THE CHANGING INCIDENCE AND MORTALITY OF INFECTIOUS DISEASE IN RELATION TO CHANGED TRENDS IN NUTRITION

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During the past century there has been a general downward trend in the incidence and mortality rates of infectious diseases, notably tuberculosis, pneumonia, diphtheria, scarlet fever, whooping cough, rheumatic fever, typhoid fever, and erysipelas; also a similar decline in puerperal and infant deaths. During the same time there has been a marked shift in the age incidence of a number of infectious diseases from infant to older age groups and a marked general reduction in the case-fatality rates.

The usual explanation offered for this changed trend in disease has been the forward march of medicine in prophylaxis, therapy, and public-health protective measures; but, from a study of the literature it is evident that epidemiologists generally recognize that these changes in incidence and mortality have been neither synchronous with, nor proportionate to such measures.

Considering each disease separately, evidence regarding the changed trend will be given, and in the discussion following an attempt will be made to track down the unidentified prophylactic factor, which the author believes to be nutritional, and fit it into the picture of each disease.

Tuberculosis

Tuberculosis, formerly known as the "Great White Plague", consumption or phthisis, was responsible for the death of one-fifth of all mankind in western Europe at the beginning of the 19th century. In London the rate was even higher—30 percent. At that time the yearly death rate from this disease in western Europe has been estimated at 1,000 per 100,000 population. From 1812 to 1840 the death rate from tuberculosis in the American cities of Boston, Philadelphia and New York was about 400 per 100,000, while in Budapest in 1874 the rate was double this amount.

During the past century there has been a consistently steady reduction in mortality from tuberculosis until at present the rate in England is 69, in Canada 45.8, and in the United States 41.3 per 100,000. The orderly rate of this reduction may be seen by reference to Table 1, from Pringle (1),

TABLE 1

Yearly average tuberculosis death rates per 100,000 in city of Ipswich, England, in ten year periods, 1840-1940

Decennia	*Males*	*Females*	*Both Sexes*
1841-1850	389	399	393
1851-1860	327	350	340
1861-1870	339	320	329
1871-1880	321	292	305
1881-1890	279	257	268
1891-1900	243	195	217
1901-1910	212	158	183
1911-1920	168	135	151
1921-1930	117	86	100
1931-1940	76	63	69

which shows a decline in death rate from tuberculosis in the city of Ipswich, England, during the past 100 years (1841 to 1940) from 399 to 69 per 100,000. These figures, indicating an almost even decline throughout the century, are closely parallel to the figures for a corresponding period in Massachusetts, in which a reduction of mortality from 444 to 36 per 100,000 occurred between 1859 and 1939. At the middle of this period the rate had declined to 254, and previous and subsequent to this date the decline followed an almost even grade.

A noticeable feature of the mortality trend of this disease has been a shift in the age incidence. Forty years ago the peak for males fell in the third decade of life. It now falls in the 50-to-60-year-age group. The rate for the under-5-year group has also shown a disproportionately greater reduction. The under-1-year mortality rate for tuberculosis dropped from 1000 to 645 per 100,000 living between 1868 and 1900. In this same age group, from 1900 to 1932, the rate fell to 39. Apparently tuberculosis is increasingly becoming a disease of older age groups.

During and following the First World War and the recent Second World War, there has been a sharp rise in the incidence and mortality from tuberculosis in Europe, particularly in the countries most involved. According to *Time* (Apr. 14, 1947), tuberculosis, on the rise for the first time in a century, is now Europe's No. 1 killer. Germany, which formerly had one of the world's lowest T. B. death rates, now has one of the highest. In Berlin alone, 150 deaths and 400 new cases are reported weekly. The U. S. occupation zone has 117,983 T. B. cases. In Poland the monthly T. B. death rate is estimated at 18,000, mostly children. In Greece there are 150,000 severe cases with only 5,000 T. B. hospital beds. Roumania, with a population of 16,500,000, has 600,000 T. B. cases. Yugoslavia has an estimated 157,000 cases.

Pneumonia

At the beginning of the present century pneumonia stood ahead of tuberculosis as a cause of death. At that time the famous Osler referred to this disease as "the old peoples' friend", because it took so many of the aged at a time when life became burdensome. During the last half century there has been a steady decline in mortality from this disease, with the exception of the up-surge in 1918 to 1920 as a result of the post-war influenza pandemic. Since 1900 the yearly death rates for pneumonia in the United States, per 100,000, at five-year intervals, were as follows: 1900-202.2, 1905-169.3, 1910-155.9, 1920-207.3, (influenza pandemic), 1925-121.7, 1930-102.5, 1935-104.2, 1940-70.3, 1944-48.6. A closely similar decline in mortality from this disease has occurred in Canada.

Diphtheria

Prior to the present century, diphtheria, known

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also as malignant angina, membranous croup, angina suffocans, garotilla, etc., was the major scourge of infancy and childhood. Following the Napoleonic wars, intensive epidemics occurred in England, France and other European countries. The virulence of these outbreaks was so great that frequently whole families were wiped out. In one French family of seventeen there were thirteen deaths in one epidemic. The case-fatality rates in these early times were very heavy. In 39 epidemics, from 1557 to 1805, an average rate of 80 percent has been reported (Ozanam). From 1805 to 1830 the case-fatality rate has been estimated at 25 percent (Academie Royale de Medicine). At present the case-fatality rate in Ontario is approximately 10 percent.

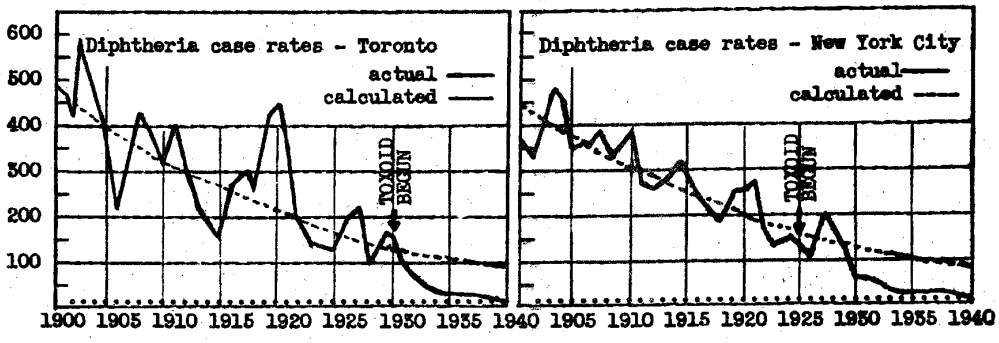
The modern trend of this disease is shown by reference to the mortality records of the city of Toronto which go back to 1885. The average yearly deaths per 100,000, for consecutive ten-year periods (1886 to 1945, inclusive), were as follows: 132.0, 66.0, 34.5, 19.7, 8.2, 0.3. The diphtheria death rates for the United States follow a closely similar trend, the figures being as follows: 1900-40.3, 1910-21.1, 1920-15.3, 1930-4.9, 1940-1.1, 1944-0.9. These figures clearly show a consistently steady reduction in mortality which began over sixty years ago.

Recently, however, there has been a war-time increase in the incidence of diphtheria in both Europe and America. In Halifax, N. S., in 1940, there was an epidemic of considerable intensity involving both the civilian and military population of the city. There were 891 cases in all,—588 civilians and 303 in the armed forces. An unusual feature of this outbreak was the high proportion of adults affected, 69.2 percent of the cases being over fifteen years of age. In Ottawa, Ontario, in the fifteen months prior to November, 1946, there were 204 cases of diphtheria and 32 deaths, including a number of non-residents who were treated in the city, thus indicating a case-fatality rate of 16 percent.

A similar war-time increase in diphtheria has been noted in the United States. According to *Health News*, Aug. 19, 1946, "the increase in diphtheria morbidity and mortality in upstate New York, which began in 1945, has continued in 1946, with 231 cases and 21 deaths being reported this year, the highest since 1934." Baltimore also has had a steady increase in diphtheria since 1941, reaching epidemic proportions in 1944 with 142 cases and 9 deaths.

Recent reports from Europe also indicate that the war-time and post-war incidence of diphtheria has assumed almost pestilential proportions, being very virulent with a high case-fatality rate. In 1943 about 630,000 cases were reported in European countries in which records were available. Including countries in which records were not available, it may reasonably be assumed that there were fully 1,000,000 cases in that year, with about 50,000 deaths. In the years 1944 and 1945, with European conditions even more chaotic, it has been estimated that the toll of 1943 has been maintained.

DIPHTHERIA - CASE RATES PER 100,000, TORONTO, CANADA, AND NEW YORK CITY, 1900-/40



Scarlet Fever

The mortality rates for scarlet fever have been on a steady decline since before the beginning of the present century. The trend of this disease is shown by the average yearly death rates per 100,000 in the cities of Toronto and Montreal for consecutive five-year periods from 1890 to 1945, which are respectively as follows: 36.6 and 66.0, 18.8 and 15.4, 24.7 and 35.8, 12.8 and 11.6, 17.9 and 22.2, 4.4 and 8.4, 5.7 and 12.8, 1.9 and 6.8, 1.5 and 3.6, 2.2 and 2.5, 0.5 and 0.4. The mortality decline for this disease in the United States has been very similar, the rates per 100,000 being as follows: 1900-9.6, 1910-11.4, 1920-4.6, 1930-1.9, 1940-0.5, 1944-0.3.

The case-fatality rate for this disease has also declined greatly in this same period. In the city of Toronto, prior to 1900, the case-fatality rate varied from 10 percent to 20 percent. This rate has gradually declined until during the last ten years it has varied from ¼ percent to 1 percent. A similar decline has occurred in the Province of Ontario as a whole.

Whooping Cough

The mortality rates for whooping cough have also shown a gradual decline since before the turn of the century. The average annual death rates per 100,000, for consecutive five-year periods from 1895 to 1945, in the city of Montreal, were as follows: 32.4, 30.6, 19.6, 21.2, 20.4, 14.7, 12.3, 8.8, 6.8, and 4.2. The rates in other large cities throughout Canada and the United States have shown a similar trend.

Rheumatic Fever

The declining mortality from this disease in the United States and Canada is well shown by the statistics of the Metropolitan Life Insurance Company (Table 2) in which the average yearly death rates per 100,000 for consecutive five-year periods from 1910 to 1945 are as follows: 6.7, 4.8, 4.6, 3.5, 3.4, 2.5, 1.7. The average yearly death rates for rheumatic fever in the city of New York, for consecutive five-year periods from 1900 to 1945 are as follows: 8.2, 9.1, 6.2, 4.3, 3.8, 4.6, 3.6, 2.1, 1.3.

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TABLE 2

Five year averages of annual death rates from infectious diseases—white children ages 1 to 14 years, Metropolitan Life Ins. Co., Industrial Department, 1911 to 1945

Cause of Death	Average Death Rates per 100,000							Percent Change 1941-1945 Since 1911-1915
	1941-1945	1936-1940	1931-1935	1926-1930	1921-1925	1916-1920	1911-1915	
Measles	1.9	2.7	6.2	11.3	14.0	23.9	26.8	—92.9
Scarlet Fever	1.1	3.5	7.8	7.4	12.8	12.6	28.5	—96.0
Whooping Cough	1.5	2.5	4.5	8.1	9.7	16.8	15.9	—90.3
Diphtheria	2.5	4.7	8.9	24.1	45.9	61.2	75.1	—96.6
Tuberculosis—all forms	4.7	6.1	9.9	16.0	20.9	36.5	46.6	—89.2
Acute Poliomyelitis	1.8	1.3	2.9	2.6	2.9	9.8	3.8	—52.2
Acute Rheumatic Fever	1.7	2.5	3.4	3.5	4.6	4.8	6.6	—74.3
Pneumonia-Influenza	14.3	27.1	40.8	59.4	64.3	151.1	85.7	—83.3
Diarrhea and Enteritis	3.1	5.4	9.6	19.2	27.6	49.2	60.9	—94.8
Appendicitis	5.1	9.4	11.5	11.9	11.3	9.8	10.0	—49.6

TABLE 4

Five-year averages of annual maternal death rates, puerperal causes, in Canada, by Provinces, per 1000 live births.

Years	P.E.I.	N.S.	N.B.	Que.	Ont.	Man.	Sask.	Alta.	B.C.
1921-1925	4.5	5.8	5.0	3.9	5.4	5.3	5.9	6.2	6
1926-1930	4.7	5.5	6.2	5.2	5.8	5.6	5.9	6.6	6
1931-1935	5.3	5.1	5.4	5.1	5.3	4.3	4.5	4.5	5
1936-1940	4.8	4.0	4.9	5.1	4.5	5.0	3.6	4.5	3
1941-1945	3.9	2.7	3.2	3.3	2.5	2.6	2.8	2.4	2
1945 alone	2.7	1.5	1.8	2.4	2.2	1.9	2.4	2.3	2

Typhoid Fever

The mortality rates from typhoid and paratyphoid fever have also steadily declined since before the turn of the century. The modern trend of this disease is shown by the average yearly death rates per 100,000, for consecutive ten-year periods, from 1885 to 1945, in the cities of Toronto, Montreal and New York, which are respectively as follows: 54.4, 32.3, 22.1; 19.8, 28.7, 17.7; 19.2, 29.9, 11.0; 2.8, 12.0, 2.9; 0.7, 11.1, 1.1; 0.1, 1.3, 0.2. (Table 3).

TABLE 3

Ten year averages of annual death rates from typhoid and paratyphoid fever per 100,000, in Toronto and Montreal, Canada, and New York City

Decennia	*Toronto*	*Montreal*	*New York City*
1886-1895	54.4	32.3	22.1
1896-1905	19.8	28.7	17.7
1906-1915	19.2	29.9	11.0
1916-1925	2.8	12.0	2.9
1926-1935	0.7	11.1	1.1
1936-1945	0.1	1.3	0.2

The case-fatality rate of this disease has also markedly declined, from about 20 percent prior to 1900 to about 5 percent at the present time.

Erysipelas

The mortality rates for erysipelas have steadily declined since 1880. The average yearly death rates per 100,000 for this disease, for consecutive five-year periods from 1880 to 1945, in the city of Montreal, are as follows: 12.0, 9.6, 6.3, 6.5, 5.2, 5.2, 5.0, 4.1, 3.1, 4.2, 3.5, 1.6, 0.5. A similar decline for this disease has been recorded in other large cities of Canada and the United States.

Puerperal Disease

Maternal deaths have been on the decline in Canada since 1921, beyond which time the records are incomplete. The death rates for puerperal disease in all nine Provinces of Canada in this 25-year period indicate an average decline from a rate of approximately 5.3 in 1921 to 2.3 in 1945. (Table 4). A very similar trend has been in evidence in the United States.

Infant Mortality

Infant mortality, under one year, has shown a steady reduction in Canada and United States since the beginning of the century. The death rates, under one year, per thousand living births, in the city of Montreal, based on the yearly average of consecutive five-year periods from 1900 to 1945, are as follows: 274.7, 268.6, 220.2, 183.0, 160.6, 126.8, 105.9, 83.0, 64.5, 61.2 (1945 alone). The infant death rates in other large American cities show a very similar trend.

Discussion

From a cursory examination of the above data it is quite obvious that there has been a general decline in mortality from practically all the common infectious diseases both before and since the beginning of the present century. There are doubtless a number of factors which may have contributed to this regression,—better nutrition and hygiene, particularly in the younger age groups, improved medical therapy, artificial immunization, and public-health measures such as quarantine, pasteurization of milk, chlorination and filtration of municipal water supplies, etc.

Regarding tuberculosis: the advent of sanitarium treatment, with the segregation of a considerable number of active cases, and the more recent mass x-ray surveys for the early detection of otherwise unrecognized cases, have saved and will save many fatalities from this disease. The fact remains, however, that this disease was definitely on the decline in both Europe and America long before any of these control measures were instituted, indeed even long before Koch's discovery of the specific etiological organism in 1882. Furthermore, the rate of mortality decline was practically as rapid before as since the adoption of these controls. Commenting on this orderly decline, Ross (2) says: "While the control measures which have been applied have possibly accentuated the decline in young adult life and influenced through public-health education all age groups, it seems reasonable to attribute the general decline to other factors, more general in character and of which but little is really known." In support of this statement Ross compares the tuberculosis mortality figures of Mexico City with those of Ontario, showing that the decline in the former has been more rapid than in the latter, in spite of the fact that "Mexico City had no sanatoria, no diagnostic clinics, no anti-tuberculosis movement."

On this same subject McKinnon (3) says: "Quite obviously, then, all the factors mentioned are not

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adequate in themselves to explain the recorded decline. Some other factor or factors must have been operating during this period and it is necessary to cast farther afield in search of them."

Regarding the general decline in tuberculosis mortality Davis (4) says: "Is it that we are effecting more cures? Yes, we are effecting more apparently arrested cases, . . . Do you think that alone accounts for the drop in the death rate? Without hesitating the answer is no—the figures are nowhere near commensurate. Can it be due to our methods of diagnosis? To some extent—yes. Does this account alone for the drop in the death rate? Again the answer is no. Can it be that we have developed more resistance to the disease? Yes, it could be, . . ."

In the epidemiological history of diphtheria we have a somewhat similar picture to that of tuberculosis. The decline in mortality was well under way long before the end of the last century, and has continued on an almost even grade until, during the last decade, it has approached the vanishing point. At the beginning of the century anti-toxin came into general use, and later (1930) artificial immunization by toxoid was adopted by the health departments of many of our large urban centers. By reference to the accompanying charts of the case rates of diphtheria in New York City and Toronto, Canada, the general decline in incidence is shown with an apparent accentuation of same following the introduction of toxoid immunization in these cities, which began in New York in 1925 and in Toronto in 1930. These graphs show one marked up-surge in New York shortly following the adoption of toxoiding which corresponds in timing with a similar upward fluctuation in Toronto before toxoiding was begun. In fact the deviations from the calculated base line of incidence in both cities, all through the 40-year period, show a striking parallel. From 1930 to 1940 the decline has been apparently more free from upward fluctuations in both cities, and this has been cited as evidence of the effect of immunization; but, from present indications, when the graph is completed to date, a disturbing upward fluctuation will be noted within the last few years. In a number of centers in the United States and Canada serious outbreaks of diphtheria have recently been reported, to say nothing of the major up-surge in Europe. In the United States as a whole there was approximately a 30 percent increase in incidence in 1945. In upstate New York, Baltimore, Halifax, N. S. and Ottawa, Ont., outbreaks of epidemic proportion have been reported. A disquieting feature of these outbreaks has been the development of a considerable number of cases in supposedly immunized subjects, and the marked invasion of adult age groups. In the Halifax epidemic (5), 66 of the cases admitted to hospitals had previously received one or more doses of toxoid or antitoxin or were Schick negative. Fifteen cases developed in persons supposedly immune by Schick test. Of these, 9 cases developed in less than three months from the time the test was made, while the remaining 6 had been negative a year or more previously. Five cases had received antitoxin within two months previously. In the Ottawa epidemic (6), of 99 cases under fifteen years of age, 36 were found to have previously received three doses of toxoid. One of 25 cases in adults had been toxoided in the army. In the Baltimore outbreak of 1944 (7), 63 percent of all cases had a record or history of prior toxoid inoculation. Of the fatal and malignant ("Bull-neck") cases 77.8 percent, and 61.8 percent of the remaining milder cases had previously been toxoided. Since the number of the pre-school and school-age children of Baltimore who had been toxoided was estimated at 75 percent, the ratio of incidence in the toxoided and non-toxoided groups was about even, with the malignant cases showing a selectivity for the toxoided group. Commenting on these findings the authors of the report say: "This may be a reflection of the increasing amount of inoculation being done in Baltimore, but it is by no means certain that this is the only factor involved".

Thus it would appear that, with the exception of the recent post-war increase in Europe and America, the decline in diphtheria mortality has generally followed a rather even course during the past sixty years or more, with up and down fluctuations prior and subsequent to the adoption of artificial immunization. The protective efficacy of the latter seems to be adversely reflected in the reports of the Halifax, Ottawa and Baltimore epidemics of the last few years. The present trend in this as in other infectious diseases seems to be toward a shift in age incidence from the younger to older age groups.

Regarding pneumonia, it will be seen by the statistical data previously presented that the decreased mortality has followed a fairly even grade, with the exception of the 1920 up-surge which was incidental to the post-war influenza pandemic. The decline was almost as rapid prior to as following the introduction of chemotherapy, which has been the only factor likely to have materially influenced the epidemiology of this disease.

Regarding typhoid fever, this enteric infectious disease, which has generally been thought to be propagated by pollution of drinking water or milk, has been on a steady decline in mortality since 1885. No one can question the favourable influence of water chlorination and milk pasteurization on the incidence of this disease; but, strange to say, the decline in mortality and case-fatality rates had begun long before the adoption of either of these control measures. This would seem to indicate, as with the diseases previously discussed, the operation of some major unidentified prophylactic factor.

Regarding the other infectious diseases listed—scarlet fever, whooping cough, rheumatic fever and erysipelas—these, as shown in the previous statistical data, have all exhibited a steady decline in mortality and case-fatality rates since before the turn of the century, although no specific control measures have been generally applicable. In recent years, however, artificial immunization for scarlet fever and whooping cough has been given a limited trial.

Regarding maternal and infant mortality (under one year): these, as previously indicated, have also shown a steady decline in keeping with that of the infectious diseases, although no specific control measures have been applicable, thus indicating the possible influence of the same unidentified prophylactic factor.

The Author's Hypothesis

From the foregoing it is clearly apparent that some unidentified major prophylactic factor or factors, general in application, must have been operating in bringing about such a uniformity in reduced mortality from so many infectious diseases in the same period of time. The fact that the decline has followed practically the same pattern in diseases

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such as scarlet fever, rheumatic fever, whooping cough, measles, erysipelas, diarrhea and enteritis, and even appendicitis (Table 2), in which no specific control measures have been applicable as in tuberculosis and diphtheria, points significantly to the over-all nature of the prophylaxis. The most logical explanation would seem to be that resistance to infection in general has been increased gradually throughout the past century, particularly in the younger age groups, and that the major factor in producing this result is most likely to have been some changed trend in nutrition. On this basis, artificial control measures, which have been applied mostly within the last two decades, have played a minor or supplemental role.

The major change in nutrition in this period has been brought about by the tremendous increase in the production, distribution and consumption of citrus and other vitamin-C containing fruits in North America and most of Europe, made possible by the gradual development of better transportation throughout the century—steamships, railways, and motor highways. Prior to 100 years ago, ocean transport by sailing ships and lack of refrigeration made practically impossible the import by the United Kingdom of citrus and other fresh fruits from Mediterranean ports or North Africa. With the advent of steamships and railways, imports of these fruits to England and other Northern European countries gradually increased from Spain, Algiers and the Middle East. The citrus fruit industry began in America in 1886, at which time the annual U. S. production amounted to nearly 3,361,000 bushels. The production has gradually increased (more rapidly in the last two decades) until in 1944 the total amounted to 278,369,600 bushels. The production of canned citrus juices began in U.S.A. in 1929, in which year the total pack was 6,150,000 lbs. By 1945 the annual output had reached a total of 1,738,170,000 lbs. The production of canned tomato juice began in U.S.A. in 1930, in which year the total pack was 6,930,000 lbs. By 1945 the annual output of this juice, second only to citrus in vitamin-C content, had reached a total of 924,000,000 lbs. The production and consumption of fresh and canned tomatoes, in ever increasing quantity, has now become general throughout the Americas and most of Europe. One hundred years ago the tomato, or love-apple as it was then called, was thought to be unfit for food and the cause of cancer. It was then grown for ornamental purposes only. Today the use of these fruits and juices has become routine as an essential part of modern nutrition, and significantly the decline in mortality rates of the infectious diseases dealt with in this treatise has been closely proportionate to the increased use of these fruits and juices. Significant also may be the fact that the inception of the citrus and tomato juice canning industry (1929-1930), which has greatly increased the consumption of these fruits, closely coincides with an apparent acceleration in the mortality decline of most of these diseases.

This nutritional revolution has, perhaps, been applied more intensively in infancy and childhood than in the older age brackets. Fifty years ago infants, when not breast fed, were fed artificially on modified cows' milk, condensed milk, or proprietary foods in powder form, which frequently was conducive to malnutrition. Even breast feeding at that time, owing to impoverished maternal diets, often had to be abandoned. Pediatricians at that time sanctioned the use of orange juice in small quantity —½ to 1 oz. after the age of ten months. Many mothers, however, hesitated to use fruit juices of any kind in the feeding of infants and young children because of the then popular fear of its producing "colic". Infant feeding today presents a greatly different picture. The infant of one month now gets its full ounce or more of orange juice daily, which is gradually increased until at six months fully four ounces or more is given, besides supplemental feedings of homogenized fruits and vegetables, wheat-germ-enriched cereal foods, etc. If orange juice should disagree, vitamin-C in tablet form is substituted.

The author believes that the major factor in the protective influence of this dietary revolution, with regard to the prevention of infectious diseases, has been the greatly increased intake of vitamin-C, which has been referred to by nutritionists as the "anti-toxic" or "anti-infection" vitamin. The anti-infection properties of this vitamin are dependent upon its effect on the reticulo-endothelial system in building up and maintaining stability and invulnerability of the submucous and subcutaneous connective tissues. The proliferation of fibroblasts and collagen fibrils is dependent upon a normal plasma concentration of vitamin-C, thus maintaining the stability of the intercellular cement substance, which in turn is essential to optimal resistance to infectious invasion. By reason of its chemical action as a reducing agent, and sometimes as an oxidizing agent, vitamin-C is also a specific antagonist of chemical and bacterial toxins. An optimal intake of this vitamin is, therefore, a means of building up natural immunity or resistance against all infectious diseases as well as counteracting their toxic manifestations.

The following references to the literature pertaining to the anti-infectious action of vitamin-C are submitted to show the prophylactic and therapeutic effect of this vitamin in the diseases under discussion:

Regarding tuberculosis: Richard Morton, one of the earliest writers on this disease, states in his famous *"Phthisiologia"* (1689) that "scurvy is wont to occasion a consumption of the lungs". Many investigators have studied the effect of vitamin-C in this disease because of its favourable effect on fibroblastic connective tissue formation, so essential to the healing of the exuditive or ulcerative lesions. Harris (8), finds that the excretion of vitamin-C is decreased in tuberculosis, that deficiency of vitamin-C reduces the resistance of guinea-pigs to tuberculosis infection, and that similar effects have been observed in man. Birkhang (9), found that C-hypervitaminosis, induced by daily administration of ascorbic acid, produced an increase in body weight and reduction in the tuberculosis lesions of guinea pigs. Microscopic examination revealed less caseonecrotic lesions and more collagenous tissue in and around the tubercular centers than was observed in the controls. Bauer and Vorwerk (10), report vitamin-C deficiencies of from 1000 mg. to 4000 mg. in tuberculosis cases. They state that there appears to be a certain parallelism between the activity of tuberculosis and the extent of vitamin-C deficiency. Albrecht (11), found that daily subcutaneous injections of vitamin-C in tubercular patients increased appetite, improved general health and blood picture, and frequently decreased the temperature. He also found it to be of value in pneumothorax therapy. Pilz (12), finds that vitamin-C favourably influences the process of recovery in tuberculosis. It increases vitality, eliminates night sweats, improves appetite, and, combined with cal-

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cium, raises blood values. A daily dose of 300 mg. is given until deficiency is made up, and thereafter sufficient to maintain normal levels. Nicita (13), reports that tubercular patients show a diminished vitamin-C urinary content, which is proportional to the severity of the disease. He advocates the administration of large amounts of this vitamin to counteract toxemia. Boissevain and Spillane (14), found that vitamin-C, in concentration of .001 per-cent inhibits the growth of human tubercle bacilli in artificial media. Radford, de Savitsch and Sweany (15), report the effect of vitamin-C on 111 far-advanced and fibroid tubercular cases. The patients were divided into three groups: the first received 500 cc. of orange juice, and the second 250 mg. of synthetic vitamin-C daily. The third group, used as controls, were given imitation orange juice. No other therapy was employed except routine rest. In three months the greater percentage of the treated patients showed a more favourable response than the controls in red-blood-cell count, lymphocytes, monocyte-lymphocyte ratio, neutrophil-lymphocyte ratio, hemoglobin and albumin-globulin. At six months the treated group still showed greater improvement in blood cells and hemoglobin. At nine months the greater amelioration of the treated groups in respect to blood-cell counts, sedimentation rates, and blood fibrogen was still maintained. Hasselbach (16), found a close relationship between fever and vitamin-C intake, and cites clinical cases to show that vitamin C reduces toxic manifestations, including fever. McConkey (17), reports that of 437 pulmonary cases admitted to a New York State Hospital for tuberculosis in 1926 and 1927, 47 developed intestinal tuberculosis; whereas, of 399 admitted in 1928 and 1929, who received a prophylactic treatment consisting of 3 oz. of citrus or tomato juice and ½ oz. of cod-liver oil with each meal, only three developed intestinal tuberculosis. Furthermore, of 913 other patients admitted during 1930 to 1938, who received the same prophylactic treatment, only nine developed intestinal tuberculosis. Borsalino (18), reports a study of the capillary resistance of 140 tubercular patients. He found that administration of vitamin-C rapidly increased capillary resistance and stopped hemoptysis, which reappeared when the treatment was discontinued. Moore *et al* (19), in a recent survey of nutrition among the northern Manitoba Indians, report a very high mortality rate from tuberculosis and pneumonia (761 and 383, respectively, per 100,000) among the Indians of Canada. In the tribes covered by their study the death rate for tuberculosis in 1942 was 1400 per 100,000. (The comparable figure for the white population of Manitoba was 27.) In their analysis of the daily per-capita food intake they found vitamin-C to be in greatest deficiency—less than 1/71 of the recommended allowance. In conclusion they say: "It is not unlikely that many characteristics, such as shiftlessness, indolence, improvidence and inertia, so long regarded as inherent or hereditary traits in the Indian race, may, at the root, be really the manifestations of malnutrition. Furthermore, it is probable that the Indians' great susceptibility to many diseases, paramount amongst which is tuberculosis, may be attributable among other causes to their high degree of malnutrition arising from lack of proper foods."

Regarding vitamin-C in pneumonia: In 1936 Gander and Niederberger (20), found that vitamin-C favourably influenced the course of pneumonia. When the vitamin-C status was brought up to normal saturation level early in the disease, preferably the first day of illness, the temperature dropped abruptly to normal and the pain subsided. The pulse remained in good tone and remarkable improvement in general condition was noted. They were led to the clinical study by the observation that the seasonal incidence of the peaks of vitamin-C deficiency (December and April) corresponded with the periods of highest mortality from pneumonia. Furthermore, they correlated the age incidence of the disease with the degree of vitamin-C deficiency usually found at different ages, the greatest deficiency occurring in age groups above fifty years in which pneumonia also has its highest incidence. In the same year Hochwald (21), independently reported similar results, his findings indicating that massive doses of vitamin-C—500 mg. every 90 minutes until the temperature drops to normal—exerted a curative effect in croupous pneumonia as shown by improvement in general condition—lessened prostration and dyspnea, earlier return to normal temperature, quicker disappearance of local findings, and normalization in white-blood-cell picture. More recently Slotkin and Fletcher (22), have reported on the prophylactic and therapeutic value of vitamin-C in postoperative pneumonia. They summarize their findings as follows: "Pulmonary complications in old debilitated patients, requiring prostatic surgery, is a common cause of death. The pulmonary lesions most noted were bronchopneumonia, lung abscess and purulent bronchitis. Most of these cases are so-called "wet chests", due to capillary secretions. Ascorbic acid, which increases the tonicity of these capillaries, has been of great value in alleviating these patients and restoring prompt pulmonary action by disappearance of this infiltration. . . . It is a valuable adjunct in tiding these aged patients over their critical postoperative period." Slotkin further reports (23), that since publication of his original paper on this subject, "ascorbic acid has been used routinely by the general surgeons in all surgical procedures in the hospital (Millard Fillmore-Buffalo) as a prophylaxis against pneumonia with complete disappearance of this complication." In this connection it may be of interest to note that bronchopneumonia is often the terminal cause of death in frank scurvy, and that the "rusty-brown" sputum of pneumonia may in reality be a sign of the hemorrhagic status of a sub-clinical scorbutic background.

Regarding vitamin-C in diphtheria: In the early history of this disease, when it was known as malignant angina or gangrenous sore-throat, many observers reported the frequent concurrence of "gangrenous gingivitis". Some physicians at that time regarded this complication as an extension of the disease from the throat. Others regarded this severe form of gingivitis as evidence of a scorbutic background. Boerhaave, a Dutch physician of international repute in the early 18th century, held strongly to this viewpoint. The quite frequent occurrence of epistaxis and the profuse bleeding from the denuded fauces upon removal of the false membrane, so characteristic of diphtheria, are very suggestive of the hemorrhagic status of scurvy. One thing is certain, scurvy was at that time very prevalent in central and northern Europe, where the available supply of fresh fruits was much less than in countries bordering on the Mediterranean.

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The basic concurrence of this condition may have determined the very high case-fatality rate (80 percent) at that time.

The close relationship between the vitamin-C status and the degree of diphtheritic intoxication is shown by Ravina (24), who observes that guinea-pigs have greater resistance to diphtheria toxin after injections of vitamin-C than controls not so treated. In 25 benign, 10 severe and 4 malignant cases of the disease a marked deficiency of vitamin-C was found in 28 percent of the subjects under fifteen years of age, and in 52 percent of those over fifteen years of age. For effective therapy he recommends large daily doses of the vitamin—150 mg. for children under three years of age, and 500 mg. for adolescents and adults. In Russia Bagasheva (25), uses a combined therapy for diphtheria, consisting of anti-serum, hypertonic dextrose, nicotinic acid and vitamin-C.

Regarding vitamin-C in rheumatic fever: Abasy, Hill and Harris (26), found a striking difference in the excretion of vitamin-C in 107 active rheumatic fever cases compared with controls. They conclude that large amounts of this vitamin are indicated both therapeutically and prophylactically. Roff and Glazebrook (27), reported the occurrence among naval trainees of a gingivo-stomatitis, commonly associated with rheumatic fever, which was shown to be due to vitamin-C deficiency. Glazebrook and Thomson (28), studied the effects of hemolytic streptococcus infection in potentially scorbutic and control groups in 1500 youths in a naval training school. Of these 335 were given liberal daily supplements of ascorbic acid, the remainder being used as controls. There developed 16 cases of rheumatic fever and 17 cases of pneumonia among the controls, and no case of either disease among the youths who received the extra vitamin-C. These authors felt that there was a close relationship between the cases of pneumonia and rheumatic fever. They noted the occurrence of a low-grade basal lung consolidation which was characterized on the one hand by its tendency to progress into rheumatism, and on the other hand by its disappearance when treated with vitamin-C. Rinehart (29), studied the effect of vitamin-P, a plant pigment found in the peeling of lemons and oranges, in conjunction with vitamin-C in the treatment of rheumatic fever. It had been found that vitamin P had a favorable influence on purpuric and hemorrhagic conditions resulting from vascular permeability in infections, notably rheumatic. All his cases showed a slowing of the sedimentation rate which was paralleled by marked clinical improvement. He concludes: "If nutritional deficiency of vitamin-C and P prove to be conditioning factors which prepare the soil for rheumatic fever, the prophylactic implications are clear."

Regarding vitamin-C in whooping cough: In 1936 Otani (30), and in 1937 Ormerod *et al* (31 and 32), reported very favorable results in the vitamin-C therapy of this disease. The former reported on the intravenous vitamin-C treatment of 81 cases of whooping cough in hospital clinics, and concluded that vitamin-C has a definite antagonistic action on the toxin of the Bordet-Gengou bacillus. The latter reported on the oral vitamin-C therapy of 29 cases —500 mg. the first day, then a daily average of 200 mg. thereafter. They concluded that "this treatment markedly decreases the intensity, number and duration of the characteristic symptoms."

Regarding nutritional deficiency as the major etiological factor in maternal and infant mortality: The epochal work of Ebbs *et al* (33, 34, 35), has furnished indubitable evidence of the life-saving effect of improved maternal nutrition on both mother and child. They studied the effect of supplemental feeding of 90 women, on poor diets and with low income, in the last half of pregnancy, as compared with 120 controls, unsupplemented, on equally poor diets; and another group of 170 women with higher incomes who were advised regarding proper diet. The supplemental foods supplied in these studies consisted of milk, eggs, cheese, oranges, tomatoes, wheat germ and vitamin D. The women on the supplemented and good diets enjoyed better health, had fewer complications throughout the puerperium, and the health of their infants was much better than those on the unsupplemented poor diet. The incidence of miscarriages, prematures, stillbirths and deaths before six months was significantly higher in the poor-diet group. In a subsequent study by Burke *et al* (36), in which 216 maternal cases were observed, very similar findings are recorded.

It is the author's belief that the gradually increased use of citrus fruits and juices in maternal and infant feeding during the past half century has been the major factor in reducing the maternal and infant death rates. The increased intake of vitamin-C would, for the physiological reasons previously stated, tend to minimize puerperal infection, decrease the incidence and severity of pre and post-partum hemorrhage (the *bête noire* of obstetrics,) and, by increasing the tensile strength of connective tissues, prevent cervical and perineal lacerations, thus still further lessening the danger of maternal infection. In the infant this dietary revolution would, for the same reasons, tend to reduce the incidence of neonatal pneumonia, diarrhea and enteritis (now taking such a heavy toll in war-ravaged Europe), and other infectious diseases of early infancy.

Regarding vitamin-C and resistance to infection in general: Jusatz (39), finds that vitamin-C has a stimulating effect on the production of antibodies. He claims that it increases the agglutinin, hemolysin and precipitin titres and the opsonic index of experimental animals treated with vaccines or toxoids. Madison and Manwaring (40), confirming these findings, were able to bring about a ten-to-thirty-fold increase in precipitin titre by optimal intake of vitamin-C. During the recent war it was found that German children receiving a supplement of 50 mg. of vitamin-C daily were less susceptible to infection than controls (41). More recently Nungster and Ames, of the University of Michigan, reported to the American Society of Bacteriologists (1947 Convention) that vitamin-C greatly increases the phagocytic action of white blood cells against infectious bacteria.

The author's hypothesis of increased vitamin-C intake associated with the increased consumption of citrus fruits, tomatoes, etc., as being the major heretofore unidentified factor in bringing about the general reduction in mortality of infectious diseases, would also account for the shift in the age incidence of tuberculosis, diphtheria, poliomyelitis and other diseases from the under-five-years to older age groups. This is explained by the fact that the infant in the nursery is given the full benefit of this nutritional reform, whereas after this age perverse dietary habits are gradually acquired through lack of parental guidance and inadequacy of public-health education. The increased use of candy, carbonated

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beverages, tea, coffee, tobacco and alcohol by our juvenile and older age groups tends gradually to displace the more wholesome nutritional habits of early childhood.

After all, we should recognize that natural resistance to disease is developed by fundamental improvement in nutrition and hygiene. Such resistance gives protection against all diseases. Artificial immunization, on the other hand, is dependent upon the conversion of a portion of this latent general resistance to a specific resistance, such as in toxoiding for diphtheria. The injection of an attenuated virus or bacterial toxin elicits a reaction of the organism to that specific morbific agent only, and draws upon our reserves of natural immunity to meet this conversion demand. If repeated demands exceed the supply we are left physically bankrupt. In other words, we cannot strike back with more than we have, and we cannot get out of anything more than we put into it. Thus the fundamental prerequisite for successful artificial immunization is an ample reserve of natural immunity. In our search for short cuts in the prevention and cure of disease we are prone to overlook this basic truth. In the modern use of chemotherapy we are already beginning to find "flies in the ointment". The specific benefit of the sulfonamides is sometimes obtained at the expense of toxic damage to some vital uninvolved part of the human mechanism. (In a previous paper (37), the author has shown that vitamin-C deficiency is conducive to sulfonamide sensitivity.) We are now beginning to find that even the more benign penicillin has its drawbacks in stepping up the virulence of certain organisms. The author is inclined to believe that the principle of trying to eradicate disease by concentrating our attack against the associated micro-organisms is fundamentally unsound. If we wish to eliminate a desert or swamp we do not proceed to cut down the sage brush and cactus of the former, or the lush characteristic verdure of the latter. Instead, we change the condition of the soil. By irrigation we make the desert blossom like a rose, and by drainage we eliminate the swamp.

Dr. Alexis Carrel (38), has said: "Microbes and viruses are to be found everywhere, in the air, in water, in our food. . . . Nevertheless, in many people they remain inoffensive. Among human beings some are subject to diseases and others are immune. Such a state of resistance is due to the individual constitution of the tissues and the humors, which oppose the penetration of pathogenic agents or destroy them when they have invaded our body. This is natural immunity. . . . But natural immunity does not exclusively derive from our ancestral constitution. It may come also from the mode of life and alimentation. . . . Some diets increase the susceptibility of mice to experimental typhoid fever. The frequency of pneumonia may also be modified by food. The mice belonging to one of the strains kept in the mousery of the Rockefeller Institute died of pneumonia in the proportion of 52 percent while subjected to the standard diet. Several groups of these animals were given different diets. The mortality from pneumonia fell to 32 percent, 14 percent, and even to zero, according to the food. We should ascertain whether natural resistance to infections could be conferred on man by definite conditions of life. Injections of specific vaccine or serum for each disease, repeated medical examinations of the whole population, construction of gigantic hospitals, are expensive and not very effective means of preventing diseases and of developing a nation's health. Good health should be natural."

A great English physician, Dr. Leonard Williams, has said: "The discovery of the vitamins has entirely altered our conception of the causes and origins of disease. Until lately disease was regarded as a sin of commission by some unseen and subtle agency. The vitamins are teaching us to regard it, in some degree at any rate, as a sin of omission on the part of civilized or hypercivilized man. By our habit of riveting our attention on microbes and their toxines we have sadly neglected the side of the question which concerns itself with our own bodily defenses."

Charcot has said: "Disease is from of old and nothing about it has changed. It is we who change as we learn to recognize what was formerly imperceptible."

Summary

Statistical data are presented to show the marked decline in mortality and case fatality of many infectious diseases within the past century.

The uniformity of this decline, in so many diseases and over such a lengthy period of time, suggests the operation of some major over-all factor improving natural resistance, compared with which our artificial control measures have played a minor or supplemental role. The existence of such a factor has been recognized by epidemiologists, but not yet identified.

The author advances the hypothesis that some major change in the trend of nutrition offers the most likely explanation, and singles out the greatly increased consumption of citrus and other fruits rich in vitamin-C as the unidentified factor. Correlated statistical data show a close parallel, in both time and extent, between the development of this nutritional trend and the mortality decline in infectious diseases.

The physiological action of vitamin-C is discussed in relation to its "anti-infection" role, and the literature relative to the prophylactic and therapeutic use of this vitamin in infectious diseases is reviewed.

Bibliography

1. Pringle, A. M. N.: Tuberculosis throughout the century. *Med. Off.*, Apr. 10, 1943.
2. Ross, Mary A.: Tuberculosis mortality in Ontario *Can. Pub. Health Jour.*, 25:73, 1934.
3. McKinnon N. E.: Mortality reductions in Ontario 1900-1942. *Can Jour. Pub. Health,* 36: 423, 1945.
4. Davis, Paul V.: Tuberculosis epidemiology. *Dis. of Chest,* page 21, Sept., 1939.
5. Morton, A. R: The diphtheria epidemic in Halifax. *Can Med. Assoc. Jour.,* 45:171, 1941.
6. Lomer, T. A.: Personal communication to the author. Dec. 16, 1946.
7. Eller C. H. and Frobisher, Martin, Jr.: An outbreak of diphtheria in Baltimore in 1944. *Am. Jour. Hyg.,* 42:179, 1945.
8. Harris, L. J.: Nutrition and its effect on infectious disease. *Lancet,* 1: 811, 1937.
9. Birkhang, K. E.: Tuberculosis in animals treated with ascorbic acid. *J.A.M.A.,* 112:2376, 1939.
10. Bauer, G. and Vorwerk, W.: Beitrag zum vitamin C-defizit bei Lungentuberkuloesen. *Beitr. z. Tuberk.* 91:262, 1938.
11. Albrecht, E.: Vitamin C als adjuvans in der therapie der lungentuberkulose, *Med. Klin.,* 34: 972, 1938.
12. Pilz, I.: Vitamin C; ein wichtiges adjuvans in der behandlung der lungentuberkulose. *Med. Klin.,* 34: 227, 1938.
13. Nicita, A.: Recerche sulla eliminzione della vitamina C nei tuberculotici. *Riv. di Patal. e Clin. d. Tuberc.* 12: 41, 1938.

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14. Boissevain, C. H. and Spillane, J. D.: A note on the effect of synthetic ascorbic acid on the growth of the tubercle bacillus. *Am. Rev. Tuberc.* 35: 661, 1937.
15. Radford, M., de Savitsch, E. C., and Sweany H. C.: Blood changes following continuous administration of vitamin C and orange juice to tuberculous patients. *Am. Rev. Tuberc.*, 35: 784, 1937.
16. Hasselbach, F.: Vitamin C und waermeregulation. *Schweitz. Med. Wschr.*, 67: 877, 1937.
17. McConkey, Mack: Cod liver oil and tomato juice in prophylaxis of intestinal tuberculosis. *Am. Rev. Tuberc.*, 43: 425, 1941.
18. Borsalino, G.: La fragilite capillare nella tuberculose polmonare e le sue modificazione par azione della vitamin C. *Gior. di clin. med.*, 18: 273, 1937.
19. Moore, P. E., Kruse, H. D., Tisdall F. F. and Corrigan, R. S. C.: *Can. Med. Assn. Jour.* 54: 223, 1946.
20. Gander, J., and Niederberger W.: Vitamin C in der behandlung der pneumonie. *München med. Wchnschr.*, 51: 2074, 1936.
21. Hochwald, A.: Beobachtungen uber askorbinsaure-wirkung bei der krupposen pneumonie. *Wien. Arch. f. Inn. Med.*, 29: 353, 1936.
22. Slotkin, G. E. and Fletcher R. S.: Ascorbic acid in pulmonary complications following prostatic surgery: A Preliminary Report. *Jour. Urol.*, 52: Nov. 6, 1944.
23. Slotkin, G. E.: Personal communication to the author, Dec. 2, 1946.
24. Ravina, A.: The vitamin-C therapy of diphtheritic intoxication. *Presse Med.* 53, 8, 1945.
25. Bagasheva, A. M.: Combined therapy of diphtheria with anti-serum, hypertonic solution of dextrose, nicotinic and ascorbic acid. *Soviet. Med.*, 8: 7, 1944.
26. Abasy, M. A., Hill, N. J., and Harris, L. J.: Vitamin C and juvenile rheumatism. *Lancet*, 2: 1413, 1936.
27. Roff, F. S. and Glazebrook, A. J.: The therapeutic application of vitamin C in peridental disease. *Jour. Roy. Nav. Med. Serv.*, 25: 340, 1939.
28. Glazebrook, A. J., and Thompson S.: The administration of vitamin C in a large institution and its effect on general health and resistance to infection. *Jour. Hyg.*, 42: 1, 1942.
29. Rinehart, J. F.: The treatment of rheumatic fever with crude hesperidin (vitamin C), Paper read before California Heart Assoc., Los Angeles, May 6 1944.
30. Otani, T.: Vitamin C therapy of whooping cough. *Klin. Wchnschr.*, 15: 1884, 1936.
31. Ormerod, M. J., and Unkauf, B. M.: Ascorbic acid treatment of whooping cough. *Can. Med. Assn. Jour.*, 37, 134, 1937.
32. Ormerod, M. J., Unkauf B. M., and White, F. D.: A further report on the ascorbic acid treatment of whooping cough. *Can. Med. Assn. Jour.*, 37: 268 1937.
33. Ebbs, J. H., Tisdall, F. F., and Scott, W. A.: The influence of prenatal diet on the mother and child. *Jour. Nutrit.* 22: 515, 1941.
34. Ebbs, J. H., Scott, W. A., Tisdall, F. F., Moyle, W. J. and Bell, M.: Nutrition in pregnancy. *Can. Med. Assn. Jour.*, 46: 1, 1942.
35. Ebbs, J. H. Brown, A., Tisdall, F. F., Moyle, W. J., and Bell M.: The influence of improved prenatal nutrition on the infant. *Can. Med. Assn. Jour.*, 46: 6, 1942.
36. Burke, S. B., Beal, V. A. Kirkwood, S. B., and Stuart, H. C.: The influence of nutrition during pregnancy upon the condition of the infant at birth. *Jour. Nutrit.* 26: 569, 1943.
37. McCormick, W. J.: Sulfonamide sensitivity and C-avitaminosis. *Can. Med. Assn. Jour.*, 52: 68, 1945.
38. Carrel, Alexis: *Man the Unknown*, New York and London, Harper Bros.: 1935, p. 207.
39. Jusatz, J. H.: Uber den influss von vitamin C auf immunitatsvorgange. *Ztschr. f. Vitaminforsch.*, 9: 75, 1939.
40. Madison, R. R., and Manwaring, M. H.: Ascorbic-acid stimulation of specific anti-body production. *Proc. Soc. Exper. Biol. Med.*, 37: 402, 1937.
41. Summary of certain public health measures adopted in Germany during the present war. *Bull. War Med.*, 2: 5, 1941.

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