one of the oedematous cases who showed serious cardiac involvement. This case will be described in more detail later.

On analysing the series the following figures were obtained:—

Systolic bruits. 23 or 21.4%.

Apical	15
Aortic...	2
Tricuspid	3
Pulmonary	1
Aortic + tricuspid	1
Tricuspid + mitral	1

Reduptication of 2nd sound. 20 or 18.6%.

Mitral...	10
Tricuspid	3
Pulmonary	1
Mitral + pulmonary...	2
Mitral + tricuspid	1
Aortic + tricuspid	2
Mitral + pulmonary + tricuspid	1

Epigastric pulsation was noted as the only sign in two cases. The accentuation of the aortic second sound noted in 13 cases was due to concomitant atherosclerosis, and had no direct connection with the beriberi. The same may be said of the two cases which showed extra-systoles and no other sign of cardiac involvement. The following case history illustrates the picture seen in an oedematous case with severe cardiac involvement:—

W.H. Male. aet. 23.

No history of any previous illnesses. For the last 5 weeks he states that his legs have been "swollen," and he has grown tired easily. He has become breathless on exertion, and has had numbness in the finger tips and toes. He has also noticed palpitation on exertion. The swelling has been increasing during the last fortnight. No sphincter involvement. No falls. Not dropping things. He has had no illness like this before.

On examination the man was noticed to be slightly busky, and dyspnoeic even at rest. The lips and fingers nails were slightly cyanosed. Extremities were cold. The face, hands and legs up to the knees were oedematous and the skin over them was tense and glossy. The oedema pitted; scrotum was not involved, but there was a slight lumbar pad. The pulse was extremely irregular and there was a marked difference between apex and pulse rate at wrist. There was obvious pulsation of the veins at the root of the neck on both sides and also epigastric pulsation. The area of cardiac dulness was enlarged to the right, and on auscultation the mitral and pulmonary second sounds were reduplicated. The heart sounds were distant and the cardiac excursion poor. No bruits were heard. The B.P. was 115-80. The tongue was furred but he stated he was not constipated. No enlargement of liver on spleen was noted. The lungs were normal and there was no sign of fluid in their pleura.

All the reflexes were abolished but cranial nerves were not involved. There was a glove-stocking loss to all forms of stimuli and the calves were tender on deep pressure. No atrophy could be made out in the legs although both legs were weak throughout. (Atrophy became evident later on as the oedema disappeared.) The arms also showed slight weakness throughout on both sides and as was the case with the legs, this weakness was more marked on the left side.

The urine was canty and high coloured. It showed no sugar and no casts.

The man's diet consisted of rice, fish, white bread, tea, sugar, salt. He never obtained fresh meat, eggs or fresh milk. He ate cabbage once a week.

He was admitted to hospital and treatment was begun with tincture of digitalis minims 10 4 hourly by fouth. In five days the pulse rate had fallen from 140 to 70, and the oedema had begun to disappear. He developed well marked bigeminy after 48 hours on digitalis and this persisted for 24 hours. The pulse was extremely variable throughout the first week in hospital.

He was ordered a dry diet and 2 grammes of dry yeast daily and on this regime he rapidly improved. He was discharged after 3 months in hospital and was able to resume work on the farm. His knee-jerks took four months to return, his ankle-jerks eleven. He continued to take 1 gramme of dry yeast daily for months after leaving hospital. He was examined eleven months after his admission to hospital. He then showed a slight inequality of the ankle-jerks; otherwise the nervous system was normal. He still had, however, a reduplicated 2nd sound at the mitral and tricuspid areas, and seven extra-systoles a minute. The pulse was 82 and the area of cardiac dullness normal. His heart and nervous system to-day appear to be normal.

A pulse chart of the case during the first five days in hospital is appended here. (Figure 6.)

THERAPY.

As the majority of the cases in this series were of the rudimentary type, treatment was carried out at home. The rational treatment of any deficiency disease is to supply the missing factor, if possible.

The cause of the disease was explained in simple language to all patients, they were given a leaflet with a list of the commoner foodstuffs containing vitamin B_1, and were advised to introduce some of these foods into their daily diet. In many cases this advice could

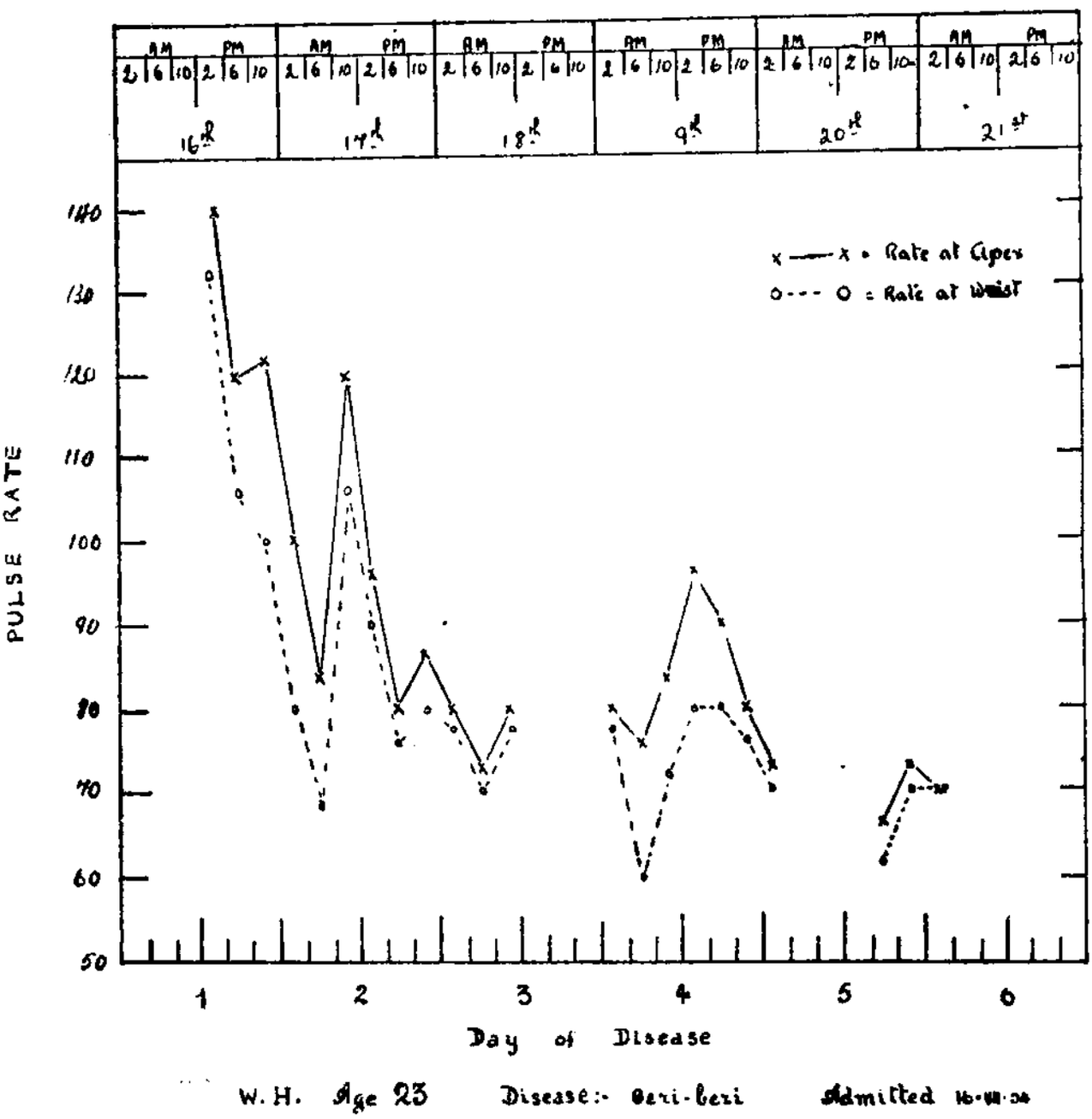


Figure 6. Pulse chart of W. H., described in text.

not be carried out owing to the profoundly depressed economic status of the average islander. Therefore, the routine practice was adopted in all cases of giving 1 gramme of dry yeast, in tablet form, daily. In most cases this acted as a specific.

The first change noted was, as a rule, the disappearance of the oedema. If a case were going to respond well to administration of B_1 by mouth, oedema invariably disappeared within one week from the beginning of treatment. The disappearance of the oedema was usually accompanied by a subjective feeling of well-being, coupled with a loss of the tired, weak 'heavy' sensations in the limbs. Not infrequently the complexion became clearer as these changes occurred. It has been the rule to find that dyspnoea on exertion and subjective feelings of palpitation disappear within one week from the beginning of treatment. The disturbances of sensation such as the dysaesthesiae and acroparaesthesiae usually take longer to clear up, and in some severe cases, numbness of the soles and 'burning' of the feet, especially at night, have persisted for months. This is also the case with reflexes which have been lost. It is unusual for lost reflexes to reappear in less than 3 months, not uncommon for them to take at least 6 months to return, and by no means rare to find them still absent 12 months after the case has come under observation.

Marmite has been used effectively in a number of cases, but its cost puts it beyond the reach of most of the islanders. Potato cream has been found to afford the most convenient way of giving B_1 to to hospital without delay all cases showing signs of an impending babies suffering from the disease. It has been the practice to admit cardiac crisis. Treatment secundum artem—venesection, intravenous strophanthin, digitalis by mouth, and a dry diet rich in B_1—has proved successful in several such cases. If they can be tided over the first week, they appear, as a rule, to recover.

Parenteral administration of B_1 became possible owing to the courtesy of Messrs. Hoffmann la Roche, who supplied 1 dozen ampoules of B_1 for clinical trial. Each ampoule contained 500 international units of vitamin B_1. This preparation was tested on a typical case of the disease, Mrs. L. F. aged 43.

Mrs. L. F. developed beriberi in 1931. Onset was sudden and she was reduced to a state of helplessness in a few days. Since that time she has had to be dressed, fed and carried about the house. She cannot stand unsupported and is incapable of taking a step alone. All her deep reflexes are absent, and she has very marked sensory loss as shown in the accompanying charts. There is also some loss of normal sphincter sensation. For the last six months she has been taking 1 gramme of dry yeast by mouth daily. This has made very little appreciable difference to the motor power of the limbs, and none whatever to their sensory condition.

She was admitted to hospital on the 20th of July this year, and her sensory loss on that date is shown by chart A. She was given 500 units of B_1 subcutaneously on the 21st, the 22nd, the 23rd, the 25th, and the 26th. Her condition remained objectively and subjectively unchanged. She was taken home on the 28th.

On the 30th she found on waking up that the level of numbness in the arms had receded from the position shown in chart A to the level of the wrist joint. The hands felt warmer. She was examined again, and the recession of the level of sensory loss was demonstrable in both arms and legs. It was much more marked in the arms (vide Chart B).

A further dose of 500 units was given on the 2nd of August, and in the following week she was able "to take a few stitches," the first sewing she has done since 1932. It is too early to say how far her improvement will go, but the improvement effected by six injections of B_1 has been very striking. While she was in hospital, she was kept on the ordinary hospital diet and had no yeast, marmite or other preparation known to be rich in B_1. It is difficult to say why there was an interval of nine days between the beginning of treatment and the first sign of improvement. There seems, however, to be no doubt but that the improvement noted is due to the parenteral administration of B_1. Several of the long standing cases in the series have proved to be similarly resistant to B_1 by mouth, and one has been forced to conclude, from clinical observation, that some change has occurred in the intestinal mucosa in those cases, which prevents B_1 from being absorbed when given by mouth.

It is quite obvious that this new method of exhibiting the vitamin opens up a further field for investigation, and it is to be hoped that adequate supplies of B_1 for injection will be speedily procured. It is also quite clear that the preparation should be of value in the treatment of the cardiac crises of the disease.

CONCLUSION.

One point of cardinal importance emerges from a study of the diets eaten by this series of cases. With one exception, every patient stated that rice formed a large part of his everyday food. One man stated that he only ate rice twice a week, but as his food consisted of white bread, fish, salt meat, tea, sugar and salt, with an occasional pumpkin, cabbage and banana, it can readily be appreciated that he was not obtaining enough vitamin B_1 to prevent the onset of symptoms. The non-rice eater also proved, on investigation, to be living on a dangerously deficient diet.

Clinical observations have afforded little or no evidence in favour of the hypothesis that some toxic factor contained in milled rice is either wholly or in part the cause of beriberi.

The one non-rice eater in the series tends to show, what is already well known, that the disease develops as a result of the deficiency of vitamin B_1.

As the standard diet of the average islander consists of white bread, milled rice, fish, tea, sugar, salt and curry, it is easy to see how prone he is to show the effects of B_1 deprivation. These effects, when they manifest themselves as frank beriberi, cannot escape notice. Little evidence has been collected to show that deficiency of B_1 produces other clinical pictures, but there is no doubt that many islanders, who never come under medical observation, are living either on the verge of beriberi or with the disease itself in its rudimentary form. In taking the case-histories special attention was paid to the question of anorexia, dyspepsia or constipation. It was surprising to find how few of the cases complained of constipation or dyspepsia of any sort. The sole clinical finding which could lead one to imagine that the intestinal mucosa was in any way implicated, is the fact that a number of cases of the disease respond little or not at all to the administration of B_1 by mouth. In only one of these cases, so far, has it been possible to give the vitamin subcutaneously, and in this case the improvement recorded up to date has been very gratifying.

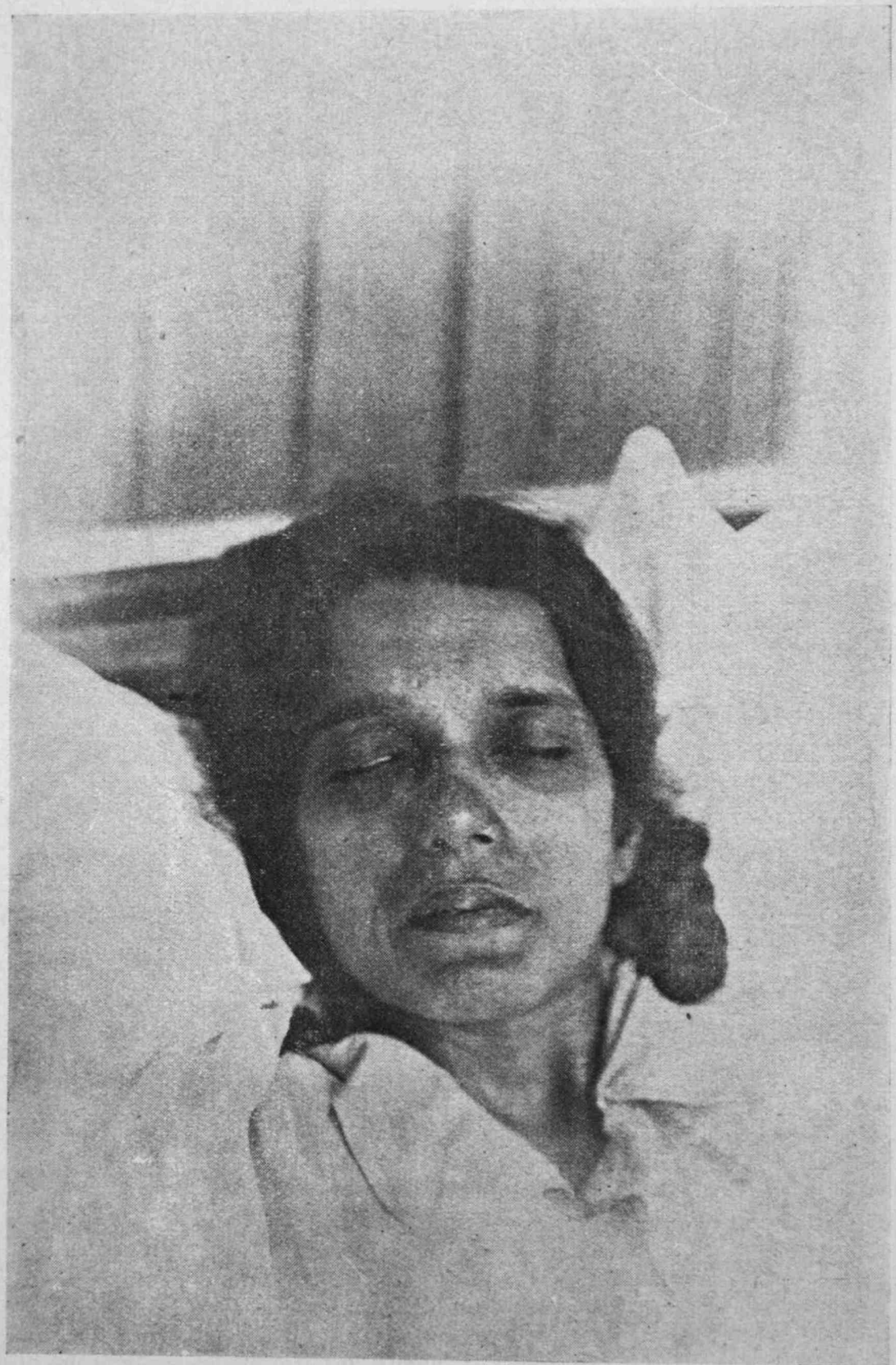
Comment has already been made on the observation that co-existent conditions such as arteriosclerosis, and morbus cordis appear to make the response to B_1 slower than usual. Age quâ age does not appear to have this retarding effect, provided the patient is otherwise healthy.

It appears unnecessary to introduce into the literature of the subject such pedantic neologisms as "ateleositetic neuritis." Entia non sunt multiplicanda praeter necessitatem. The so-called ateleositetic neuritides, if they are in fact due to a deficiency of vitamin B_1, should be called beriberi and treated as such.

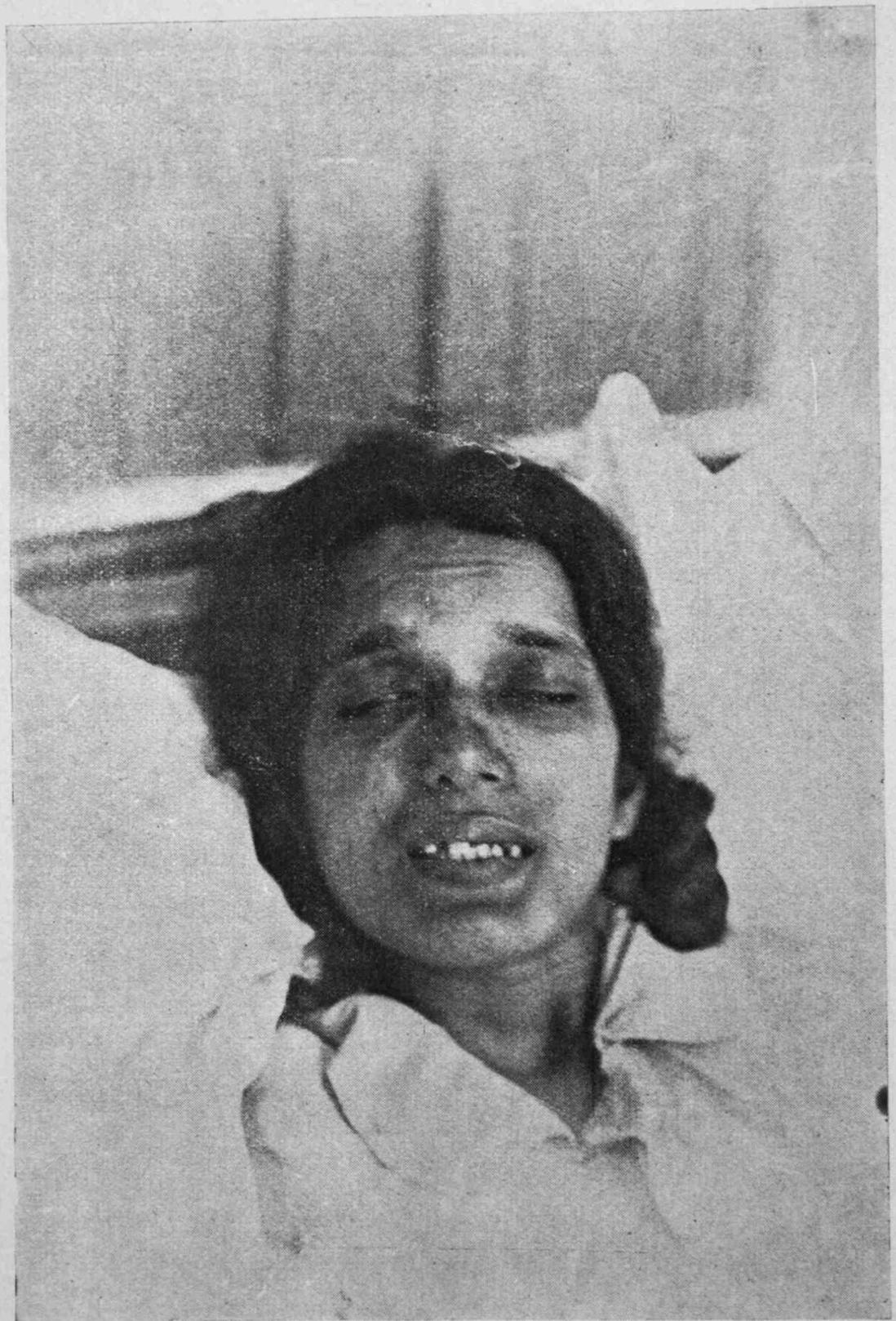
SUMMARY.

1. One hundred and seven cases of beriberi in St. Helena have been investigated as far as the resources of the Island allowed.
2. The incidence of the disease has been correlated with the deficiency in vitamin B_1 of the diet of the average islander.
3. Evidence has been adduced to show that the disease did not occur among the islanders until polished rice became one of their staple foods.
4. The suggestion is put forward that it would be worth while to introduce legislation making the importation of any but brown (unmilled) rice illegal, in view of the fact that 2½% of the population of the island are now suffering from a preventable disease.

In conclusion I should like to thank my friend Mr. G. C. Kitching for the great help he gave me in writing the historical section of this paper. I must also thank Mr. Cecil George for typing the manuscript and Mr. A. P. Pereira for his help with the diagrams.



Mrs. W.S. Facial diplegia in uncomplicated beri-beri.



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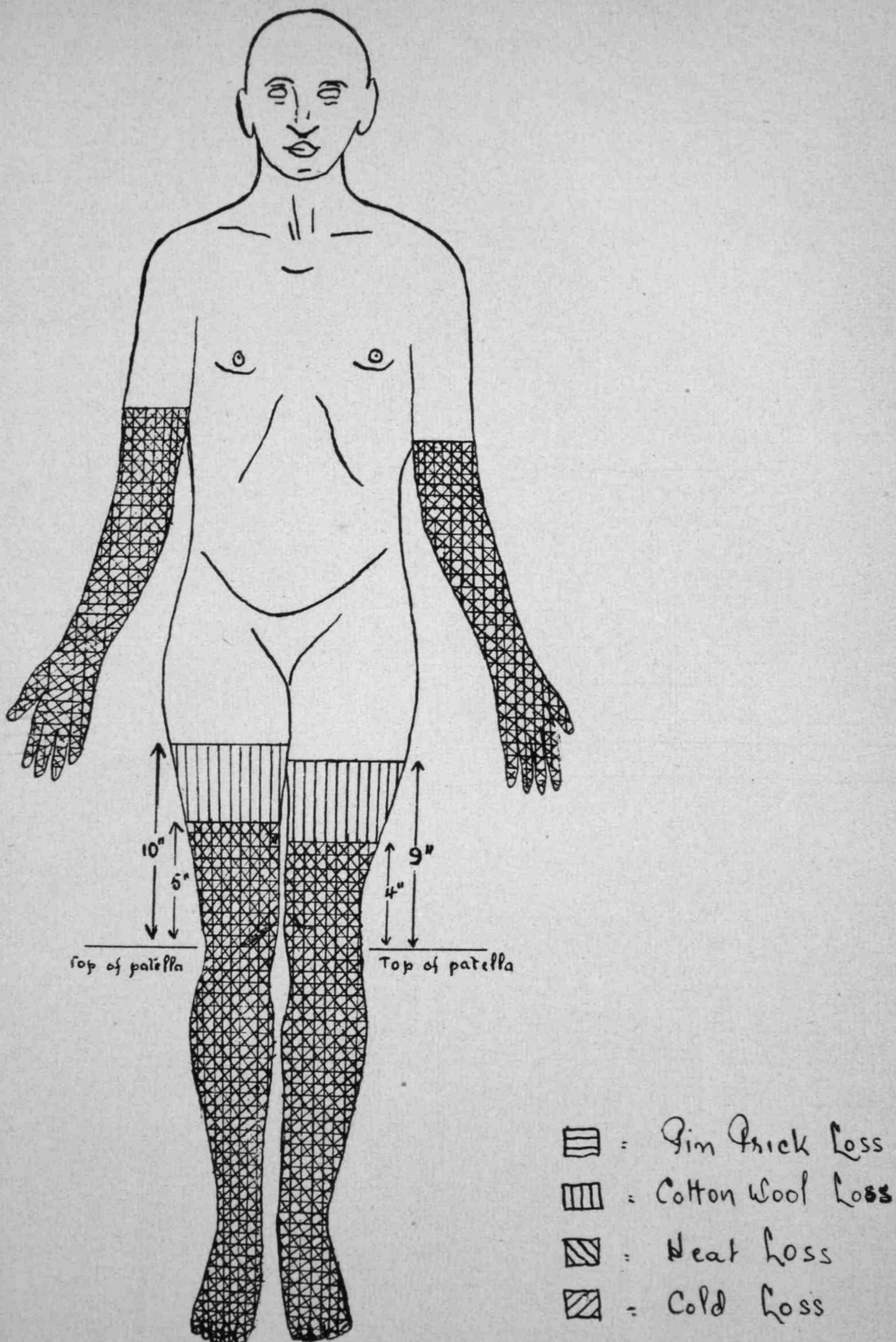


CHART A.

Mrs. L. F., aet., 45. 21 : VII : 36.

Before administration of B_1 subcutaneously.

Joint sensation. Complete loss, toes, ankles, fingers, wrists. Inpaired at knees and elbows.

Tuning fork. Only perceived on skull, clavicles, ribs, upper humerus.

Deep pain. No tenderness on pressure.

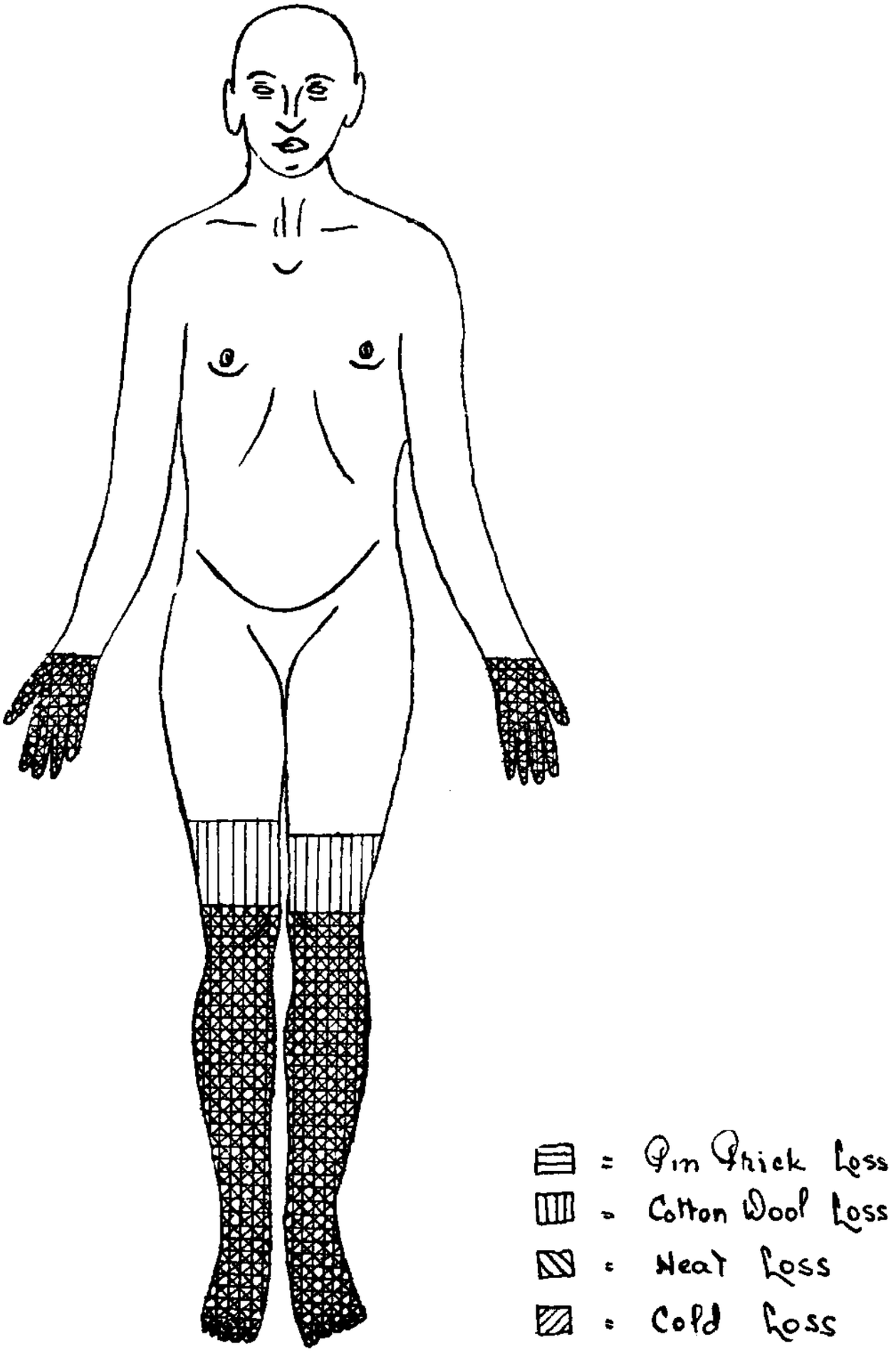


CHART B.

Mrs. L. F., aet., 45. 2:VIII:36.
Thirteen days after 2500 U. B_1 subcutaneously.
500 U. B_1 21:VII:36.
500 U. B_1 22:VII:36.
500 U. B_1 23:VII:36.
500 U. B_1 25:VII:36.
500 U. B_1 26:VII:36.
Joint sensation. Kees and elbows normal.
Tuning fork. Perceived weakly, styloids, malleoli, B. S.
Deep pain. No tenderness on pressure.

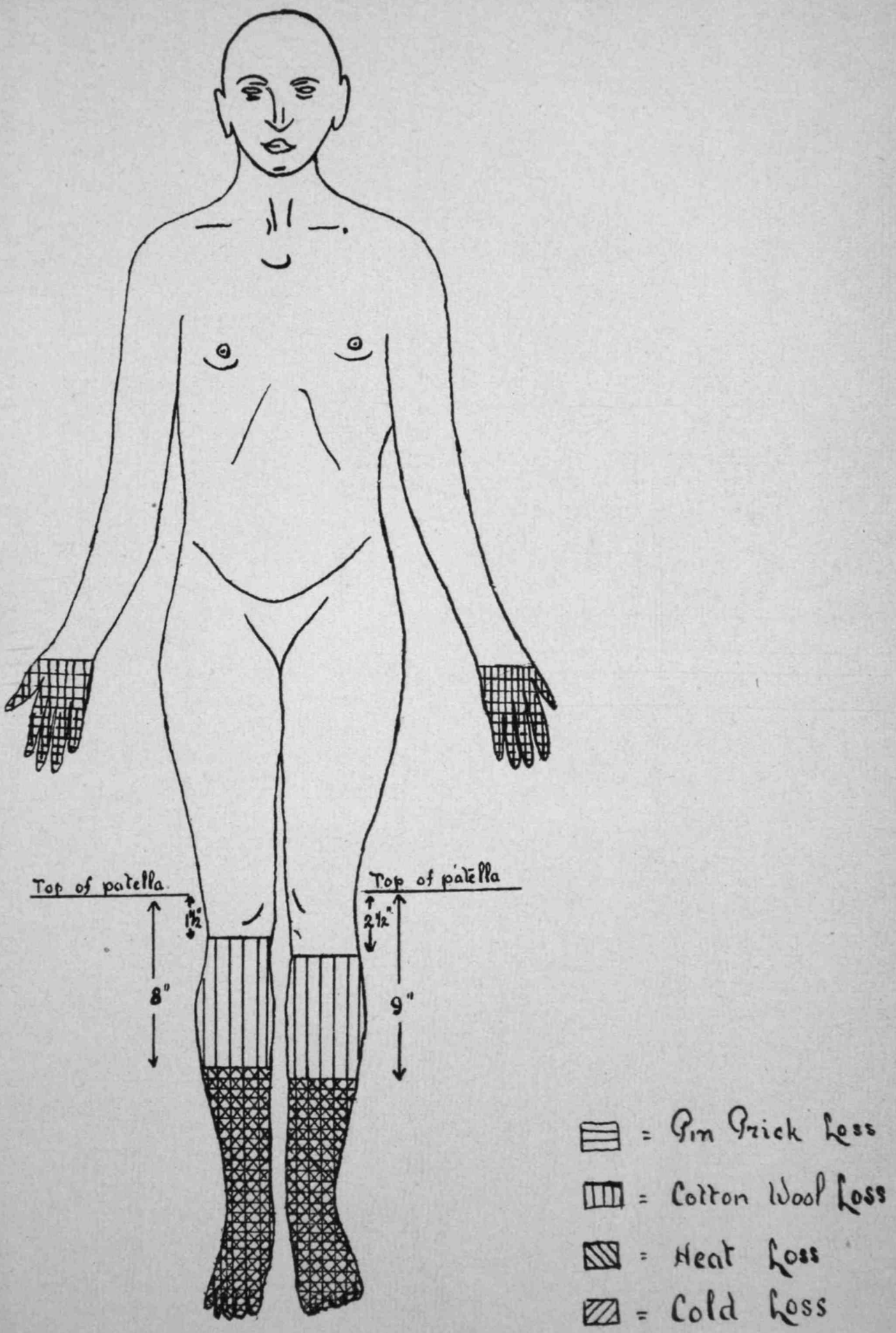


CHART C.

Mrs. L. F., aet., 45. 7:VIII:36.
500 U., B_1 subcutaneously. 2:VIII:36.

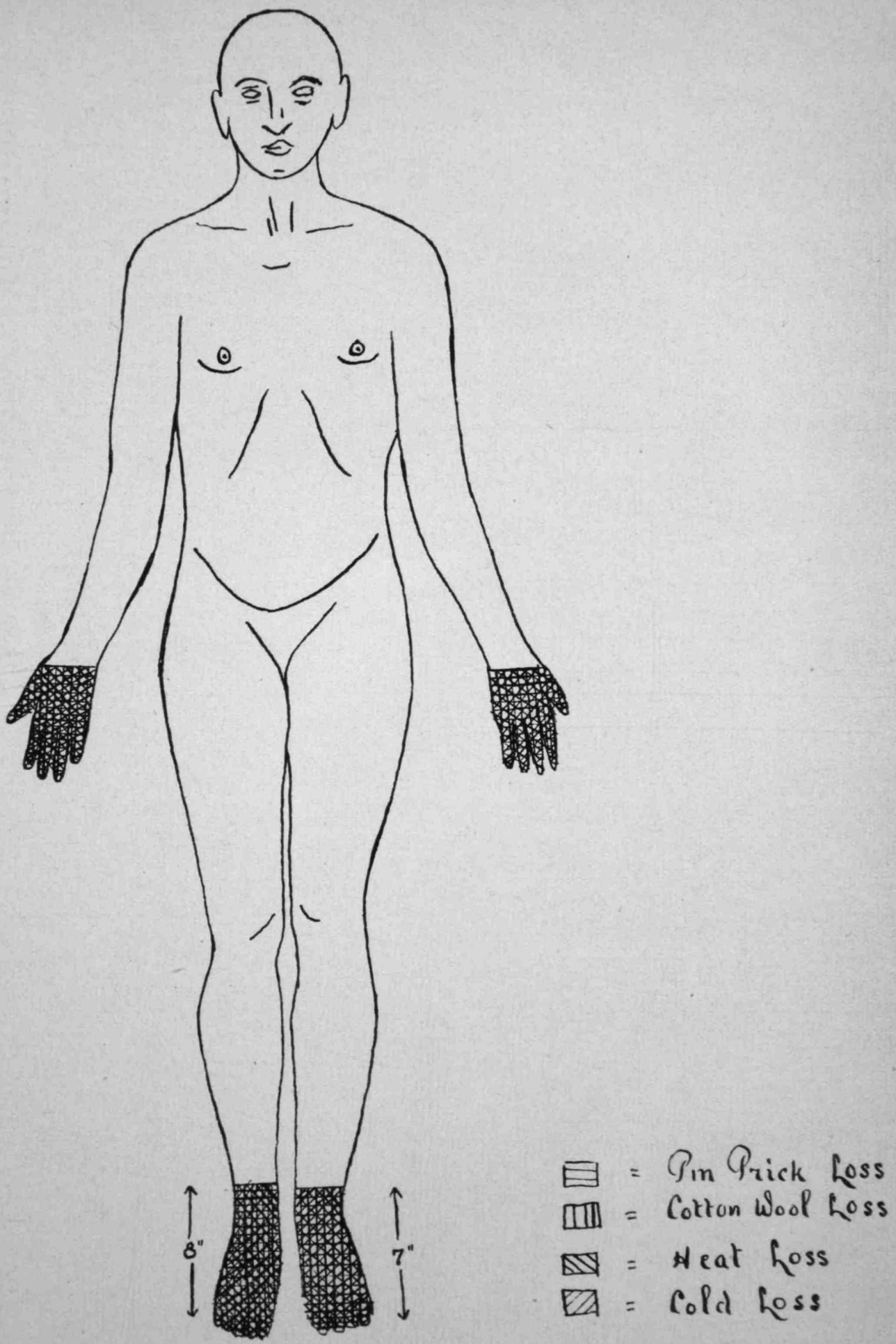
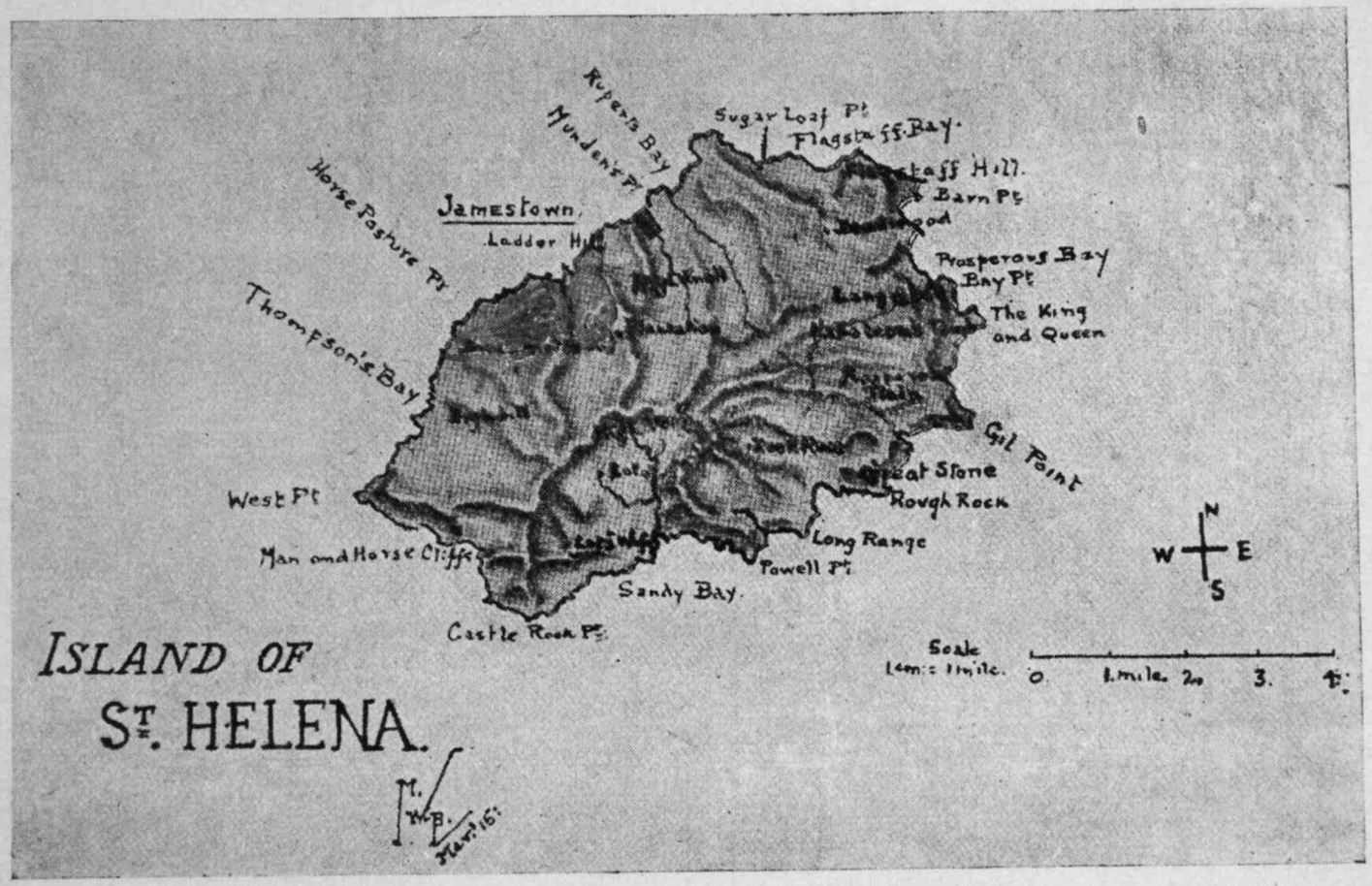


CHART D.

Mrs. L. F., act. 45. 21 : VIII : 36.
500 U. B_1 subcutaneously 9 : VIII : 36.
500 U. B_1 subcutaneously. 16 : VIII : 36.



ISLAND OF St. HELENA.

M. W. B. Mar. 16.

TRACE ELEMENTS IN NUTRITION

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During the last two decades chemical and physical methods of detection and estimation of minute amounts of chemical elements have attained a degree of delicacy and precision out of all proportion to the cumbersome and inaccurate methods of the last century. Hand in hand with this advance in technique has come a wider knowledge of the distribution of the so-called "trace" elements in nature, and the part they play in metabolic processes. Progress in the first-mentioned field is easy and rapid, and is limited mainly by the amount of material available and the existence of suitably accurate and convenient methods of analysis, but advance in our knowledge of the eventual functions of the various elements which are found in association with living tissues is slow and hardly won, and depends not only on our knowledge of their distribution in different species and in the different organs of individuals, but also on the general advance in biochemical knowledge.

There is considerable scientific basis for the belief that the various forms of living organisms have developed in the course of evolution from marine ancestors. In the salty environment which was offered to these primitive forms of life almost all the mineral elements were present in some degree or other, for the sea is a solution of all the soluble salts of the earth. Nature no doubt made many experiments, there were successes and failures, but the wealth and variety of the materials offered were sufficient to ensure that always a suitable alternative could be found. Under the continual pressure of their chemical and physical environment these primitive creatures diversified through long evolutionary ages, selecting and being selected, all the time developing along paths of least resistance new and more complex vital processes as the need arose. Under the stress of competition and environment the skeleton principles of biochemistry were hammered out in this marine laboratory.

Extra-marine life is a relatively recent innovation, and was reached only through long and anxious periods of substantial readjustment on the littoral. In order to meet new conditions as they arose, many new biochemical tricks had to be learnt, others, essential enough in the sea were gradually modified or fell into disuse as their importance declined. Nevertheless, in spite of the great changes that have taken place in the course of evolution, there still remain many recognisable links with the fishy past. It is sufficient perhaps in this regard to mention the close similarity which exists between the respiratory pigments. Haemoglobin in land animals is, as we know, a compound containing the element iron in chemical combination. In the haemocyanin of molluscs and crustaceans copper takes the place of iron.

The lamellibranch *Pinna squamosa* has been shown to contain a respiratory pigment in which manganese is used instead of copper. In plants, chlorophyll, which is in a sense a respiratory pigment, contains magnesium. From these facts it is clear that certain metals may play a specific rôle in the vital processes of one class of organisms, and yet be of no consequence to another. The fact that a metal is not universally distributed in nature does not preclude its possible importance as a limiting factor to certain forms of life. Conversely the fact that a metal is universally present in all biological material may merely denote an acquired universal tolerance and not a universal need.

The presence of relatively large quantities of certain metals in certain organs or structures may not be taken as conclusive evidence that these metals are secreted for a definite purpose. It may mean that these organs or structures merely possess a greater degree of tolerance or a greater chemical affinity for the metal or metals in question. Arsenic, zinc and copper for instance are found in hair and fingernails. In the absence of other evidence this can only be taken to mean that these metals have an affinity for keratin and are conveniently eliminated from the body in this manner. There is however evidence which suggests that copper may be concerned in the production of melanin. The deposition of certain metals in the liver of the growing fetus is usually accepted as strong evidence of their necessity.

Some of the elements found in the various organs of the body have their source in the utensils used for storing or cooking foodstuffs; the amounts so found will therefore reflect to some extent the domestic habits of the people concerned. For example, copper is more likely to be found in greater quantity in the organs of Asiatics than in the organs of Europeans for the simple reason that copper and brass utensils are still used in Asia for culinary purposes particularly in the towns among the more well-to-do. In the West, copper is no longer used for making pots and pans largely owing to the high cost of copper relative to the cost of aluminium which is being used to an ever increasing extent and also because of a widespread fear of copper poisoning. Copper vessels such as stills, evaporators, are however used in the manufacture of certain pharmaceuticals and food preparations. Medicinal glucose for example frequently contains heavy traces of copper. Silver is more likely to be found in the organs of those people whose racial peculiarity it is to eat with knife and fork. The organs of Eastern people who use chopsticks, on the other hand, are likely to contain less silver, but this short-coming is in all probability more than offset by their gold content, if the popularity of wearing gold-teeth in the East is any criterion.

Another aspect of the problem which greatly adds to its complexity is the fact that certain elements, such as lead, aluminium and

tin which, while occurring to a relatively limited and harmless extent in natural foodstuffs, find their way into prepared foodstuffs in much greater quantity during manufacture. Care is usually taken by manufacturers to keep the purity of their preparations within the limit of safety so far as concern elements which are known to be toxic, but no special care is usually exercised unless and until a metal has been shown to be harmful. Aluminium which finds its way into our daily bread as an ingredient of baking powder, is now believed to be quite harmless, but it was used for many years before the question received careful attention. Arsenic has been found in cocoa, and there is one well-known case where the manufacturers found it necessary to destroy a very large quantity of cocoa in the interest of the public.

Acid fruits are particularly liable to pick up traces of metals from utensils used in cooking and from the tins in which they are preserved. Milk is also very susceptible to contamination.

The widespread use of processed foods especially amongst western peoples makes it particularly difficult to obtain reliable values for the amounts of the various metals which can be regarded as normally associated with the various organs, and the research worker has to pick his way through a jungle of uncertainties. Nevertheless many of these values have been determined for the most part within reasonable limits and in so far as a full knowledge of the occurrence and distribution of minor elements in the various organs is essential to an understanding of their function, if any, it may be said that very considerable progress has been made in recent years.

Apart from the elements, carbon, hydrogen, oxygen, nitrogen, sulphur, phosphorus, calcium, sodium, potassium and chlorine which enter into the composition of protoplasm, and the elements iodine, iron and magnesium, the need for which has been established beyond all doubt, the only three elements which may be regarded as equally necessary for man, albeit in minute amounts, are copper, manganese and zinc. Their precise rôles, however, are not yet fully understood. Bromine and cobalt also have claims. Fluorine, beryllium and selenium are of importance, not as essential elements, but as elements which in certain natural circumstances can give rise to pathological conditions. Of the rest the most that can be said is, that their eventual rôle is still undisclosed. It may transpire that many will be found to be of the nature of tolerated adulterants rather than essential ingredients.

COPPER

Copper is one of the few elements which have been shown to play an important rôle in vital processes. It is extremely widely distributed in nature. In plants it is present in greatest amounts in the actively growing tissues, and is accumulated principally in the seed. It is universally present in all animal tissues, being located

mainly in the liver, heart, lung, brain and spleen. It is deposited also in teeth (Tiede and Chromse 1934, Jost 1934), particularly the first dentition (Sheldon and Ramage 1931), hair (Uichiro 1935), and gall-stones (Schoenheimer and Herkel 1931), and is a normal constituent of urine (Rabinovitch 1933, Tompsett 1934), blood (Tompsett 1934, Sachs, Levine and Fabian 1936), milk (Zbinden 1931), and bile (Judd and Thomas 1935). It is stored to an appreciable extent in the foetal liver during the three months preceding birth (Gerlach 1934, Tompsett and Anderson 1935, Lesne, Zizine and Briskas 1936). This is regarded as affording the strongest evidence of its indispensability.

The average human daily intake of copper is estimated (Tompsett 1934) to be of the order of 2-2.5 mg., the daily requirement being estimated (Tung-Pi Chou and Adoph 1935) to be 2 mg. Urinary copper has a concentration of .08-.48 mg./l. (Tompsett 1934, Ross and Rabinovitch 1935), with a daily urinary excretion (Tung-Pi Chou and Adolph 1935) of the order of .25 mg. Tung-Pi Chou and Adolph (1935) have estimated that the human body contains 100-150 mg. of the metal.

In bovine aqueous humour (Nitzescu and Georgescu 1935) it is present to the extent of .14-.18 mg./l. This is of particular interest in view of the recent finding (Policord, Bonnet and Bonamour 1936) that in Wilson's disease (hepato lenticular degeneration) the green ring which forms on the cornea contains appreciable quantities of copper.

Deeply pigmented hair is stated by Uichiro (1935) to contain 5.8-6.7, and colourless hair from the same head to contain 3.8-4.7 mg./kg. of dry matter. The senile depigmentation of hair is also associated with a reduction in the copper content (Hiroshi Yoshikawa 1937). This association of copper with pigmented hair is of particular interest in view of the fact that the ink sac of the octopus has been reported to contain the astonishing amount of over 900 mg./kg. of dry matter (Cunningham 1931). The ink itself, which contains a melanic pigment as does hair, contains only a small amount of copper. Cunningham has shown that copper has a catalytic action on the oxidation of "dopa" (3.4. dihydroxyphenylalanine), the precurser of melanin, to melanin, so that it would appear that the copper is playing a part in the production of the pigment. Oddly enough however Saccardi and Giuliani (1935) find more copper in the hair of albinos than in the red or black hair of normal animals. The pigment of the tail feather of the touraco is due to the presence of a copper porphyrin compound (Sheldon 1934).

It is in its participation in the formation of haemoglobin, however, that copper may be said to fill one of its most important rôles. Tompsett (1934) finds that normal blood contains 1.85-2.29 mg./l. According

to Sachs, Levine and Fabian (1936) the blood of the new-born contains only .83, but rises to the region of 1.71 mg./l. a few months after birth. Lesne, Zizine and Briskas (1936), however, find the blood copper of 5-6 months foetuses to be in the region of 1.95-2.35 mg./l., as compared with .73-1.06 for new-born infants, and an average of 1.35 for children of 1-2 months. Still-born children at term had the somewhat lower values of .80-1.12. Bence, Lendvai and Szekely (1936) find the whole blood copper to lie between the limits .70-1.33 with an average of .98 mg./kg. for ten normal persons. Tompsett (1934) and Bjerrum Jannik and Henriques (1935) consider that the blood copper is distributed equally between corpuscles and plasma, but Uichiro (1935) finds .337-.635 in plasma and .679-.729 mg./l. in the erythrocytes, his value for whole blood being .912-1.081 against the somewhat higher values found by Tompsett, and Sachs, Levine and Fabian. In the serum the copper is considered to be present in combination with the albumin fraction (Eisler, Rosdahl and Theorell 1936). The activity of the female reproductive organs appears to be associated with the presence of copper, for although during the intermenstrual period the blood copper content is approximately the same as it is in males, the premenstrual period is characterised by a definite increase both in the plasma and cells, followed by a decrease during the menstrual hemorrhage (Uichiro 1935) when iron is also lost (Ohlson & Daum 1935). Uichiro observed a marked increase in the plasma copper during the first half of pregnancy, tending to return to normal at parturition. The erythrocyte copper, however, showed hardly any change. Tompsett and Anderson have also noted an increase in the whole blood copper during pregnancy, but in their experience the increase was confined to the last three months. Strong evidence of the hematopoietic action of copper is afforded by the fact that copper feeding at this time reduces the amount of iron in the liver and tissues and increases the amount in the blood.

In hemachromatosis copper as well as iron is deposited in the tissues. Iron is deposited chiefly in the pancreas, and also in the liver, thyroid, lymph nodes, salivary glands, pituitary, choroid plexuses and heart. Copper is deposited in the liver, and in most other tissues, but not apparently in the kidney, small intestine and omentum (Ramage & Sheldon 1935).

According to Uichiro (1935) the production of hemorrhagic anemia is accompanied by an increase in the amount of copper in the erythrocytes and in the bone marrow. In hemorrhagic anemia in rabbits intravenous injections of .3-.6 mg. of copper per kg. of body weight increase the number of erythrocytes.

Pure iron as $FeCl_3$ does not stimulate regeneration of haemoglobin when fed to anemic rats at a level as high as 10 mg. daily, but intraperitoneal injections of iron as the chloride or citrate definitely

induce hematopoiesis. Intraperitoneal injections of copper also influence hematopoiesis favourably, but similar injections of Ni, Zn, Ge, Mn, V, As, Ti, Se, Hg, Rb, and Cr salts fail in this respect. (Keil and Nelson 1933). Usher, MacDermot and Lozinski (1935) have shown that a group of children who received 1.5-3.0 grains of iron as Ferric Glycero Phosphate and 1/64-1/32 grain of copper sulphate had a higher hemoglobin concentration at the age of one year than another similar group who received only iron. Both groups showed substantial increases over a control group. The group receiving the copper supplement showed the greatest gain in weight, the greatest resistance to disease, and a lower mortality rate.

Iida (1936) considers that hematopoiesis by copper is due not to its direct action on the bone marrow but to its action through the spleen, thyroid, and the whole reticulo-endothelial system.

MANGANESE

Manganese is a very common constituent of soil, though present as a rule in very small quantities. Scheele is credited with having first detected its presence in plants as early as 1785. The amount of manganese assimilated by plants, in which it is widely distributed, depends on the physiological nature of the plant, and on the amount present in the soil, where it occurs in organic combination in plant debris as well as in the free state as manganese dioxide. Cooper (1935) has shown that plankton contains appreciable quantities of manganese. The plankton from a cubic metre of sea-water contained from 0.5 to 3.0 gamma of manganese, and waters rich in plankton are low in dissolved manganese (Thompson and Wilson 1935). Since plankton occupies such an important and fundamental position in the marine food-chain it will be appreciated that fish also serve as an important source of manganese in human nutrition. Webb (1937) has shown by spectrographic means that manganese is very widely distributed amongst marine invertebrates, but that it is nowhere very abundant. In plants, manganese appears to be far more abundant in those parts in which active chemical changes occur. In leaves, it appears to bear some relation to the formation of chlorophyll, for according to Bertrand and Rosenblatt (1932) it is found in amounts proportional to their greenness. Riou, Delorme and Hormisdas, who investigated the distribution of manganese in the pines of Quebec, found that the amount of manganese (and iron) in the ash differed in the bark, twigs, needles, sapwood, heartwood and cones of a given species but was similar for the corresponding parts of white pine (*P. strobus*), red pine (*P. resinosa*), and grey pine (*P. banksiana*). They found also that a relatively high manganese content was associated with a low iron content, and that the largest amounts of these metals were present in the active parts of the tree—the twigs and needles. Ramage (1933) gives figures which show that in various seeds the coat of the endosperm is much

richer in manganese than either the outer coat of the seed or the endosperm itself. The amount of manganese present in the whole seed was greater than that present in other parts of the plant, a fact which Ramage (1933) suggests is proof of the plant's need for manganese, and the other metals present, since in this way the offspring is guarded against shortage. Scharrer and Schropp (1934) have recently investigated the influence of manganese on the germination of cereals, maize and peas and find that although small amounts of manganese definitely stimulated growth, the effect was toxic at concentrations above 10 mg. in 800 grams of soil (.0013 per cent.). This confirms the conclusions reached by Bishop (1928) who also pointed out that calcium has the power of protecting the plant from this toxic action. Scharrer and Schropp also studied the interrelations of iron and manganese and noted that when iron was replaced by manganese maize did not develop as well as when both metals were present. They obtained the best results from the point of view of germination when Fe: Mn=7: 1, which suggests that although necessary, manganese is required in considerably smaller quantities than is iron. It should be pointed out, however, that optimum conditions for germination are not necessarily optimum conditions for subsequent growth. Ferruccio has also studied this question. He found that grain absorbed manganese from the soil in proportion to the amount present in the soil, and observed also that iron was absorbed to a lesser extent and could not be substituted for manganese. This result agrees with that obtained by Scharrer and Schropp in so far as both results show that iron and manganese are both necessary and are not interchangeable. Carsten Olsen has recently carried out some work in Copenhagen in which he showed that various species of plants varied very widely in their degree of tolerance to the presence of manganese in the growth medium. For example, a concentration of 0.5 mg./l. in the form of $MnSO_4.4H_2O$ was toxic to water cultures of *Lemna polyrhiza,* whereas no toxic effect was noted for *Hordeum distichum* and *Sinapis alba* with a culture solution containing five times as much manganese. The growth of *Zea mays* was promoted by increasing the concentration of manganese up to 50 mg./l., and was not inhibited until the concentration reached 250 mg./l. Another interesting contribution to our knowledge on this subject has been made by Summer and Howell who have studied the rôle of the bivalent metals in the reversible inactivation of jack-bean haemaglutinin. According to these authors Concanavalin A, one of the four crystalline globulins of the jack-bean, consists of an organic part, the globulin, united with the three metals, calcium, magnesium and manganese. They come to this conclusion since they found that on treatment with dilute acid these three elements are removed, whereupon the protein loses its power to agglutinate erythrocytes and starch granules and also loses its power to precipitate

glycogen. These properties were restored, they found, by neutralisation and also by the addition of salts of these three elements to Concanavalin which had been irreversibly inactivated by acid treatment followed by dialysis. A solution containing as little as 0.3×10^{-6} *M* of Ca, Mn and Mg produced a perceptible effect in reactivation. The concentration of each metal is about 1:5000 million. The protein does not crystallise readily when it has been deprived of its Ca, Mn, and Mg, but does so in the normal manner on addition of the salts of these metals. On this basis they conclude that the ash of a protein is not necessarily to be regarded as an impurity, but that proteins in nature may be composed of an organic part united with one or more metals.

In animal tissues manganese is of widespread occurrence, the liver and pancreas usually containing the largest quantities. Sheldon and Ramage (1933) have frequently found notable amounts in the suprarenals and in meconium. These workers also report a considerable variation in the manganese content of corresponding tissues of various species, man, for example, having much smaller values than herbivorous animals such as the guinea pig. Manganese occurs in blood, where it is principally located in the serum, the amount ranging between 0.16-0.3 mg. Urechia, Pamfil and Retzeanu (1934) could trace no connection between pathological condition and the level of blood manganese.

For the last decade manganese has been generally regarded as being of definite physiological importance. McHargue as early as 1926 came to the conclusion that manganese together with copper and zinc were indispensable. The growth and condition of rats reared on synthetic diets with and without the addition of salts of manganese, copper and zinc singly and in mixtures indicated that all three metals were necessary for normal growth and development. McHarrison (1927) also found that a daily dose of 0.889 mg. of MnO_2 exercised at first a favourable effect on young rats but later retarded their growth. The retarding effect was apparent after 32 days. A smaller daily dose of 0.0327 mg. was found to exert a markedly favourable influence on growth. Bertrand and Nakamura (1928) have also described feeding tests with and without manganese. Thirteen mice fed without manganese survived on the average 24.4 days and fifteen fed with manganese survived on the average 27.4 days. Little importance can be attached to this small difference. However, they noted that the animals fed on manganese retained about ten times as much in their bodies as those that were fed none. Ramage, Sheldon and Sheldon (1933), who carried out a spectrographic investigation of the metallic content of the liver during childhood showed that the manganese concentration of the foetal liver was definitely increased during the last three months of foetal life. They noted also that the amount decreased during the nursing period but increased again after weaning.

With regard to the influence of manganese in fertility Keil, Keil and Nelson (1934) were able to obtain satisafctory reproduction in first generations of rats fed on milk plus iron and copper, but the second generation failed to reproduce unless manganese was added. Daniels and Everson (1935) studied the cause of the high mortality in the young born from rats on a diet poor in manganese. Rats born under these conditions contained 65% less manganese than those from mothers receiving adequate manganese, and were not strong enough to survive birth, or if they did survive, they were not active enough to suckle. However, mothers on the low manganese diet were able to suckle young taken from mothers on a normal diet. Manganese thus appears to play a more important part in the development of the foetus during gestation than in normal lactation after parturition as was suggested earlier by Orent and McCollum (1931). Daniels and Everson also observed a considerable increase in the manganese store of young rats during suckling, but very little increase after weaning, when they were fed on cow's milk, which may merely mean that rat's milk is richer in manganese than cow's milk. As a result of their experiments Daniels and Everson suggest that the daily diet of children should contain between 0.2 and 0.3 mg. of manganese per kg. of body weight.

ZINC.

Zinc is a very widely distributed element. It is present in most soils and has always been found in small amount in natural waters. The water of the English Channel contains about 8 mg./cu. metre, but sea water remote from land contains only traces. It occurs, it is believed, in all plants, and consequently in the tissues of all animals, although exceptions have been recorded. For example, using the spectrograph, Boyd and De (1933) failed to find any trace of the element in Rangoon rice, brinjal, lady's finger, puin shak and palong shak, although all other plants tested gave positive results. In marine animals, Webb (1937) was unable to demonstrate its presence spectrographically in a few species, whereas in other closely related species it occurred in abundance. Apart from this recorded exception it is widely distributed in marine animals, oysters being particularly rich in zinc (Birckner, 1919, Hiltner and Wichman, 1919). Paulais (1937) has reported that *Gryphaea* also contains large quantities, particularly in the hepatopancreas. Over an exceedingly wide range of land animals its presence in all organs and tissues has been noted so far without exception. In certain organs and structures it occurs in relatively large amounts, notably in liver and pancreas but the largest amounts are secreted in hair, 207 p.p.m., finger and toe nails, 182, 197 p.p.m. (Eggleton 1938) and in teeth, 250 p.p.m. (Cruickshank 1936, 1937). Skin contains about 24 p.m., sciatic nerve about 40 p.p.m., but cerebro spinal fluid contains only 2-3 mg./l. (Eggleton

1938). The amounts of zinc deposited in the various tissues is influenced largely by the nature of the diet, predominantly carbohydrate diets contributing appreciably less zinc than diets containing a large proportion of protein (Eggleton 1938). The daily intake of zinc from an average well balanced diet has been calculated by Eggleton to amount to 8-15 mg. so that the average human being consumes something over half a pound of the metal during a lifetime of three score years and ten.

Deficiency of zinc in soils of certain areas in the Florida Everglades is understood to be the cause of certain physiological growth disturbances known as mottled leaf, or little leaf disease of citrus and other plants growing in these localities. Beneficial results have followed not only from the application of zinc salts to these soils but also from injection into the trunk of the tree and even from spraying of the foliage. So far as land animals are concerned there is now considerable evidence to show that it is an essential mineral. In addition to copper and iron there is a pre-natal storage of zinc in the liver, the birth value being approximately three times the normal adult value of about 300 p.p.m. Colostrum, according to Koga (1934) contains three times as much zinc as milk. Following on the work of Bertrand and his school, Hubbell and Mendel (1927) observed that rats fed on a relatively zinc-free diet supplying only 0.005 mg. per mouse per day made somewhat slower growth than animals receiving a similar diet containing four times as much zinc: eight times as much appeared to have a slight retarding effect. Later Newell and McCollum (1933) designed a diet which they estimated by spectrographic means to contain only one part of zinc in ten million, and found that rats reared on this diet appeared to develop just as well as did similar animals receiving a small supplement of zinc. Normal reproduction, however, was not obtained either on the experimental diet or on the control diet, although conception and successful gestation took place when both parents were raised on the zinc-free diet. The authors concluded that zinc was necessary for normal reproduction in the rat but not necessary for growth. Todd, Elvehjem and Hart (1934) on the other hand came to the conclusion that zinc was indispensable in the proper nutrition of the rat, their zinc deficient rats having a markedly low efficiency for converting food to body weight. The growth of fur was also abnormal (Elvehjem and Hart, 1934). Later, Stirn, Elvehjem and Hart (1934) criticised Newell and McCollum's work which failed to show a deficiency effect on growth as being due to imperfect purification of the food materials used. More recent work by Elvehjem and his associates (1937) again showed that a low zinc ration interfered with normal growth. The effects arising from zinc deficiency were prevented when the animals received 40 gamma per day. The growth rate of animals which received only half this amount was halved. These workers also noticed a distinct

irregularity in the glucose tolerance curves of zinc-low rats and in view of the fact that no sugar was lost in the urine and that the blood sugar and liver glycogen were normal, put forward the suggestion that the disturbance in glucose tolerance was due to a delay in the absorption rate from the intestine. Amongst other things this suggestion received support from the fact that the weight of the dry feces excreted per day by zinc-low rats was greater than for the control even though the former consumed less food: the nitrogen per gram of dry feces was the same for both groups. Furthermore they found that whole pituitary gland transplants produced a definite improvement in food utilisation and growth response in the zinc-low rats. It was shown by suitable Anuitrine-G "growth" hormone injections that this effect could not be due to the zinc content of the transplanted pituitary gland (estimated to be about 0.3 microgram) nor to its "growth" hormone content. On this basis the authors felt justified in assuming that zinc is involved in the production or utilisation of some hormone which controls the motility and tonus of the intestinal tract.

It can be said therefore that there are very substantial grounds for believing that zinc may be classed as one of the essential minerals. Precisely what rôle it plays is however still a matter for speculation. There is a growing body of evidence to show that in common with some other metals it is associated with the synthesis of enzymes and hormones and such like bodies or with their activity—possibly with both. Rost (1921) was one of the earliest workers to suggest that the zinc in the body is in organic combination principally with protein and protein derivatives and is not present as a free salt. It should be mentioned however that Delezenne (1919) in his work on snake venoms arrived at the conclusion that the zinc which he showed to be associated with the venom is in firm chemical union since he could not remove it either by H_2S or dialysis. Since he found that the relative activity of venoms from different strains of several species closely paralleled their zinc content he assumed that zinc is the specific component of the enzyme. He found that the sulphur content closely paralleled the zinc content. Bertrand and Vladesco (1921) showed that during the period of sexual activity of the herring the testicles of the males contain twice as much zinc as the rest of the body. During the same period there was practically no difference in the zinc content of the ovaries and of the remainder of the body. Akao (1935) has also shown that the total zinc content of the adult female silkworm, *Bombyx mori,* L., is higher than that of the male, and that the total zinc content of the ovaries is about twenty-four times as great as that of the testicles although the amount per kg. of dry matter is about the same in both organs. After gonadectomy the zinc content of the blood of the females is increased to four or five times that of the normal female. This operation produced no change in the zinc content of the blood of the males.

McHargue (1927) suggested that since most of the zinc, manganese and copper of plants is concentrated in the seed, the plant uses these metals in synthesising complex organic combinations which have important functions as catalysts, enzymes, and vitamins, and that when these complex organic compounds are consumed by animals they are assimilated and re-synthesised into catalases, oxidases and hormones. In order to test this point Turnwald and Haurowitz (1929) separated liver extract which contains copper, zinc and manganese into four fractions each of which was examined for esterase and catalase. By spectrographic analysis they showed that the bulk of the metals was present in the enzyme-free fractions. Nevertheless, these authors consider that individual metals may occur in chemical compounds and be catalytically active only in some particular type of molecular linkage. It is of course a well known fact that the activity of enzymes can be very much modified by the presence of a metallic salt. Whether or not the effect is accelerated or inhibited depends usually on the particular metal present, its concentration and on the pH of the medium. As examples, the work of Andreitchewa (1930) and of Linderstrom Lang (1934) may be cited. The first mentioned showed that peroxidases are accelerated at $M/1000$ concentration but inhibited at higher concentrations of zinc salts, and according to the last mentioned worker the cleavage of alanyl-glycine by enteric pepsidase at pH 8 is activated by low concentrations of zinc acetate and inhibited at higher concentrations. Zlataroff (1930) goes so far as to suggest that accumulation of zinc in the skin is one defence of the organism against abnormal metabolism of the cancer cell, the zinc tending to inhibit the enhanced activity of proteolytic enzymes and catalase and stimulate the decreased activity of peroxidase.

With regard to the action of zinc on hormones Maxwell (1934) and Hisaw, Fevold and Greep (1936) have reported that the addition of zinc salts to hypophyseal sex hormone preparations produces a marked augmentation of response. The effect of zinc in combination with insulin and protamine is now well known and the preparation "zinc-protamine-insulin," because of its modified hypoglucemic action, is finding increased favour in place of insulin alone. Finally there is Kohn and Bulgar's (1937) work on the action of zinc on the effect of subcutaneous adrenalin injections. The adrenalin effect as measured by blood sugar concentration was definitely diminished when the adrenalin was administered in conjunction with zinc sulphate. Blood pressure curves told the same story.

CADMIUM

The presence of cadmium in living tissues was first reported by Fox and Ramage in 1931, who detected it spectroscopically in the common scallop (*Pecten maximus*). Oddly enough these authors detected the presence of this metal in every specimen of this species

from four different localities, but failed to find a trace of it in other species from the same locality. Webb (1937) reports its frequent occurrence in marine invertebrates. Salant and Connet (1920) have shown this element to have a toxic action on the isolated frog's heart. Rossi and Scandellari (1932) have recorded its inhibiting action on invertase production in *Aspergillus Niger*. Sinichi Okajima (1931) has shown that when administered *per os* and parenterally this metal is quickly distributed to all organs of animals, and is only slowly discharged in the urine, feces and bile. In sand and water culture experiments Scharrer and Schropp (1934) have shown it to be more toxic and less stimulant than zinc at equivalent concentrations. Schnetz (1935) has shown that cadmium salts in doses up to 2 mg./kg. had no effect on the blood sugar level of rabbits when injected subcutaneously, but did inhibit the duration and extent of the adrenalin hyperglucaemia. Torsten Thunberg has shown that, in common with zinc, cadmium promotes the discoloration of oxidation-reduction indicators by extracts from a variety of plant seeds. The evidence so far available suggests that this element is of very infrequent occurrence, but when present its action is similar to zinc, the two metals being to a limited extent interchangeable.

BROMINE

This element is widely distributed in nature. It is particularly to be found in marine organisms, more especially in marine vegetation (Neufield 1936). Sea water contains about 0.008 per cent. of bromine and is one of the principal sources of the element. In this connection it is of interest to note that one American plant recovers no less than 45,000 lb. of bromine daily from sea water. The magnitude and efficiency of the process is appreciated when it is realised that this involves the treatment of some 1,370,000 lb. of sea water each minute (Fielder 1937). Von Damiens and Blaignan (1931, 1932) have demonstrated the occurrence of bromine in land plants, where it is usually present in amounts of the order of 2-20 parts per million of dry matter. Its presence has been established in almost all animal organs and was at one time thought to be much more concentrated in the hypophyses (Bernhardt and Ucko 1926) than in the blood. Beluchi and Baldanzi (1934) give the values 56 and 302 mg./kg. respectively for two samples of human blood, and 1184 mg./kg. for human hypophyses (3140 mg./kg. of dry matter). Dixon (1935) and Neufield (1936, 1937) however, find the pituitary bromine to be of the same order as the blood bromine. The amount present in the blood, where it is largely concentrated in the erthrocytes (Leipert, 1935), is now agreed (Dixon, 1935, Ucko, 1936) to be of the order of 4-15 mg./litre. Moruzzi (1936) gives the following values expressed in parts per million of fresh material, for some of the principal organs: brain, 0.2; liver, 7.2; spleen, 4.6; lung, 3.5; kidney, 6.3; suprarenals, 4.2; testicles, 2.6; thyroid, 2.5; hypophyses,

10.2. According to Boronino, Schteingart and Ferramola (1934), the spinal fluid contains only 2.0 mg./litre. The daily excretion of urinary bromine has been found by Ucko (1936) to be of the order of 1-2.5 mg. per day.

In 1932 Zondek and Bier claimed that the bromine content of the blood of manic depressives was much lower than that of normal persons, and several other groups of workers (Klimke and Holthaus 1932, Sacristan and Peraita 1933, and Urechia and Retzeanu 1933, 1935) claim to have confirmed this observation. It has been pointed out subsequently, however, by Dixon (1934) and Quastel and Yates (1934) that the method of Pincussen and Roman which was used by Zondek and Bier, and by the workers who claimed to confirm their results, is subject to large errors. Not only does the blood bromine vary very greatly among cases of mental disorder, but similar variations also occur among normal subjects (Quastel and Yates 1934, Henelly and Yates 1935). Dixon (1935) found the blood bromine of ten psychotics to lie within the range of 2.8-17.6 mg./l., corresponding closely with the figures given above for ten normal persons. Chatagnon and Chatagnon (1936) similarly failed to find a characteristic decrease in the blood bromine of manic-depressives, and Ucko (1936) also reached similar conclusions. Since the methods used by these workers represent a substantial advance in accuracy, and since the greatest care was taken to exclude all cases of known or suspected bromide therapy, it would appear that blood bromine is not necessarily related to certain forms of insanity as was previously supposed. Not only does the blood bromine of individuals show a wide variation, but it also varies (Moruzzi and Guareschi 1936) with age and sex, and is greater in the morning than in the evening (Moruzzi 1936). The bromine in the cerebro spinal fluid also varies between wide limits for different individuals according to Mihaly Nagy and Janos Straub (1936), and similarly bears no relation to nervous diseases and insanity. Furthermore, it has been shown (Dixon 1935, Leipert and Watzlowek 1935) that the bromine contents of the hypophyses from insane persons shows as large a degree of variation as those from normal persons. Quastel and Yates (1934) have observed that during the process of digestion the amount of bromine in the blood is decreased while the amount in the gastric juice is increased. It is possible therefore that this may provide an explanation of the anomalous results obtained by Zondek and Bier, in the event of their having consistently taken post-prandial samples from their psychotics.

Zondek and Bier (1932) also put forward a theory that a bromine-containing hormone was associated with the pituitary, and was the agent responsible for producing sleep and sedative effects. This suggestion receives some support from the results of Suomalainen (1935) who observed that the bromine content of the blood and pancreas of hedgehogs increases during hibernation, while that of the liver, spleen

and other organs decreases, but this may be merely a reflection of the fact that no bromine enters the system during hibernation and that the bromine already within the body becomes disposed about the various organs according to their ability to retain it. Moruzzi and Guareschi (1936) find that the hypophyseal bromine is almost completely non-diffusible and Dixon (1935) also could find no evidence in support of the theory that a bromine-containing hormone exists in the pituitary. The function of bromine therefore in vital processes is still unknown.

FLUORINE.

Fluorine is widely distributed as fluoride in rocks, soils and waters being estimated to constitute 0.1 per cent. of the first half mile of the Earth's crust, land and sea. The minerals fluorspar and cryolite are rich in florine as are biotite, muscovite and apatite: all are widely distributed. As a result of its universal occurrence in vegetation, animals cannot avoid consuming it. Consequently it is found in all tissues and organs. Zdarek (1910) has reported the following figures for the normal fluorine content in parts per million of dry matter of various human organs: brain, 2.7; lung, 2.2-7; heart, 4.6; spleen, 8.2-23.5; liver, 6.8-8.0; kidney, 15.4. Gautier and Clausmann (1913) give further figures for various other organs and structures: muscle, 0.4-4.6; cartilage, 4-14; hair, 61-197; epidermis, 164; thymus, 39-111; testicle, 12-42. Cow's milk according to the same authors, contains 1.8 and human milk 0.5 parts per million. Blood contains about 23-44 parts per million.

Whether or not the element plays an essential rôle in vital processes is not known for certain. Some of the available evidence suggests that it is an accidental constituent of tissues being unavoidably ingested in almost all foodstuffs, but the fact that bones and teeth normally contain fluorine in the form of apatite, $3Ca_3(PO_4)_2 CaF_2$, may indicate a special function in bone and tooth building. So far it has not been found possible to design a diet which is free from fluorine so that critical experiments to show whether the element is essential or not are lacking. Most of the work that has been done has been concerned with the effect of feeding fluorine in amounts greater than those normally occurring in foodstuffs in order to determine its degree of toxicity and the effects which it produces on the system under these conditions.

Sollman, Schettler and Wetzel (1921) three of the first workers to study the effect of fluorine on growth ascertained that a concentration of sodium fluoride greater than 10 mg./kg. of body weight per day interfered with the growth of rats and diminished the amount of food consumed although the food was equally palatable to the animals. Below this level no harmful effect was observed. In 1925, Schultz and Lamb reported briefly that a level of 0.1 per cent. sodium fluoride

in the ration interfered with the growth of rats and stated that an "unfavourable effect in reproduction begins at a level of about 0.025 per cent. of sodium fluoride." In the same year McCollum and co-workers reported that when sodium fluoride was added to an adequate mixed ration at the level of 0.05 per cent. the teeth of rats were observed to be abnormal in appearance and defective in structure. Later they noted defective dentition when the diet contained half this amount of fluorine, 0.0226 per cent. Christiani and Gautier reported that fluorine tended to accumulate in the bones of guinea pigs producing a conditon resembling osteomalacia. Two years later Begara (1927) noticed that feeding excessive amounts of fluorine to rats retarded calcification of the osseous tissues and produced dark bands on the incisors.

Up to this time interest had centred mainly around the fluorine content of teeth and bones and the relation of excessive amounts of ingested fluorine to the condition of the teeth known as "mottling" was unknown. In 1931 Smith, Lantz and Smith definitely established the fact that fluorine was the causative agent. Mottled teeth are not only disfiguring in appearance but are so defective in structure and strength that they often need to be replaced by false teeth at an early age. Smith and Smith (1935) carried out an extensive survey of the conditions in Arizona by means of which the concentration of fluorides in water supplies was correlated with the degree of severity of the disease, and showed that the continued use of water containing as little as one part per million of fluorine was sufficient to interfere with normal tooth development. Since this time the question of fluorine has assumed a much greater importance. Not only have deposits of fluorine bearing minerals been found to be very widespread but many kinds of phosphate rock used as fertiliser have been found to contain appreciable quantities of fluorine. Furthermore fluorine compounds are also becoming more commonly used as spray insecticides in place of arsenicals the toxic action of which is known and feared. Most of the damage to teeth which arises from fluorine occurs during the time of formation of the teeth. In after life exposure to similar conditions has little or no effect in this regard. Fluorine can be transferred to the young during suckling and even during foetal life (Reid and Cheng, 1937). Reid (1936), and Cheng and Reid (1937) have drawn attention to the wide distribution of fluoride deposits in Shansi, Kiangsu, Shantung, Liaoning and Jehol. In all of these provinces mottled teeth are of frequent occurrence. Reid (1936) has also shown that many Chinese teas particularly the cheaper brands contain relatively large amounts of fluorine.

ALUMINIUM

Aluminium is a constant constituent of plant and animal tissue. It is quite harmless to the living animal when presented in the amounts

normally present in foodstuffs. The interest in aluminium centres mainly about the possible harm which might arise from its use in baking powders and from the use of aluminium cooking ware. Until within the last decade opinions have varied with regard to the amounts of aluminium present in various materials and particularly in regard to the amounts of aluminium which may be brought into solution during the process of cooking in aluminium vessels. This lack of agreement was due largely to the difficulty of accurately of estimating small amounts aluminium. For example, Carnot's well-known gravimetric method in which aluminium phosphate is precipitated has been shown to involve serious errors if calcium is present. Gwyer and Pullen have also shown that the figure obtained varies according to the pH at which the aluminium phosphate is precipitated. Recently however more accurate methods of estimation have become available, and it can now be said with a fair degree of certainty that the amount of aluminium brought into solution on boiling in an aluminium saucepan is of the order of 1 p.p.m. The amount of aluminium dissolved is of course largely influenced by the reaction of the material which is cooked. When neutral foods are cooked in aluminium vessels there is no appreciable removal of the metal. Acid juices however remove anything from 10 to 40 p.p.m. according to the degree of etching of the pan. Experiments on University students have shown that the daily consumption of a fifth of a gram of aluminium for long periods produces no ill effect.

For some years the natural occurrence of aluminium in cereals, vegetables and fruits was doubted, but from the results obtained in recent work using improved methods of estimation it is now apparent that aluminium occurs widely as a natural constituent of foodstuffs. It has recently been estimated that the daily intake of aluminium is of the order of 12 mg. of which about half is naturally contained in the foodstuffs.

We have no knowledge whether aluminium has any special significance in vital processes, or whether the amounts found in the body are merely tolerated. Kahn (1911) using dogs which were fed a diet containing aluminium reported its presence in the urine and blood. Analysis of the organs showed that the element was present in perceptible amounts in the liver, spleen, kidney and muscle. Steel (1911) also observed that aluminium is present in the blood of dogs receiving aluminium in the diet. Balls (1917) found that dogs under similar conditions of feeding absorbed aluminium especially into the liver, but that much of this aluminium was speedily eliminated in the bile and urine. Leary and Scheib (1917) stated that puppies fed on a diet of low phosphorous content to which was added a comparatively large amount of aluminium hydrate showed symptoms of under-nourishment. Flinn and Inouye (1928) using rats which received aluminium as an aqueous solution reported that 70 per cent. was

excreted in the feces and 30 per cent. in the urine. Myers and Morrison (1928) found that dogs fed on aluminised diet showed markedly higher aluminium content in most of the internal organs than animals fed on control diets. Underhill (1929) observed that dogs fed on diets containing aluminium showed a higher level of aluminium in the organs than dogs on a control diet, but could not find any definite relation of absorption to ingestion, though the amounts found usually increased with the age of the animal. Aluminium could be detected in human blood after a meal containing aluminium and a slight urinary excretion, not usually exceeding half a milligram in 24 hours, was sometimes observed. Mackenzie (1930) as a result of experiments with pigs concluded that no harmful effect on growth and metabolism results from feeding comparatively large amounts of aluminium. Mackenzie was also unable to find any conclusive evidence of urinary excretion, the small amounts found in the urine could be attributed in his opinion to fecal contamination which was unavoidable. Mackenzie was also unable to confirm the suggestion of Leary and Scheib that aluminium may affect metabolic processes by combining with available phosphorous in the intestinal tract, thereby immobilizing it. In Mackenzie's experiments urinary excretion of phosphate was no less with aluminium feeding than without. Further work by Mackenzie on rats (1931) confirmed his work on pigs. He found no evidence of absorption of aluminium by the internal organs and no aluminium was excreted in the urine. It is probable that the aluminium occurring naturally in foodstuffs is in organic combination in which form it may be more readily assimilated. At all events it would appear that it is entirely harmless in the amounts ordinarily presented. So far as is known aluminium performs no special function in vital processes.

LITHIUM, RUBIDIUM AND CAESIUM.

Lithium is occasionally found in human and invertebrate tissues. It appears to be always present in marine animals. Plankton are especially rich in lithium, and its presence in other marine animals is presumably a reflection of this fact. With the possible exception of plankton it is doubtful whether this metal can be regarded as an essential element.

Rubidium is widely, but not universally, distributed in nature. According to Boyd and De (1933) rubidium is commonly present in the organs of the human body. Lundegardh (1934) reports an average value of 14 p.p.m. in the fresh liver of both sexes. Its presence in plant ash, particularly in the seeds of *Hevea braziliensis* from Malaya, has been detected by Ramage (1929) who also reported that fungi not infrequently contain a very large amount of rubidium, sometimes as much as 2 per cent. of the dry matter. Wright and Papish (1929) and Blumberg and Rask (1933) report its presence in human milk

and regard this as indicating that it may be of physiological importance. The average amount of rubidium in the bodies of people dying from congental pyloric stenosis is stated by the same authors to be much higher than in normal tissues, which fact they regard as indicating that it may play some part in muscle metabolism. In specimens of snails and earthworms obtained in Cambridge and London it was found to be absent, whereas it was present in specimens from Liverpool and Marlborough. Rubidium cannot be said therefore to be of universal importance. Its presence may be merely a reflection of its fairly wide distribution in soils and consequently in the herbage and foodstuffs.

Caesium is far less widely distributed in soils than rubidium. Although it is readily absorbed when present, its occurrence in animal tissues is rare. It has been detected in plant ash (Robinson 1918). It is present in sea water, and has been detected in oyster shells. There is no evidence so far that caesium is of biochemical importance.

COBALT AND NICKEL.

Cobalt and nickel although fairly widely distributed in small amounts in soils appear to be of somewhat restricted occurrence in plants and animals. Small quantities of cobalt and nickel occur in the soils of Kentucky, and McHargue (1925) detected their presence in all plants growing under natural conditions in these soils. Berg (1925) has also recorded their presence in foodstuffs and excreta. However Boyd and De (1933) working in India failed to find by spectrographic means any trace of these metals in the whole range of foodstuffs and human organs which they examined. Du Toit and Zbinden (1930) on the other hand noted their presence in human pancreas with traces in other organs but none in the liver. Ramage (1933) frequently found considerable quantities of nickel in tropical plants. Newell and McCollum (1931) occasionally found nickel in marine products and Mueller (1936) detected the presence of nickel and cobalt in human gallstones, and nickel also in the ash of human bladder bile, but not cobalt. Thus it would appear that nickel and cobalt are not universally distributed in nature as are copper, manganese and zinc. The selectivity exercised by certain organisms for these two metals is strikingly illustrated (Fox and Ramage, 1931) by the fact that *Archidoris tuberculata* contains appreciable quantities of cobalt but no nickel, whereas *Haliotis* has a high nickel content and no cobalt. Webb (1937) finds these two metals present in relatively large quantities in *Pleurobranchus*, a tectibranch mollusc.

With regard to the possible function of cobalt and nickel in nutrition, the evidence is scanty. Truffaut (1926) records the results of experiments which show that both cobalt and nickel stimulate bacterial activity with resultant solubilisation of the slightly soluble

food complexes of the soil. Konishi and Tsuge (1936) have found both metals in the underground parts of certain leguminous plants, particularly in the nodules, and suggest that they play an active part in the process of symbiotic nitrogen fixation. Ulloa (1936) claims to have found that cobalt influences beneficially the formation of red cells in the rabbit, and Beard and Andes (1934) also have shown that .15-.3 mg. of cobalt produced polycythemia in rats, with no change in the amount of hemoglobin. Josland (1936) has also produced intense polycythemia and loss of body weight in rats within seven weeks by addition of cobalt sulphate to the diet. Storage was low in the kidney as compared with relatively high storage in the liver. Canjolle and Lafitte (1937) find that the metal is deposited mainly in the kidney and pancreas following intravenous and intramuscular injection in dogs. Orten (1936) has recently reported that both oral and subcutaneous administration of cobalt to young and adult rats produces an increase in the proportion of reticulocytes in the blood and increases the concentration of bilirubin in the serum.

During the last few years attention has been focussed on the work which has been carried out in New Zealand by Askew, Dickson, Denham and others. These workers made the very interesting observation that cobalt chloride as a dench was completely effective both as a preventive and a cure in the control of lamb-sickness at Mortain Mains and other places in the South Island of New Zealand. Post mortem examination of the animals showed that the sickness was associated with thin blood of poor supply, soft breast bones and liquid in the abdominal cavity. They found that drenches made from acid extracts of soil from the regions where the disease does not occur were also effective, and that these extracts contained more cobalt than those from the areas where the disease was prevalent. Supplements of iron, copper and nickel were not helpful. This suggested that cobalt had a haematopoietic action, but subsequent work has shown that certain other elements, for example arsenic, were also capable of curing bush-sickness in individual animals. Zinc also comes into the picture, for it has been found that the zinc content of testes of rams from bush-sick areas ranged from nil to 44 p.p.m. of dry tissue, as against from 64 to 81 p.p.m. for rams from healthy areas. The liver of a bush-sick sheep contained 141 p.p.m. of zinc in the dry tissue, as compared with 255 p.p.m. in the liver of a healthy sheep from the Wellington district. Whether or not this deficiency of zinc is of importance or not is not known for certain.

It will be seen therefore that there is no clear evidence so far available to show that either nickel or cobalt are necessary for nutrition. That they may be of importance to certain species of organisms cannot be denied, and it would appear very probable that they both possess a degree of interchangeability both with each other and with some other essential elements.

Further light on this subject has recently come from America where Neal and Ahman (1937) in controlled experiments with calves on a spectrographically cobalt-free ration of Natal grass hay, shelled corn and dried skim milk from Florida soil were able to produce a state of malnutrition which was corrected by a cobalt supplement. These authors are of the opinion that cobalt is definitely essential for the nutrition of calves.

TIN.

Tin cannot be said to be of widespread occurrence in soils. No great amount of work has been done concerning its distribution in plants, but its occasional occurrence in Indian foodstuffs has been noted. Webb 1937 reports that tin is abundant in *Aeolidia* and in the Echinoderms. Bertram and Ciurea have reported its presence in the organs of oxen, horses and sheep, being present in greatest amount in pancreas. In human beings Du Toit and Zbinden by spectographic analysis showed it to be present in all organs particularly in brain, spleen and thyroid. Boyd and De also by spectrogràphic means demonstrated its presence in pancreas, kidney, liver and spleen but failed to find it in muscle, brain and heart. It is a constant constituent of cow and human milk, and is present in tooth pulp and salivary glands and particularly in the mucous membrane of the tongue. Information concerning this metal is too scanty to permit any conclusions to be drawn. In human beings its presence may arise to some extent from the widespread use of tinned vessels. While the amounts arising from the use of tinned iron in the canning industry are probably quite small tinned kettles and tinned baking tins more especially if the latter are frequently cleaned with glass paper may be expected to contribute larger amounts.

TITANIUM.

Titanium is widely distributed in small amounts in soils. Berg (1925) has recorded its presence in foods and excreta. Its occasional presence in marine animals has been detected spectroscopically by Newell and McCollum (1931). Zbinden (1931) found it to be a constant constituent of cow and human milk. Its presence in human tissues and in human milk has also been recorded by Blumberg and Rask (1933). According to Maillard and Ettori it is found in all organs of the human body in quantities ranging between 1.5 and 10 gamma per 100 gm. Drea (1935) has shown that the element readily passes from the feed or water into the hen's blood, into the egg, and finally into all of the chick's tissues and blood. Konishi and Tsuge (1936) record its presence in leguminous plants, where it was more concentrated in the root nodules. According to these authors optimum concentrations of titanium salts increase the number of nodules and promote a greater fixation of nitrogen in alfalfa grown on agar media and on soil. There is no evidence so far to hand that titanium performs any specific function in the animal organism.

GOLD AND SILVER.

Silver is not of widespread occurrence in nature, which is no doubt due to the insolubility of its chloride. Nevertheless Du Toit and Zbinden (1930) found that it was a very frequent constituent of human milk and organs, being derived in all probability from metallic sources such as table cutlery and dental alloys. It appeared to be concentrated chiefly in the uterus, ovaries and thyroid, the heart, kidneys and spleen containing only traces. Newell and McCollum (1931) have frequently detected its presence in marine products, and Boyd and De (1933) have detected its presence spectrographically in Indian plants with certain exceptions. Its presence in tooth pulp and in the salivary glands has been demonstrated by Jost (1934) who was unable to show however that any relation existed between the occurrence of the metal and the condition of the teeth. Strangely enough Ramage (1929) has recorded its unfailing presence in English and South African edible fungi, often in remarkable amounts—up to 0.2 per cent. of the dry matter. Sheldon and Ramage (1931) have confirmed the findings of Du Toit and Zbinden and noted that the thyroid gland and tonsils contain notable amounts of silver.

Gold is of less frequent occurrence than silver though it is common knowledge that it occurs in sea water. Recently however it has been found by Nemec (1936) in plants growing in certain localities in Czecho-Slovakia. The soil from these areas is known to contain gold to the extent of a tenth of a gram per ton—approximately one part in ten million. The ash of plants growing in this auriferous soil contains up to six thousand times as much gold as the soil itself. The gold is accumulated principally in the seeds and fruit, certain plants being apparently more efficient collectors of the precious metal than others. For example, *Zea Mays* fruit contained only 1.5—2.0 p.p.m. in the ash whereas the fruit of *Clematis alba* was found to contain about 600 p.p.m. Recognisable amounts of gold were also found in plants from other places in Czecho-Slovakia where gold was known to occur, but none was found in the same species grown where gold was known to be absent. Some interest attaches to the fact that some of this gold has actually been isolated by reduction and fusion into a small ingot.

SELENIUM.

Another element on which considerable attention has been focussed during the last two or three years is selenium. This element, well known for its photo-chemical property, closely resembles sulphur in some of its chemical properties, but differing from sulphur by reason of its extreme toxicity to animals. For many years certain areas in the U.S.A. have been known to produce a herbage which is extremely harmful to grazing stock. It has been found recently that the toxic principle is selenium and that certain plants accumulate much greater

stores of this poisonous element than others. In normal times the cattle are able to detect some disagreeable quality in the more poisonous herbage, but in times of drought the wretched beasts under pressure of starvation resort to the poisonous herbage with usually fatal results. Heavy applications of sulphur to the soils of these areas have been found to have an ameliorating effect, the sulphur being taken up by the plants preferentially.

SUMMARY.

Present knowledge of the occurrence, distribution and biochemical importance of copper, manganese, zinc, cadmium, bromine, fluorine, aluminium, lithium, rubidium, caesium, cobalt, nickel, tin, titanium, gold, silver and selenium in plant and animal tissues is reviewed and discussed. One hundred and seventy references are given.

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PASSING THE RYLE'S TUBE IN FRACTIONAL TEST-MEALS.

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In the course of performing a few hundred fractional test meals, the writer found that the passage of the Ryle's tube occasioned considerable difficulty in certain cases; the difficluty lay mainly in the initial passage of the tube through the fauces and oral pharynx—a procedure which, in spite of the customary precautions taken, often invoked a good deal of coughing, retching or actual vomiting in sensitive patients or those with an "irritable throat" e.g. smokers, etc. In such cases anaesthetising the throat was naturally resorted to, but, in spite of this, failures were not uncommon; moreover patients, as a rule, disliked the procedure which often caused excessive salivation.

As an alternative the nasal route was employed and it was surprising to note how easily the tube slipped down by this route, the patient being asked to swallow as soon as the tube reached the oral pharynx, otherwise it might coil out through the mouth. The writer has since demonstrated again and again to his satisfaction the successfulness of the nasal route when the oral route had failed repeatedly.

The advantages of the nasal method are as follows:—

1. Passage of the tube causes much less irritation because it descends behind the fauces and parallel to the posterior pharyngeal wall.
2. Excessive salivation due to presence of tube in mouth or repeated unsuccessful attempts at swallowing the tube by the mouth is eliminated; swallowing large amounts of saliva will naturally upset the results of the test-meal.
3. Patient can spit out saliva without disturbing the position of the tube.
4. Patient finds it easier to swallow the oatmeal in the absence of a tube in the mouth.
5. Speech is not encumbered by the presence of a tube in the mouth, a comfort to the patient.
6. One attempt is usually successful; hence a great saving of time on the part of the clinician and much less discomfort for the patient.

The only contra-indications to the nasal route are nasal obstruction and hypersensitive mucous membranes.

The writer feels that it may not be out of place to point out the practicability and usefulness of this method and would plead for its more general use.

Review of Books

"*Surface and Radiological Anatomy.*" By A. B. Appleton, W. J. Hamilton and I. C. C. Tchaperoff. 1937 Edition, Publisher, Hecer, Cambridge. Price, 15/- nett.

This book is specially addressed to the student during his period of clinical study and to the practitioner. It is easy to conceive a great sphere of usefulness to eiher because it contains many a useful reminder as well as a mass of facts that any practitioner may welcome as a fresh exposition.

The book is well printed and the index is good. Illustration by diagrams, photographs and radiographs is lavish; indeed, exclusive of preface and index, 338 illustrations are included in 298 pages of text.

The reproduction of photographs and radiographs alike is excellent. The radiographs are uniformly "negatives" as the clinical observer and the radiologist are accustomed to see them.

In the Introduction are found notes on varying types of body physique and some technical notes on radiology, which though elementary are informative. Unexpected notes are those on skin sensation, referred pain and muscle action.

The authors evidently seek to put before the reader a mass of concise information such as may be gleaned under ordinary clinical conditions from surface and X-ray examination of the body, and to point the way to a scientific analysis of the findings. The subject matter is treated on a regional basis. The upper limb, the chest and back, the abdomen, the head and neck, the vertebral column and the lower limb are dealt with in that order.

In the chapter on the upper limb are found first an excellent photograph of the shoulder and the base of the neck clearly annotated. Next are found, side by side, a drawing of a dissection and a photograph of the scapular region—the dissection and the photograph being in exactly the same position and from exactly the same view point. The idea is most strongly to be commended—the exposition of the surface features with an exact analysis based upan anatomical findings.

Next come radiographs of the shoulder region in various positions of the limb and at various ages, to show the varying positions of the joints as well as the condition of the epiphyses at different ages.

The elbow, forearm and hand are similarly dealt with by photograph and radiograph. The elbow region receives peculiarly careful attention, but all the joints become the subjects of radiographical study.

Facts of a more purely anatomical nature such as the course and position of the nerves and arteries as well as the lymph glands and lymph vessels are presented by surface projections upon excellent photographs.

The chapter on the Chest and Back contains some twenty pages which are mostly devoted to definitions and to generalities which precede the radiological examination of the thorax.

The anatomical explanation of the different shadows met with in radiographs of the chest is original, vigorous and admirable.

Anatomical analysis is not confined to antero-posterior views but to radiographs in oblique planes designed for the examination of the aortic arch and the posterior mediastinum.

The radiography of the heart is fully presented. Radiographs of the lungs are shown and shadows of the bronchial tree are interpreted by lipoidol and normal radiographs side by side. Unexpected but welcome notes include notice of the azygos lobe, of the normal oesophagus made visible by barium and there is a note even on oesophagoscopy.

The chapter on the abdomen opens with accounts of the anatomical structure of the abdominal wall, of surface anatomy and some useful memoranda. An account that follows of the surface examination of the abdomen by percussion has a practical value which must be rather debatable.

The radiigraphy of the stomach, duodenum and the whole intestinal tract is admirably presented. Even gastroscopy and proctoscopy receive notice though in the second case, being now expectant of the most complete exposition one is moved to regret the absence of illustration. Radiography of liver by the method of pneumo-peritoneum and the use of iodophthalein for demonstration of the gall bladder are both illustrated.

The radiography of the urinary tract is dealt with at length. The pelvic viscera form the subject matter of useful anatomical notes and the methods of demonstration of the pelvic organs by radiological means are fully explained.

The chapter on the Head and Neck contains some most varied information quite apart from radiography. Here are reviewed the age changes of the skull as well as the surface anatomy of the whole head and neck. The clinical examination of the eye, the nose, the mouth and larynx is illustrated by numerous drawings which picture the findings when these organs and regions are examined by the instruments appropriate for the purpose—the laryngoscope, the ophthalmoscope and the like.

Many purely anatomical notes are to be found in addition on the organs mentioned and on the nerves, the arteries, the veins and the lymphatics. A more than usually complete account is given of the superficial veins, the diploic veins and the venous sinuses with an account of their intercommunications and clinical importance.

The section on radiology includes descriptions of the methods by which radiographs of all the various air sinuses of the skull may be made. Of course the radiology and the anatomy of the sella turcica receives special attention. Demonstration of the ventricles of the brain by thorotrast and by air injection is described, as well as the radiography of the salivary ducts.

The vertebral column receives rather less attention than was hoped for in comparison with the full description of other regions.

The lower limb is described on similar lines to the upper limb, and again the analytical method of placing photographs side by side with dissections is used with great effect.

The radiology of all the joints of the limb, hip, knee, ankle and foot are very fully dealt with.

The book ends with useful appendices such as Tables of ossification, prenatal postnatal and later, and also a table of the segmental innervation of muscles.

This volume must be regarded as a piece of "team work" on the part of the Anatomy Department of the Medical School of St. Thomas' Hospital with the collaboration of the X-ray Department of the same Hospital. The result is most successful and should be a source of gratification to the Medical School and to the authors who are most heartily to be congratulated.

If a moral for the teacher and for those who frame the medical curricluum may be drawn from this work, it is that the interpretation of normal radiological appearances and the teaching of surface anatomy of the living body should be presented to the student during the period of his study of anatomy in the dissecting room. Though we may have to wait long for this to become an established custom, it is an ideal to which the teacher should strive.

Acknowledgements

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