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## SICKNESS AMONG MALE INDUSTRIAL EMPLOYEES DURING THE SECOND QUARTER AND THE FIRST HALF OF 1936<sup>1</sup>

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The data upon which this report is based were obtained from establishments in various sections of the United States, the greater percentage of them being located north of the Ohio and Potomac Rivers and east of the Mississippi.

The sickness rates for the second quarter and the first half of the years 1935 and 1936 were derived from analyses of reports from a group of 28 identical sick-benefit organizations. The rates for the first half of the years 1931-35 include 24 of these companies.

The rise in sickness incidence which was recorded for a group of approximately 154,000 male industrial employees in the first quarter of 1936 extended into the second quarter of the year. During the 6 months, January to June, inclusive, of 1936 as compared with the corresponding period of former years, the frequency of illness causing disability for 8 calendar days or longer reached 100 cases per 1,000 male industrial workers for the first time since 1932.

For all respiratory diseases the rate for the second quarter of 1936 was 1.9 per 1,000 employees higher than the rate for the corresponding 3 months of 1935, due to an increase in the number of cases reported as bronchitis (acute and chronic), influenza, and pneumonia (all forms). With the exception of the diseases of the pharynx and tonsils and tuberculosis of the respiratory system, every subgroup in the category of respiratory disease showed higher rates for the first 6 months of 1936 than for the corresponding period of 1935.

The favorable downward trend in the frequency of new cases of tuberculosis of the respiratory system (as shown in the table) as well as the lower death rate among the 17,000,000 industrial policyholders of the Metropolitan Life Insurance Co.<sup>2</sup> continued throughout the second quarter of 1936.

As in the first quarter of 1936, the incidence rate of cases of pneumonia in the second quarter of 1936 exceeded the corresponding

<sup>1</sup> The report for the first quarter of 1936 was published in the Public Health Reports for July 24, 1936, vol. 51, no. 30, pp. 989-991.

<sup>2</sup> Statistical Bulletin, Metropolitan Life Insurance Co., vol. 17, no. 7, July 1936, p. 11.

quarter of the preceding year. Indeed, 3.8 cases per 1,000 males for January-June of 1936 is the highest rate recorded for any first half-year period since 1929. As stated in a former report,<sup>2</sup> this is suggestive of correlation between pneumonia frequency and the rate of industrial activity.

The increase in the incidence rate of all nonrespiratory diseases for the second quarter of 1936 as compared with the second quarter of 1935 was negligible; it amounted to only 0.4, while for the entire first half of 1936 the increase was 1.7 when compared with the same period of 1935. The incidence rates for the first 6 months of 1936 and the average for the first half of the years 1931-35 are approximately the same.

**TABLE 1.**—*Frequency of disability lasting 8 calendar days or longer in the second quarter of 1936 compared with the same quarter of 1935, and in the first half of 1936 as compared with corresponding period of preceding years. (Male morbidity experience of industrial companies which reported cases to the U. S. Public Health Service)*<sup>1</sup>

Diseases and disease groups which caused disability. (Numbers in parentheses are disease title numbers from the International List of the Causes of Death, fourth revision, Paris, 1929)	Annual number of disabilities per 1,000 men				
	Second quarter of—		First half of—		
	1936	1935	1936	1935	1931-35
Sickness and nonindustrial injuries <sup>2</sup> .....	86.9	84.0	100.2	93.9	98.8
Nonindustrial injuries.....	10.2	9.6	10.8	9.9	10.8
Sickness <sup>2</sup> .....	76.7	74.4	89.4	84.0	88.0
Respiratory diseases.....	29.8	27.4	41.6	37.9	40.1
Bronchitis, acute and chronic (106).....	4.7	3.6	6.0	4.2	4.0
Diseases of the pharynx and tonsils (115a).....	5.1	6.5	5.8	5.9	5.6
Influenza and grippe (11).....	12.3	10.0	20.6	18.8	22.3
Pneumonia, all forms (107-109).....	2.6	2.2	3.8	3.0	2.6
Tuberculosis of the respiratory system (23).....	.7	1.1	.7	1.1	1.0
Other respiratory diseases (104, 105, 110-114).....	3.9	4.0	5.2	4.9	4.6
Nonrespiratory diseases.....	47.4	47.0	47.8	46.1	47.9
Disease of stomach, cancer excepted (117-118).....	4.1	3.5	3.8	3.6	3.7
Diarrhea and enteritis (120).....	1.0	.9	1.1	1.0	1.0
Appendicitis (121).....	4.6	4.1	4.3	3.8	3.7
Hernia (122a).....	1.6	1.7	1.7	1.5	1.6
Other digestive diseases (115b, 116, 122b-129).....	2.9	2.9	2.9	2.9	3.0
Rheumatic group, total.....	10.6	9.8	10.4	10.1	11.2
Rheumatism, acute and chronic (56, 57).....	5.0	4.5	4.7	4.6	5.7
Disease of organs of locomotion (166b).....	3.2	2.6	3.3	2.8	3.2
Neuralgia, neuritis, sciatica (87a).....	2.4	2.7	2.4	2.7	2.3
Neurasthenia and the like (part of 87b).....	1.2	1.5	1.0	1.2	1.2
Other diseases of nervous system (78-85, part of 87b).....	1.2	1.5	1.2	1.3	1.4
Diseases of the heart and arteries, and nephritis (90-99, 102, 130-132).....	2.4	3.8	3.9	4.1	4.2
Other genito-urinary diseases (133-138).....	2.2	2.8	2.4	2.7	2.4
Diseases of the skin (161-163).....	2.3	2.2	2.4	2.3	2.5
Infectious and parasitic diseases (1-10, 12-22, 24-33, 36-44).....	3.0	3.6	3.3	3.1	3.0
Ill-defined and unknown causes (200).....	2.8	2.2	2.6	2.1	1.9
All other diseases (45-55, 58-77, 88, 80, 100, 101, 103, 154-156a, 157, 162).....	6.5	6.5	6.8	6.4	7.1
Average number of males covered in the record.....	153,670	138,214	149,901	138,089	145,356
Number of companies included.....	28	28	28	28	-----

<sup>1</sup> In 1935 and 1936 the same companies are included. The rates for the first half of the years 1931-35 include 24 of these companies, which employed an average of 114,961 men during these months, or 79 percent of the 145,356 men representing the sample population for the 5 years.

<sup>2</sup> Exclusive of disability from the venereal diseases and a few numerically unimportant causes of disability.

<sup>3</sup> See footnote 1.

The most marked increase in disorders of the digestive system both for the second quarter and the first half year of 1936 occurred in the diseases of the stomach (cancer excepted) and appendicitis. The incidence rate for appendicitis during the first 6 months of 1936 was 4.3 per 1,000 employees as compared with 3.8 for the same period of the preceding year, and with an average of 3.7 for the years 1931-35 inclusive. However, mortality from appendicitis according to the records of the Metropolitan Life Insurance Co.<sup>4</sup> was lower during the first 6 months of 1936 (10.7 per 100,000 policyholders) than during the same months of 1935 and 1934 (11.7 and 12.7, respectively). The second quarter reveals, moreover, a higher incidence for the rheumatic group of diseases than was recorded in the 1935 period, namely, 10.6 as against 9.8.

The frequency rates for diarrhea and enteritis, hernia, "other digestive diseases," and diseases of the skin were approximately the same in the second quarters of 1936 and 1935. A small decrease is shown both in the second quarter and the first half of 1936 in the incidence of diseases of the heart, arteries, and nephritis and in "other diseases of the genito-urinary system."

The records show an increase of 0.6 and 0.9, respectively, in the frequency of nonindustrial accidents per 1,000 employees in the second quarter and in the first half of 1936 as compared with the corresponding periods of the preceding year.

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## THE PHYSIOLOGICAL RESPONSE OF PERITONEAL TISSUE TO CERTAIN INDUSTRIAL AND PURE MINERAL DUSTS<sup>1</sup>

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The behavior of certain dusts when introduced into the peritoneal cavity as foreign bodies has been described in previous reports.<sup>2</sup> In 1924, experiments were begun at the Pittsburgh station of the United States Bureau of Mines to determine the action and fate of various dusts when injected into the peritoneal cavity of guinea pigs. The conclusions reached at that time were that live animal tissue in all parts of the body tends to react in essentially the same manner to foreign bodies and that fibrous tissue is formed in the peritoneal cavity by quartz and is not formed by limestone and coal. This paper reports a continuation and elaboration of these earlier studies.

<sup>4</sup>Footnote 2 and *ibid.*, vol. 16, no. 7, July 1935, p. 11.

<sup>1</sup>From the Laboratory of Industrial Hygiene of the Office of Industrial Hygiene and Sanitation.

<sup>2</sup>Miller, J. W., and Sayers, R. R.: *The Response of Peritoneal Tissue to Dusts Introduced as Foreign Bodies*. Pub. Health Rep., 49:80-89 (Jan. 19, 1934). (Reprint No. 1608.) J. Am. Med. Assoc., 103: 907-912 (Sept. 22, 1934). Am. J. Pub. Health, 25:452-456 (April 1935).

Miller, J. W., and Sayers, R. R.: *Microscopic Appearance of Experimentally Produced Dust Nodules in The Peritoneum*. Pub. Health Rep., 50:1619-1628 (Nov. 15, 1935). (Reprint No. 1717.)

Owing to the length of time required to obtain a reaction by inhalation methods and the desirability of determining the harmfulness of a dust in a relatively short time, other methods of introducing the dusts to be studied were considered. Injection into the peritoneal cavity seemed to give the most promise, because of the relatively circumscribed area of the cavity, the ease in controlling the amount of the dose, and the preservation of the sterility of the material introduced—a factor to be considered in inhalation and intratracheal methods. Mortality from peritonitis or peritoneal damage following intraperitoneal injection was found to be negligible. Identical reactions were found in each animal injected with the same dust under the same conditions and examined at the same time interval after injection. (Animals in groups of from 5 to 20 were used for each set of test conditions.)

The dusts investigated produced distinct types of reaction, which made it possible to classify them into the following three groups: (1) A group in which the dust was absorbed or disappeared without visible gross damage; (2) a group in which the dust initiated cellular proliferation followed by fibrosis and retrograde changes; (3) a group in which the dust remained inert in the tissues, neither being absorbed nor causing gross proliferation. Since the development of this classification on the basis of physiological response, an additional number of industrial and other dusts have been examined and classified. The results are reported in this paper.

#### PREPARATION OF THE DUSTS FOR INJECTION

It was desirable that the particle size of each dust tested conform as closely as possible to that of the other dusts used, and also be as small as possible without change in the physical or chemical composition. Particles passed through 100-, 200-, and 325-mesh standard sieves were used in one series of tests with several dusts.

The 325-mesh size was found to be the most suitable, because of the greater facility with which a reaction is produced. The particles obtained by passing a dust through a 325-mesh sieve were less than 43 microns in size.

In later series an air separator was used. This method of elutriation did not separate all the dusts in the series into fractions of the same size; yet it did produce samples less than 10 microns in maximum measurement. The median size of the dusts used in this series varied from 0.45 to 3.25 microns. Such variations in particle size appeared to be of no importance in comparing the physiological responses produced by the dusts. It can be readily seen that the air-separated particles more closely approximate those inhaled under industrial conditions.<sup>3</sup> While the smaller particles were prefera-

<sup>3</sup> Bloomfield, J. J.: *The Size Frequency of Industrial Dust*. Pub. Health Rep., 48:961-968 (Aug. 11, 1933).

ble, because of their greater assimilation by the cells, the particles that had been passed through a 325-mesh sieve gave the same gross reactions and, in the case of all dusts mentioned in this study, can be used in place of the more difficultly obtained smaller particles. Water separation was not attempted, because of the possibility of removing soluble portions of the dusts and thus producing a change in their chemical composition.

#### TECHNIQUE OF INTRAPERITONEAL INJECTIONS

A weighed portion of the dust and a few glass beads to facilitate suspension were placed in a small wide-mouthed flask and sterilized in a hot-air oven for 1 hour at 150° C. After cooling, sufficient sterile physiological saline solution to make a 5- or 10-percent suspension was added, the bottle was closed with a sterile rubber stopper, and the whole was thoroughly shaken. Owing to the fact that a suspension of fine dust causes a locking of the plunger of a hypodermic syringe, air-bulb syringes of 3-cc capacity were used. Any small hypodermic syringe, fitted with a rubber bulb in place of the plunger, will serve the purpose. Needles of 21- or 24-gage were found most suitable for the injections. The needles and syringes were sterilized in boiling water before use.

The hair on the right side of the animal's abdominal wall was clipped and tincture of iodine was applied. For injection, 2 cc of the 5- or 10-percent suspension, equivalent to 0.1 or 0.2 gm of dust, was introduced, intraperitoneally, into each pig at the iodine-painted site.

In the early series of experiments, animals were killed at intervals of 7, 14, 30, 56, 90, 112, 180, and 360 days after injection. It has been found that intervals of 14, 30, 60, and 90 days are sufficient to produce a reaction that can be differentiated. In most of the tests a series of animals has been kept for 180 days to confirm the earlier observations. With a great many dusts, classification into one or the other of the three groups can be made in 60 days.

#### DISTRIBUTION OF THE DUST IN THE PERITONEAL CAVITY

With the exception of bituminous coal, the greater part of each of the dusts in this series was found in the peritoneum of the anterior abdominal wall, the most dependent portion of the peritoneal cavity. The site of the next largest collection was the omentum. Small nodules and dispersed collections of particles were also found in the inguinal canals, on the mesentery, liver, intestines, testes or uterus, and diaphragm. A very little was occasionally found on the posterior abdominal wall. In the case of bituminous coal, the greater portion was found in the omentum and mesentery, while a relatively small part was present on the anterior abdominal wall. As a basis of comparison (in describing the reactions caused by the dusts), the nodules

formed on the anterior abdominal wall were used, since they were more accessible and were more constant and uniform in appearance. The response in the omentum or at any other point in the peritoneal cavity was, however, the same as that found on the anterior abdominal wall. Nodules were only infrequently found in the peritoneum at the site of the entrance of the needle—so rarely, in fact, that it was safe to assume that the trauma produced by the introduction of the needle was negligible.

#### ADHESIONS IN THE PERITONEAL CAVITY

Adhesions between the various abdominal viscera and the anterior abdominal wall or omentum were at first thought to be of some significance. However, it was noted that while the presence of adhesions was more frequent when dusts of a high silica content were used and correspondingly less frequent with such dusts as calcite and limestone, they were not of sufficient constancy to be used to draw any definite conclusions as to the activity of the dust. Adhesions were formed occasionally by calcite and by limestones of a very low silica content. They were likewise present to a marked degree in the animals injected with cement; yet subsequent observations showed that these dusts decreased in amount in the tissues as the tests progressed. It was concluded that the formation of adhesions was a result of the initial foreign body injury caused by the dust in the peritoneal cavity. This injury may be mechanical or it may be the result of a chemical irritation, due to some readily soluble constituent of the dust. The formation of peritoneal adhesions does not appear to be related to the subsequent behavior of the dust but may indicate a violent early reaction in the peritoneum.

#### THE ABSORPTIVE GROUP OF DUSTS

Dusts of the absorptive group, after being injected into the peritoneal cavity, formed nodules, the gross appearance of which was irregular, more or less discrete, but often clumped. The nodules became progressively smaller in size as the interval between injection and examination increased, and this decrease in size was accompanied by the production of brown pigment particles, which were first noted at the edges of the nodules, and later covered their entire surfaces and diffused into the adjacent peritoneum. This brown pigment, which did not respond to the iron reactions, varied in amount depending on the kind of dust used. The original dust eventually disappeared, leaving a small area of fine, brown pigment particles at the site of the nodule. These, in turn, disappeared without the formation of scar tissue. The speed with which the dust was absorbed and the severity of the initial reaction varied somewhat with the composition of the dusts. Pure calcite, for example, disappeared more rapidly

from the peritoneal tissue than did a relatively pure sample of limestone. The decrease in amount of and the disappearance of the dust from the peritoneum is a well-marked characteristic of this group of dusts.

After 7 days, microscopic examination showed that the nodules consisted almost entirely of large clumps of dust mixed with fine, granular, necrotic material. A narrow, cellular zone, composed principally of fibroblasts, enclosed the mass of dust and necrotic material. A few macrophages were found in this zone, usually adjacent to the dust clump. As the interval between injection and examination increased, capillary buds, accompanied by macrophages and fibroblasts, extended into the dust mass. Fine, brown pigment particles had made their appearance and were engulfed in the cytoplasm of the macrophages, a process that reached its peak of activity about 90 days after injection of the dust. At this time, pigmented connective tissue cells were conspicuous and only a few particles of the original dust remained. After 180 days, and also after 360 days, the nodules consisted exclusively of pigmented connective tissue cells and fat cells, and even these appeared to have decreased in number. The necrosis noted in the early stages had disappeared.

#### DUSTS CAUSING AN ABSORPTIVE REACTION

*Calcite*.—A pure mineral dust. Chemical analysis: Acid insoluble matter, 0.0 percent; silica, 0.0 percent. Petrographic examination: A calcite of high purity. Dust used passed through a 325-mesh screen.

*Calcite*.—A pure mineral dust. Chemical analysis: Acid insoluble matter, 0.1 percent, all of which was silica. Petrographic examination: A calcite of high purity. Median particle size, 1.2 microns. Geometric standard deviation, 1.4 microns.

*Precipitated calcium carbonate*.—A chemical byproduct. An industrial dust. Chemical analysis: Silica, 0.4 percent; calcium carbonate, 87.9 percent; magnesium carbonate, 10.1 percent; magnesium oxide, 0.1 percent; iron and aluminum oxides, 0.6 percent. Petrographic examination: Precipitated calcium carbonate, about 98 percent; crystals, probably sodium carbonate, about 2 percent. Median particle size, 1.05 microns. Geometric standard deviation, 1.4 microns.

*Limestone*.—An industrial dust. Chemical analysis: Silica, 1.5 percent; calcium oxide, 54.4 percent; magnesium oxide, 0.4 percent; iron and aluminum oxides, 0.4 percent. Petrographic examination: Irregularly rounded calcite. No impurities noted. Median particle size, 0.95 micron. Geometric standard deviation, 1.6 microns.

*Limestone*.—An industrial dust. Chemical analysis: Silica, 2.73 percent; calcium carbonate, 95.21 percent; magnesium carbonate,

1.17 percent. Petrographic examination: A dolomitic limestone; no impurities observed. Median particle size, 2.35 microns. Geometric standard deviation, 1.8 microns.

*Limestone*.—An industrial dust. Chemical analysis: Acid insoluble matter, 7.2 percent; silica 5 percent. Petrographic examination: Only an infrequent quartz crystal was noted. A high calcium carbonate content. Dust used passed through a 325-mesh screen.

*Gypsum*.—The uncalcined, natural mineral. An industrial dust. Chemical analysis: Silica, 1.3 percent; calcium sulphate, 97.1 percent. Petrographic examination: Gypsum, about 70 percent; calcite, about 30 percent. Median particle size, 1.1 microns. Geometric standard deviation, 1.5 microns.

*Portland cement*.—An industrial dust. Chemical analysis: Silica, 21.1 percent; calcium oxide, 74.4 percent; magnesium oxide, 2.8 percent. Petrographic examination: Normal portland cement. Median particle size, 0.65 micron. Geometric standard deviation, 1.4 microns.

#### THE PROLIFERATIVE GROUP

The dusts of this group, after an initial stage of foreign body irritation, manifested by edema and congestion about the collections of dust in the peritoneum, produced nodules that progressively increased in size. These nodules, when occurring in clumps, fused together, forming a large single mass. Numerous capillaries were present on the surfaces and throughout the nodules. The appearance was that of cellular proliferation and was apparently due to the chemical irritation supplied by the solution of the silica in the tissues. The maximum size of the nodules was observed 90 days after injection. After this period they became more firm, contracted, and fibrous in appearance. At the end of 360 days this induration was quite marked. The rate of development and the size of these nodules varied with the composition of the dust. Pure free silica produced the most rapid response. The presence of certain inert constituents, such as limonite or clay, produced variations, not only in the rate of development, but also in the color of the nodules. Any progressive increase in the size of the nodules up to a period of 90 days after injection can be designated as a proliferative reaction.

Seven days after injection, microscopic examination of the nodules showed a central mass of dust particles, mixed with, and surrounded by, a fairly wide zone of fine, granular necrotic material. The cellular elements were most conspicuous at the periphery and base of the nodules. The cellular portion was composed of many fibroblasts in various stages of development and a few scattered macrophages containing engulfed dust particles. The fibroblasts were arranged in concentric whorls and interlacing bundles, and those adjacent to the dust mass assumed a layer-like arrangement, forming an apparent

inner capsule. The fibroblast was the predominant type of cell. Capillaries occurred in large numbers in the cellular portion of the nodule. As the duration of the tests increased, the macrophages became more numerous and many were filled with dust particles. This increase was most marked in the 30-day tests. After 90 days, fibroblasts and adult connective tissue cells were again predominant, occurring in about equal numbers, although numerous dust-bearing macrophages were still present. The necrotic material appeared to decrease progressively in amount from the seventh to the sixtieth day, but at 90 days an increase was noted. Areas of early calcification were present in the centers of the necrotic material. In the 180-day nodules, the cellular portion consisted of fibrous tissue cells, fat cells, and a few fibroblasts. The areas of necrosis and calcification were larger. These retrograde changes had advanced markedly in 360 days with calcification being the most prominent feature of the nodule.

#### DUSTS CAUSING A PROLIFERATIVE REACTION

*Quartz*.—A pure mineral dust. Chemical analysis: Silica, 99.4 percent. Petrographic analysis: Normal crystalline quartz of high purity. Median particle size, 1.30 microns. Geometric standard deviation, 1.8 microns.

*Quartz*.—A pure mineral dust. Chemical analysis: Silica, 99.3 percent. Petrographic examination: Normal crystalline quartz of high purity. Dust passed through a 325-mesh screen.

*Quartz*.—An industrial dust. Chemical analysis: Silica, 99.1 percent. Petrographic examination: Normal quartz. Median particle size, 1.25 microns. Geometric standard deviation, 1.8 microns.

*Tripoli*.—An industrial dust. Chemical analysis: Total silica, 98.9 percent; calcium oxide, 0.2 percent; magnesium oxide, 0.1 percent; iron and aluminum oxides, 0.3 percent. Petrographic examination: Chalcedonic silica (crystalline aggregates) with an occasional crystal of normal quartz. Dust passed through a 325-mesh screen.

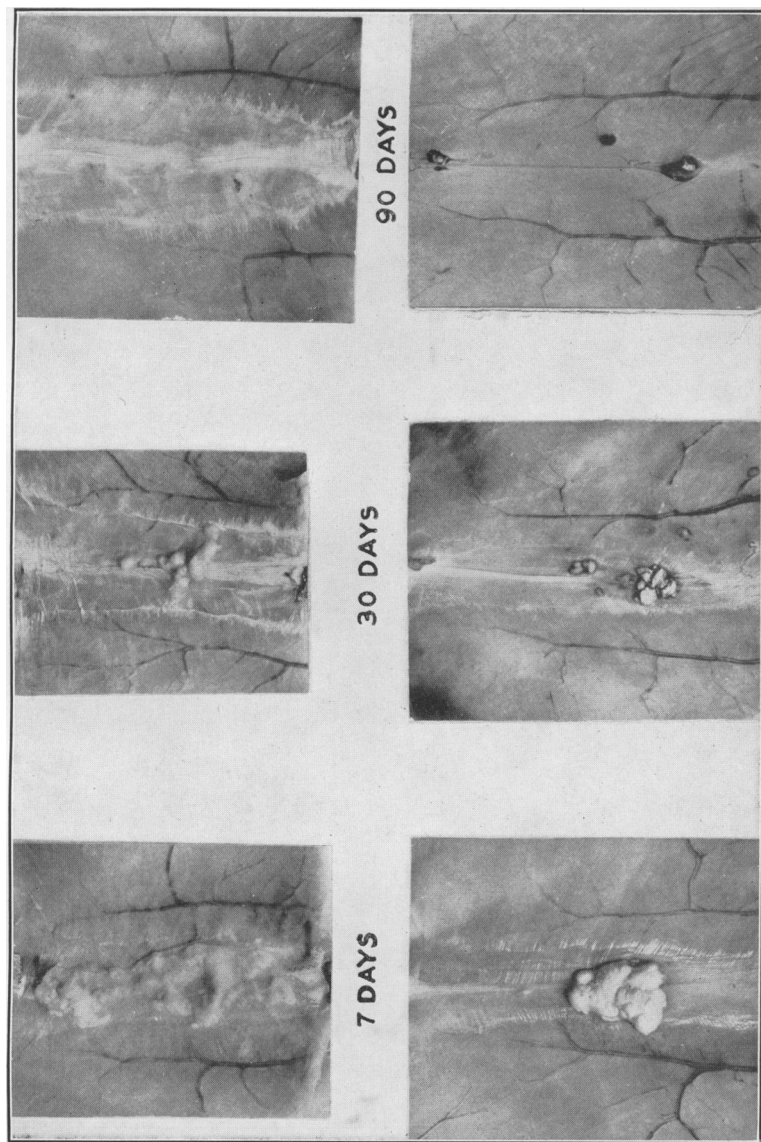
*Chert*.—An industrial dust. Chemical analysis: Total silica, 76.1 percent. Petrographic examination: Quartz and chert about 60 percent (about 25 percent of the silica is normal quartz). Calcite about 40 percent. Median particle size, 0.95 microns. Geometric standard deviation, 1.3 microns.

*Quartz-sericite*.—The source of this dust is not known. Chemical analysis: Total silica, 81.04 percent; calcium oxide, 0.30 percent; magnesium oxide, 0.45 percent; sodium oxide, 0.10 percent; potassium oxide, 0.98 percent; iron oxide, 0.25 percent; aluminum oxide, 14.26 percent; total water, 2.61 percent. Petrographic examination: Quartz, about 50 percent; muscovite (variety, sericite), about 45 percent; fibrous sericite, less than 5 percent. Dust passed through a 325-mesh screen.

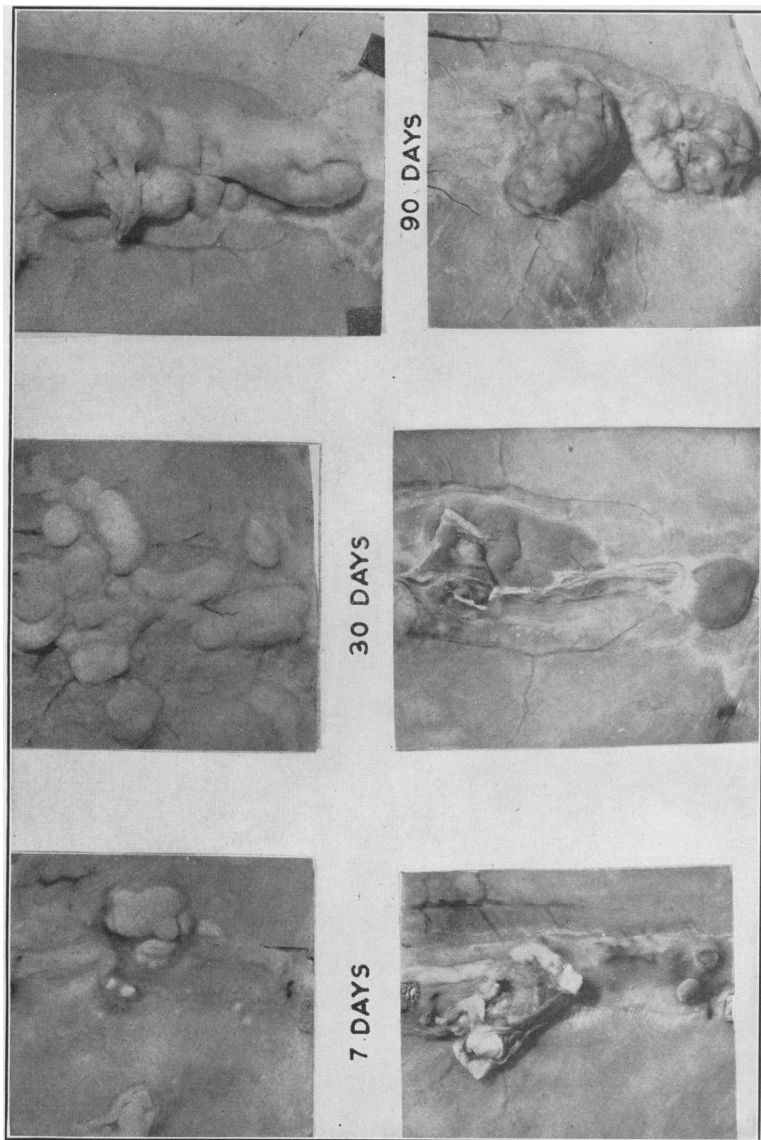
## THE INERT GROUP

Dusts of this group produced the same type of reaction in the first 2 weeks after injection that was noted in all of the other dusts; namely, an initial foreign body irritation. This early fixation reaction was not severe and subsided quite rapidly. As the time between injection and autopsy increased, the nodules, at first raised and rounded, became flattened and spreading. The edges became irregular, and numerous fine dust particles were noted in the peritoneum adjacent to the edges of the nodules. Collections of these particles were found at various other points in the peritoneum. The amount of dust in the peritoneal cavity found 360 days after injection was approximately the same as that noted in 7 days. The injected dust was not absorbed and did not initiate a cellular proliferation. The only change noted was that of the distribution of the dust in the peritoneum. The particles became more widespread in their dispersion as the interval between injection and examination increased, and this dissemination was shown microscopically to have been effected by macrophages. Variations in the reactions of these dusts were primarily in the color of the nodules, produced by the characteristic color of the individual dust.

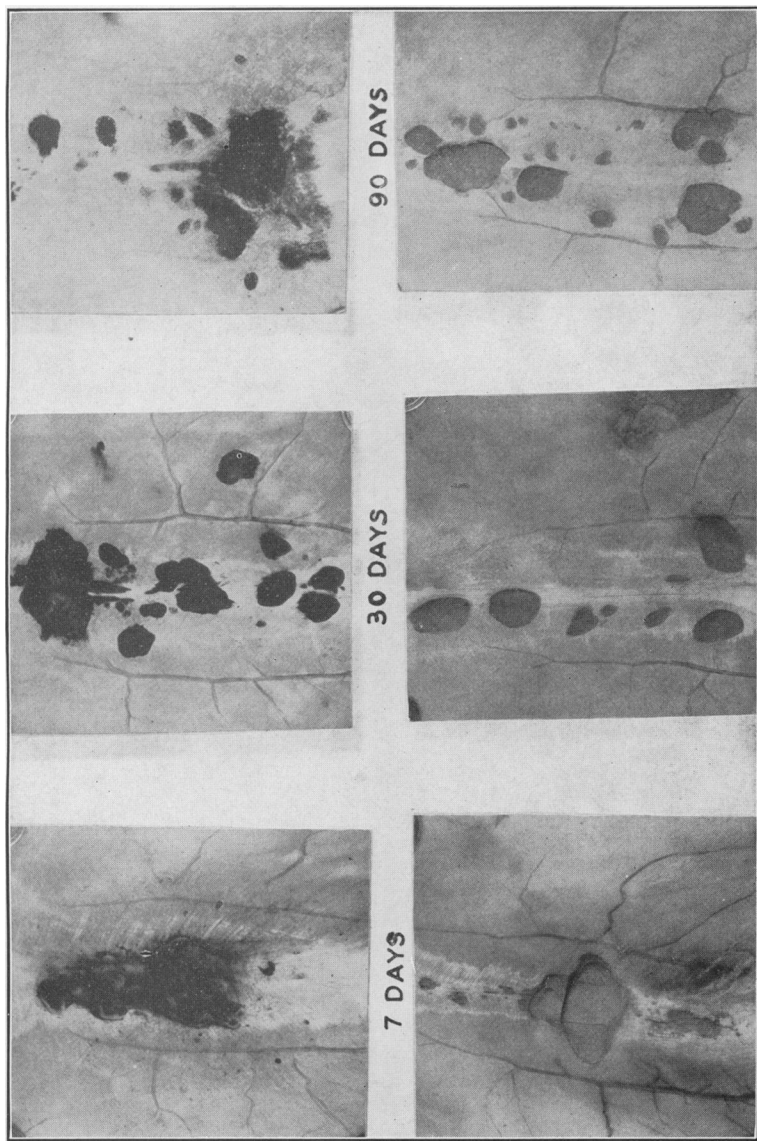
In 7 days microscopic examination showed that the dust nodule consisted of a large clump of densely packed dust with irregularities and lighter areas at its margin. No necrosis was noted with or about the dust. A narrow cellular zone, widest at the base, surrounded the dust. The nodule was covered by a thin layer of connective tissue merging into an underlying layer of fibroblasts. The basal portion was composed of fibroblasts, mostly in parallel arrangement. Some strands of fibroblasts were seen penetrating the dust mass. Only an occasional macrophage was noted near the dust. Isolated dust particles and small clumps of dust, some intracellular, were scattered throughout the cellular portion, and a few similar particles and clumps extended to a considerable distance in the peritoneal connective tissue adjacent to the edges of the nodules. Some of these particles were clearly in connective tissue cells and others were apparently in macrophages, but the color of the dust often obscured identification of the cells. Few to a moderate number of capillaries occurred throughout the nodules. As the duration of the tests increased, the macrophages became more numerous up to the sixtieth day of the tests. Fibrous tissue cells, many containing dust particles and a lesser number of fibroblasts, were also noted. After the peak of the increase in macrophages, connective tissue cells predominated in the remaining series. Fatty metamorphosis often occurred in about 60 days and increased progressively for the remaining period of the tests. Necrosis was not noted in nodules produced by inert dusts.



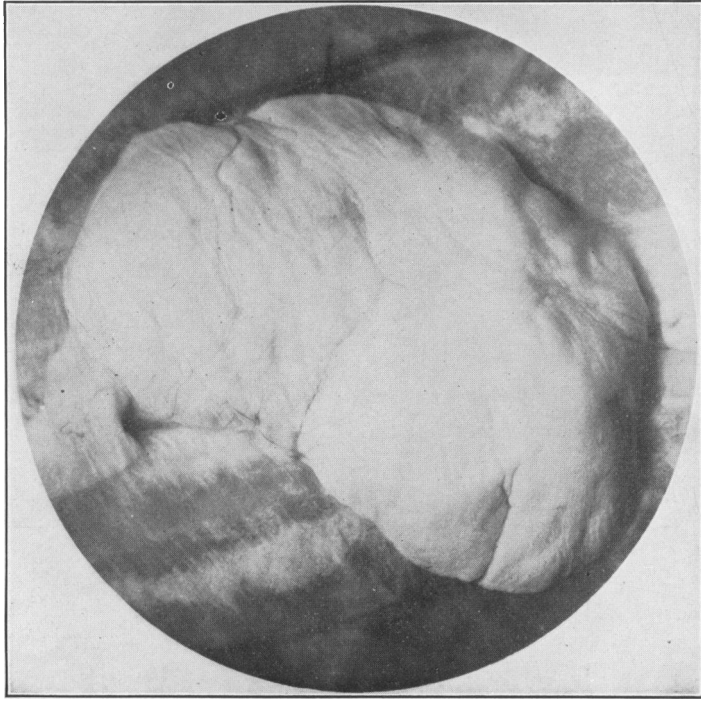
Above, calcite; below, limestone. Appearance of nodules on anterior abdominal wall 7, 30, and 90 days after injection.



Above, flint; below, chat. Appearance of nodules on anterior abdominal wall 7, 30, and 90 days after injection.



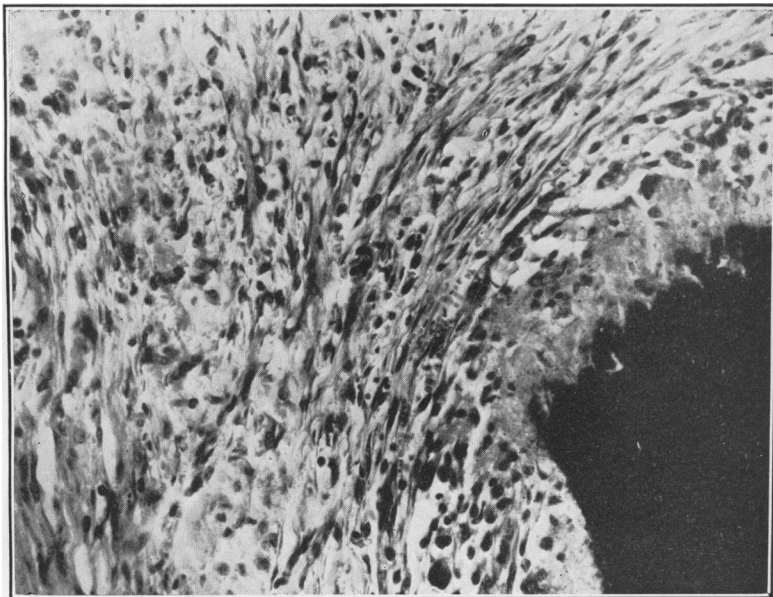
Above, anthracite coal; below, jewelers' rouge. Appearance of nodules on anterior abdominal wall 7, 30, and 90 days after injection.



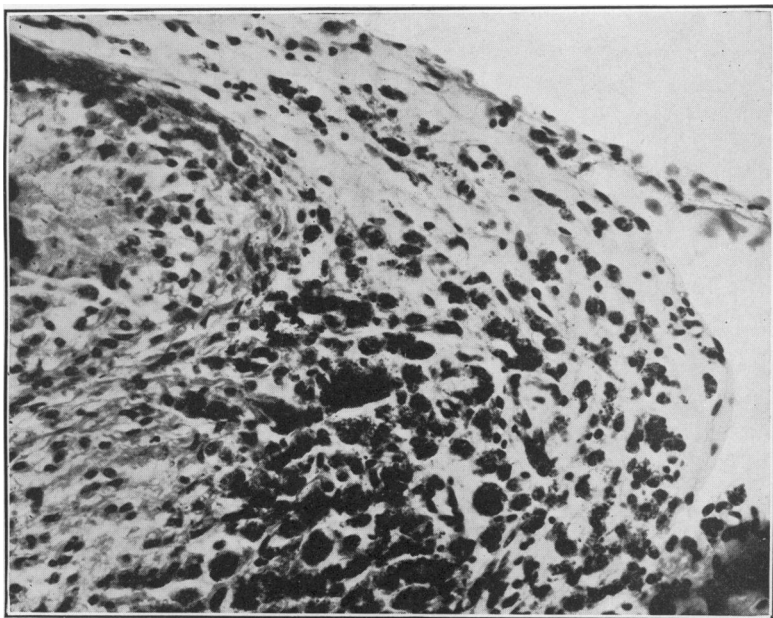
Quartz nodule, 90 days after injection.



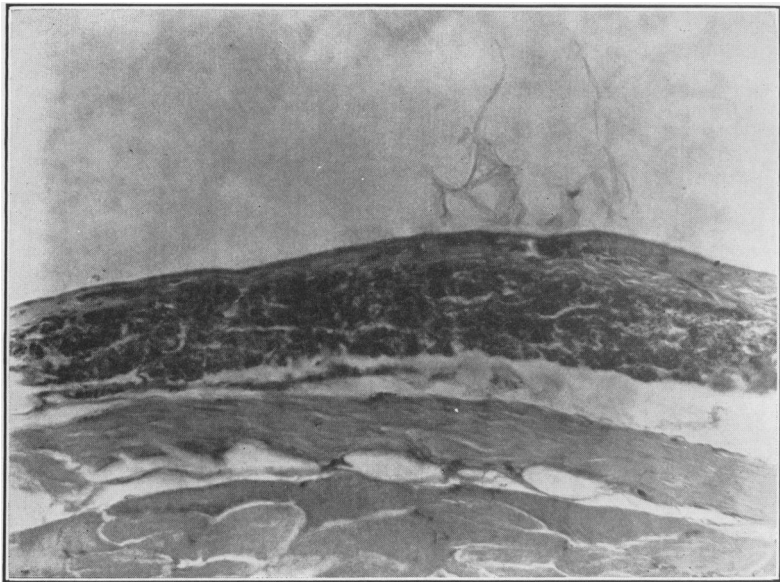
Calcite, 90 days after injection. Note fine, brown pigment granules in the peritoneum. These are all that remains of the nodule.



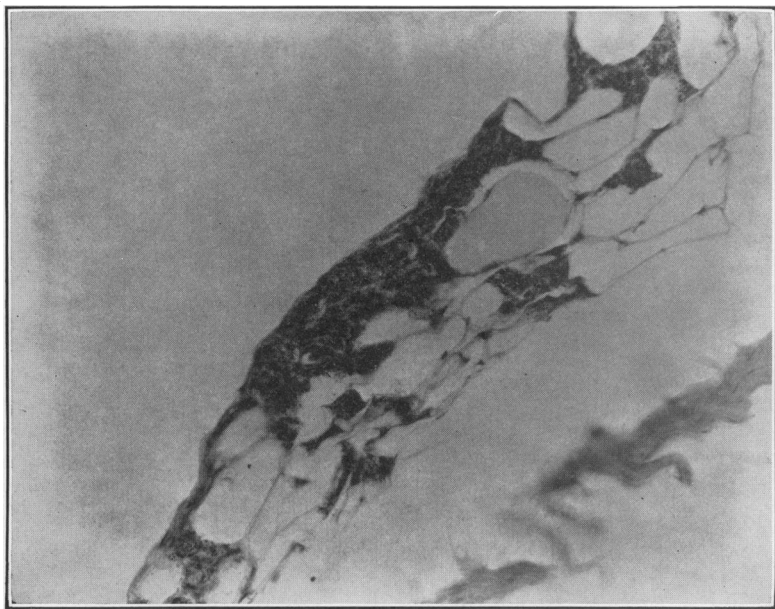
Limestone, 7 days after injection. X 655.



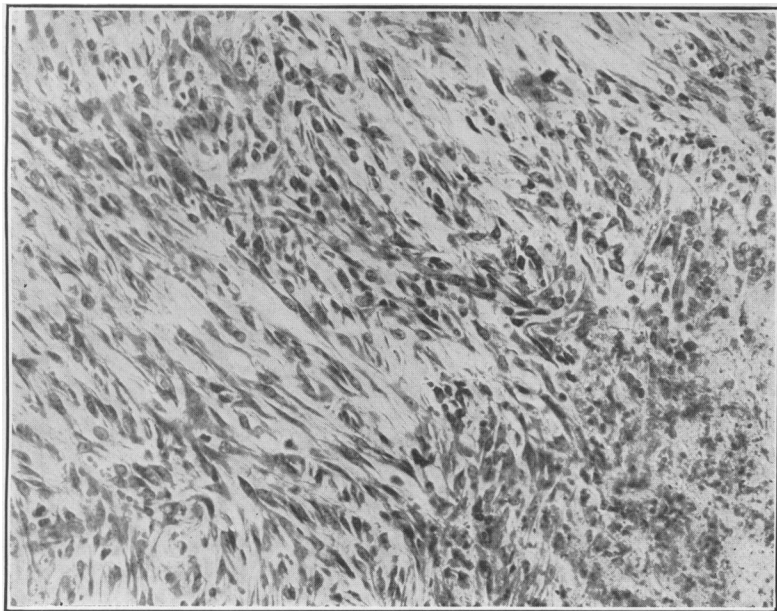
Limestone, 30 days after injection. X 655.



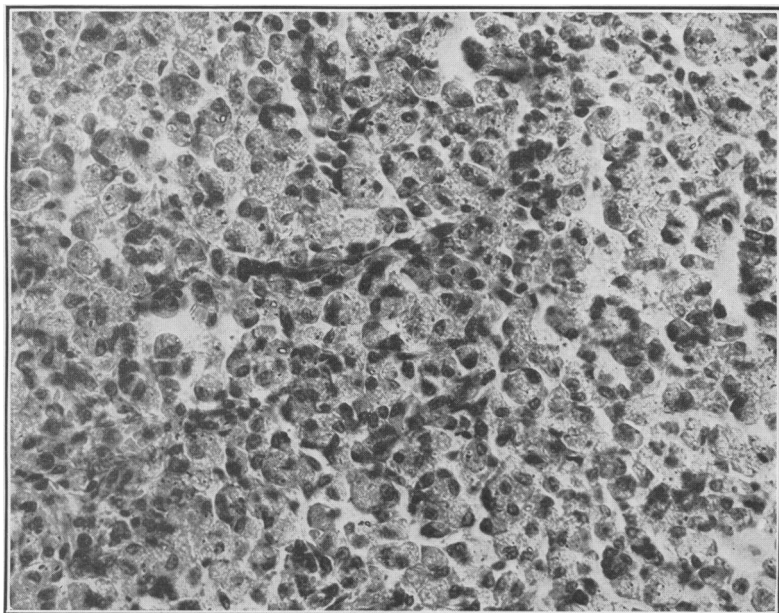
Limestone, 180 days after injection. X 655.



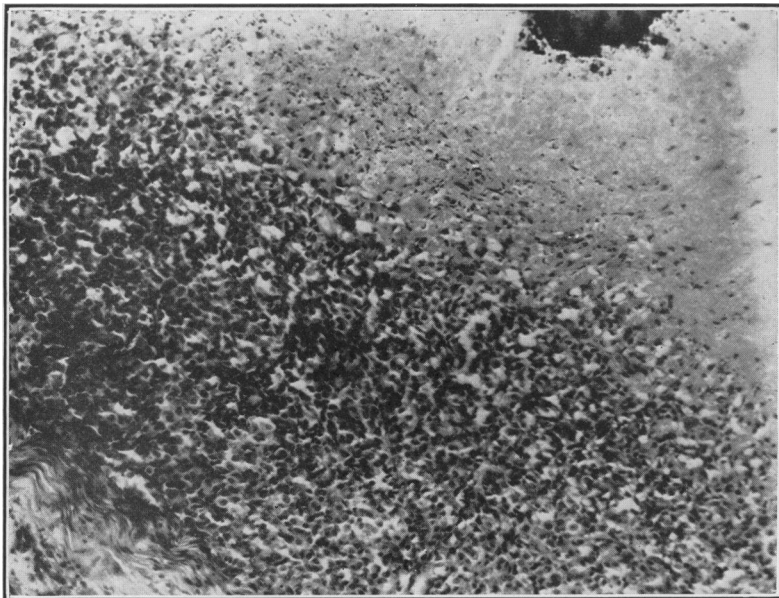
Limestone, 360 days after injection. X 655.



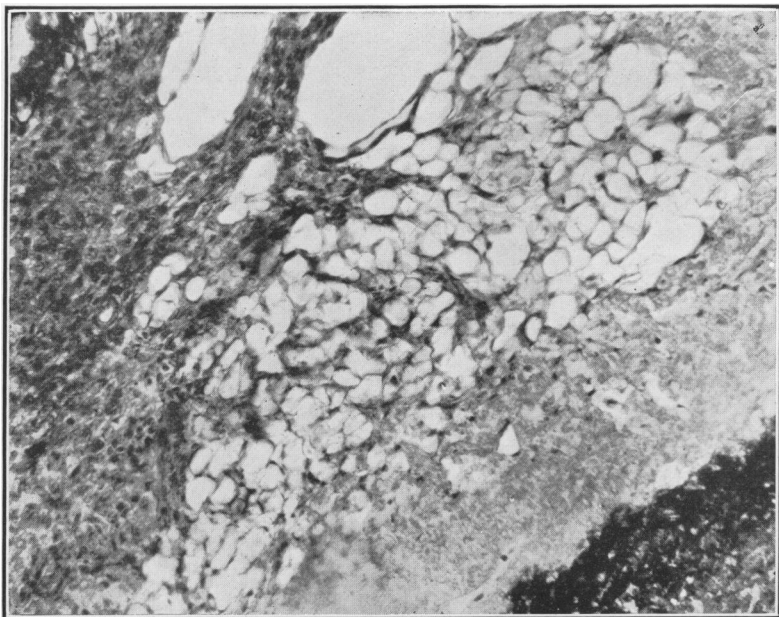
Quartz, 7 days after injection. X 655.



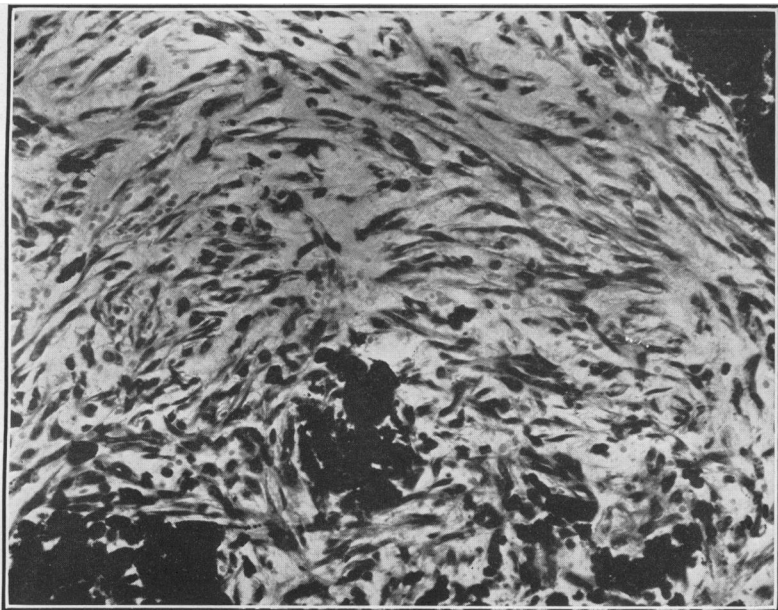
Quartz, 30 days after injection. X 655.



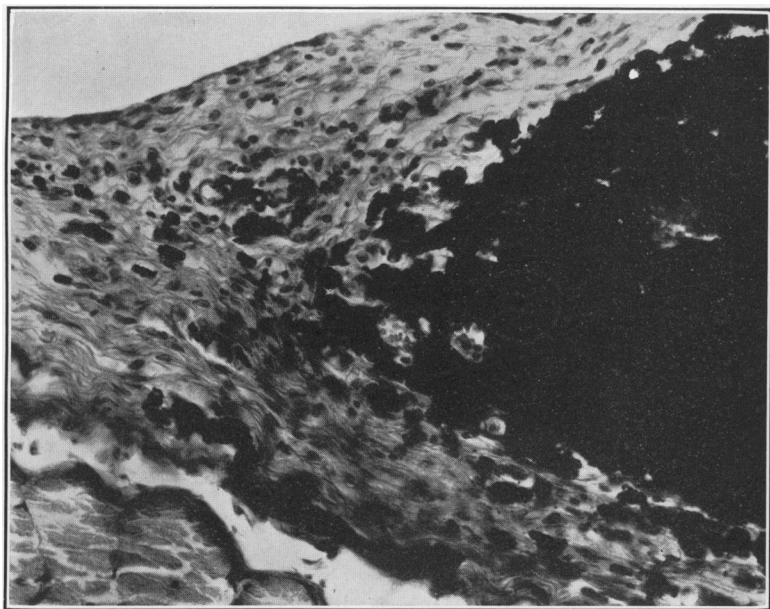
Quartz, 180 days after injection. X 305.



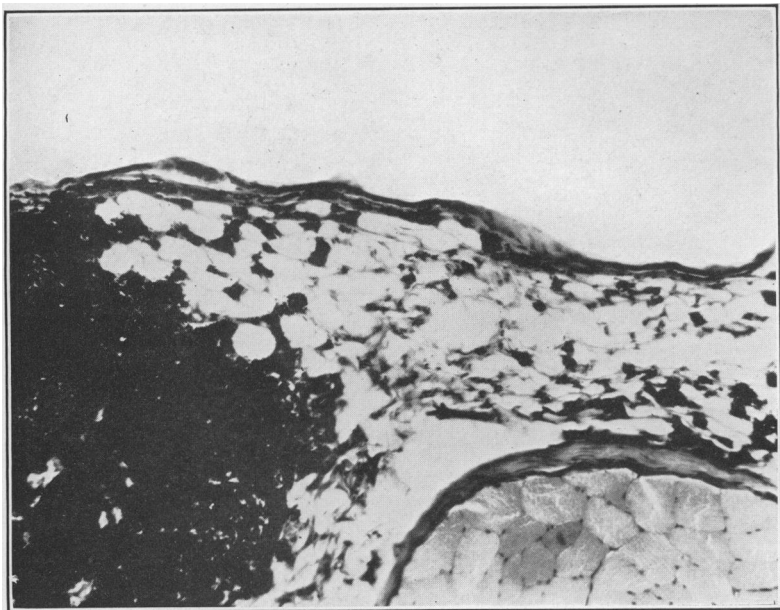
Quartz, 360 days after injection. X 655.



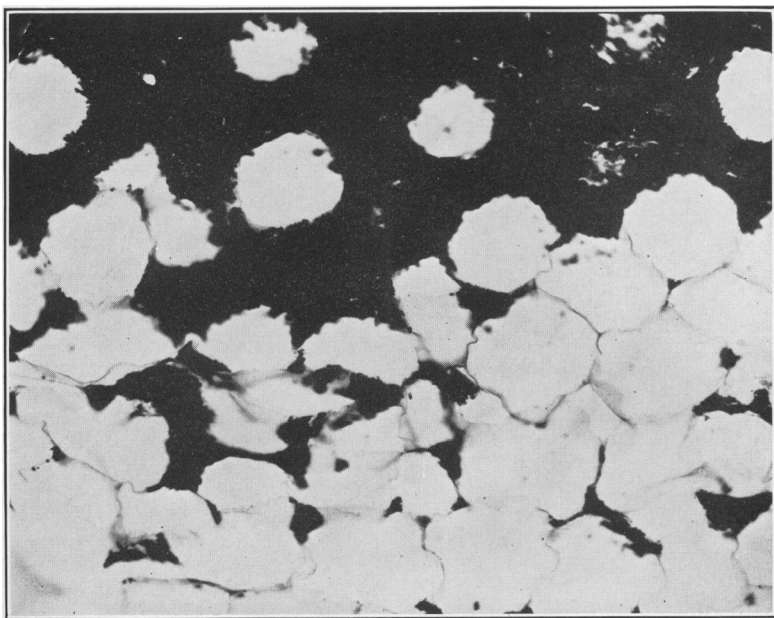
Anthracite coal, 7 days after injection. X 655.



Anthracite coal, 30 days after injection. X 655.



Anthracite coal, 180 days after injection. X 305.



Anthracite coal, 360 days after injection. X 655.

With certain dusts having a relatively large particle size (e. g., soapstone) and other physical characteristics there was a tendency for the slender dust particles to clump together in bundle-like groups. Macrophages arranged themselves concentrically about these groups and later fused together, forming aggregation giant cells with regularly spaced peripheral nuclei. These eventually assumed the appearance of an encircling capsule of a single layer of fibrous connective tissue cells. Other variations consist in changes in the speed with which isolated and grouped dust particles were carried into the peritoneum adjacent to the nodule and in colorations produced by characteristic tints of the individual dusts.

#### DUSTS CAUSING AN INERT REACTION

*Anthracite coal*.—An industrial dust. Chemical analysis: Ash, 16.0 percent; silica, 8.6 percent. Petrographic examination: Coal, about 95 percent, inorganic material, about 5 percent. About 95 percent of the inorganic material is quartz, about 5 percent is calcite, siderite, limonite, and rutile. Median particle size, 0.70 microns. Geometric standard deviation, 1.6 microns.

*Anthracite coal*.—An industrial dust. Chemical analysis: Ash, 12.6 percent; silica, 6.6 percent. Petrographic examination: Coal about 95 percent; inorganic material, about 5 percent. About 60 percent of the inorganic material is quartz; about 40 percent is calcite, with an occasional crystal of rutile. Median particle size, 0.45 microns. Geometric standard deviation, 2.1 microns.

*Bituminous coal*.—An industrial dust. Chemical analysis: Ash, 8.5 percent; silica, 0.8 percent. Petrographic examination: Mineral content (calcite) about 1 to 2 percent. Median particle size, 0.80 microns. Geometric standard deviation, 1.3 microns.

*Bituminous coal*.—An industrial dust. Chemical analysis: Ash, 8.0 percent; silica, 3.5 percent. Petrographic examination: Mineral content (quartz, calcite, clay) between 1 and 3 percent. Median particle size, 0.70 microns. Geometric standard deviation, 1.8 microns.

*Precipitator ash*.—An industrial dust. Chemical analysis: Total silica, 44.7 percent; moisture, 0.1 percent. Petrographic examination: Mostly spherical fused glass particles, with some semifused masses of crystallites, quartz, possibly calcite and coal fragments. Median particle size, 1.10 microns. Geometric standard deviation, 1.6 microns.

*Precipitator ash*.—An industrial dust. Chemical analysis: Total silica, 49.86 percent; calcium oxide, 6.03 percent; magnesium oxide, 3.01 percent; iron and aluminum oxides, 40.46 percent. Petrographic examination: Loosely consolidated, white, soft, grit-free ash, about 40 percent; partly rounded aggregates of semifused ash, about 45 percent; smooth fused glass globules, about 10 percent; normal quartz

fragments, about 5 percent; unburned coal, less than 1 percent. Dust passed through a 325-mesh screen.

*Soapstone*.—An industrial dust. Chemical analysis: Total silica, 36.8 percent; calcium oxide, 5.0 percent; magnesium oxide, 22.7 percent. Petrographic examination: Talc, about 55 percent; dolomite, about 30 percent; tremolite, about 15 percent. No quartz observed. Dust passed through a 325-mesh screen.

*Soapstone*.—An industrial dust. Chemical analysis: Total silica, 49.9 percent; calcium oxide, 1.7 percent; magnesium oxide, 26.2 percent. Petrographic examination: Talc, as plates or fibrous splinters, about 65 percent; tremolite, as long, fibrous crystals, about 30 percent; dolomite, about 5 percent. Median particle size, 3.25 microns. Geometric standard deviation, 1.7 microns.

*Talc*.—An industrial dust. Chemical analysis: Total silica, 49.0 percent; calcium oxide, 8.8 percent; magnesium oxide, 22.6 percent. Petrographic examination: Tremolite, about 60 percent; talc, about 40 percent. Dust passed through a 325-mesh screen.

*Talc*.—An industrial dust. Chemical analysis: Total silica, 56.54 percent; calcium oxide, 6.25 percent; magnesium oxide, 30.74 percent; calcium silicate, 11.00 percent; calcium carbonate, 1.88 percent; iron and aluminum oxides, 1.04 percent; ignition loss, 4.60 percent. Petrographic examination: Talc, mostly fibrous, about 75 percent; tremolite, partly altered to talc, about 25 percent; calcite and (or) dolomite, about 1 percent. Median particle size, 0.85 microns. Geometric standard deviation, 1.4 microns.

*Asbestos* (chrysotile).—An industrial dust. Chemical analysis: Total silica, 37.52 percent; calcium oxide, 2.00 percent; magnesium oxide, 36.85 percent; sodium oxide, 0.54 percent; potassium oxide, 0.08 percent; iron oxide, 7.70 percent; combined oxides, 10.30 percent; total water, 12.86 percent. Petrographic examination: Serpentine, in part chrysotile, about 85 percent; dolomite, about 5 percent; magnetite and (or) chromite, about 5 percent; talc, less than 5 percent. Dust was injected as received.

*Crocidolite*.—An industrial dust. Chemical analysis: Total silica, 50.86 percent; calcium oxide, 0.68 percent; magnesium oxide, 2.76 percent; sodium oxide, 5.72 percent; potassium oxide, 0.08 percent; iron oxide, 38.33 percent; combined oxides, 39.03 percent; total water, 5.02 percent. Petrographic examination showed fibrous material only. Dust was injected as received.

*Amosite*.—An industrial dust. Chemical analysis: Total silica, 48.31 percent; calcium oxide, 0.48 percent; magnesium oxide, 0.66 percent; sodium oxide, 0.72 percent; potassium oxide, 0.02 percent; iron oxide, 44.22 percent; combined oxides, 46.37 percent; total water, 3.62 percent. Petrographic examination showed predominating

individual fibers and about 1 or 2 percent of dolomite. Dust was injected as received.

*Feldspar*.—Chemical analysis: Total silica, 65.9 percent; calcium oxide, 0.81 percent; magnesium oxide, 0.10 percent; aluminum oxide, 19.55 percent; iron oxide, 0.28 percent; potassium oxide, 8.98 percent; sodium oxide, 3.18 percent. Petrographic examination: Feldspar (plagioclase-microcline), about 95 percent; normal quartz, about 5 percent. Dust passed through a 325-mesh screen.

*Silicon carbide*.—Pure manufactured silicon carbide. Chemical analysis: Silicon, 67.5 percent. Petrographic examination showed no impurities. Median particle size, 0.95 microns. Geometric standard deviation, 1.2 microns.

*Hematite* (jewelers' rouge).—An industrial dust. Chemical analysis: Total silica, 1.5 percent; iron oxide, 98.3 percent. Petrographic examination showed no impurities. Median particle size, 0.75 microns. Geometric standard deviation, 1.5 microns.

*Calcium phosphate*.—An industrial dust. Chemical analysis: Calcium phosphate, 75.38 percent; calcium carbonate, 3.98 percent; calcium fluoride, 6.80 percent; magnesium carbonate, 0.51 percent; iron oxide, 3.08 percent; aluminum oxide, 3.12 percent; free silica, 2.70 percent; combined silica, 1.87 percent. Petrographic examination: Earthy phosphates (not apatite), about 97 percent; normal and chalcedonic quartz, about 3 percent. Dust passed through a 325-mesh screen.

*Sericite*.—A pure mineral dust. Chemical analysis: Total silica, 51.74 percent; calcium oxide, 0.61 percent; magnesium oxide, 1.74 percent; sodium oxide, 3.40 percent; potassium oxide, 4.48 percent; iron oxide, 5.83 percent; combined oxides, 31.82 percent; total water, 6.26 percent. Petrographic examination: Sericite and feldspar residues (fibrous sericite predominates), about 95 percent; quartz, less than 5 percent. Dust passed through a 325-mesh screen.

#### SUMMARY

1. A definite quantity of dust in suspension was injected intraperitoneally into guinea pigs.

2. The response caused by the dust in the peritoneal cavity was constant in all of the animals injected with an individual dust and could be classified as an absorptive, proliferative, or inert reaction.

3. In the absorptive reaction the injected dust disappeared from the peritoneal cavity without the production of scar tissue.

4. In the proliferative reaction the nodules produced by the dust continued to increase in size up to 90 days after injection.

5. In the inert reaction the amount of injected dust remained approximately the same in the peritoneal cavity throughout the

various periods, but the nodules became more flattened and fine particles of dust were carried over rather extensive areas in the peritoneum by phagocytes.

6. Calcite, limestone, precipitated calcium carbonate, gypsum, and cement exhibited an absorptive reaction.

7. Quartz, tripoli, and siliceous chert produced a proliferative reaction.

8. Anthracite coal, bituminous coal, precipitator ash, soapstone, talc, asbestos, crocidolite, amosite, feldspar, silicon carbide, hematite, calcium phosphate, and sericite were inert in reaction.

#### CONCLUSIONS

The tissue of the peritoneal cavity responds actively to a dust introduced as a foreign body, and this response is of such a character that it may be used as a basis for the classification of industrial dusts. This response falls into three groups; namely, one of absorption, one of proliferation, and one of inertness. While, in these experiments, animals were kept on test for as long as 360 days, the response is sufficiently well marked in 90 days to determine the type of reaction, and often conclusions can be reached in 30 days, particularly if the reaction is one of absorption or proliferation. The reaction elicited by each dust was constant and uniform in all the animals injected with that dust.

The results obtained by the method used so far seem to indicate that some relationship exists between the types of reactions produced in the peritoneal tissue by a given dust and the ability of this dust to produce a characteristic type of pneumoconiosis. Thus, an absorptive reaction may indicate that the dust is relatively harmless, while a proliferative reaction, characteristic of pure silica (quartz) may be associated with definite ability to produce a nodular type of pulmonary fibrosis.

Interpretation of the significance of the dusts causing inert reactions is more difficult, but it appears logical to assume that dusts which show a tendency to remain in the tissues should be considered as potentially harmful, though not as dangerous as those causing a proliferative response. It is likewise logical to assume, and it has been proved to some extent in this laboratory, that silica mixed with an inert dust causes a modified proliferative reaction.

With this biological method of classification, which, in a number of instances, has been correlated with clinical observations and industrial surveys, it is quite possible to use intraperitoneal injection methods to determine the pneumoconiotic potentialities of a dust in a relatively short time, usually 60 days.

## ACKNOWLEDGMENTS

Acknowledgment is made of the kindness of Mr. W. A. Selvig of the United States Bureau of Mines and of Associate Chemist F. H. Goldman of the United States Public Health Service for the chemical analyses of the dusts used in these experiments. The petrographic examinations were made by Dr. Alton Gabriel of the United States Bureau of Mines.

Acknowledgment is also made to Technical Editor T. I. Edwards and Passed Assistant Sanitary Engineer J. M. DallaValle, of the Public Health Service, for assistance in preparing this report.

## GLUTATHIONE AND MALIGNANT GROWTH

By CARL VOEGTLIN, *Medical Director*, J. M. JOHNSON, *Senior Chemist*, and J. W. THOMPSON, *Associate Pharmacologist, Division of Pharmacology, National Institute of Health, United States Public Health Service*

Fifteen years have passed since the discovery of glutathione as a normal constituent of mammalian tissues. During that time much work has been done with this interesting substance, but our present knowledge is quite insufficient to give a clear picture of its physiological functions. However, there are definite indications that glutathione can exert a marked influence on the proliferation of cells and on the activity of certain intracellular enzymes. It is of interest, therefore, to ascertain whether under certain conditions glutathione can influence the proliferation of neoplasms. This question has never before been submitted to an experimental test.

The plan of procedure in the present investigation is based on the following considerations. The tripeptide glutathione is composed of cystine, glutamic acid, and glycine. A diet deficient in cystine and methionine, but adequate in all other respects, does not permit normal growth of young rats. Therefore, the first problem to be solved is to determine whether neoplastic growth can be inhibited by feeding adult tumor animals on a diet deficient in cystine and methionine, but adequate enough for maintenance. If, under these conditions, tumor growth is inhibited, then the next question is whether the administration of glutathione to animals maintained on the deficient diet will accelerate tumor growth.

## EXPERIMENTAL

The diet used has the following composition:

	<i>Parts</i>
Whole-milk powder.....	16.7
Cod-liver oil.....	3.0
Brewers' yeast.....	4.0
Starch.....	52.3
Salt mixture no. 185.....	4.0
Butterfat.....	20.0

Based on the total nitrogen determinations (Kjeldahl), 16.7 g of whole-milk powder supplies 5 g of milk protein, and 4 g of brewers' yeast are equivalent to 1.6 g of yeast protein. However, allowance should be made for the presence in yeast of considerable amounts of non-protein nitrogen, such as nucleic acid. The vitamin B<sub>1</sub> and B<sub>2</sub> potency of the laboratory sample of brewers' yeast (no. 2) used is given by Smith and Seidell (1936). The salt mixture is no. 185, devised by McCollum. As will be noted, this basal diet is similar in composition to that used by Jackson and Block (1932) for proving that methionine is capable of stimulating normal growth in rats on a diet low in cystine.

*Growth of young mice on deficient diet.*—In order to furnish evidence that this basal diet does not permit normal growth, healthy young male mice from our breeding colony were placed on this diet for about 2 months. Chart 1 illustrates the results which were obtained. It is evident that normal growth is greatly inhibited. Furthermore, it is obvious that supplementing the diet with 0.4 percent of *l*-cystine results in an abrupt stimulation of growth, the rate approximating that obtained with an adequate diet (Thompson and Mendel, 1917–18).

*Tumor growth on deficient diet.*—For the study of the influence of the deficient diet upon malignant growth we again chose, as in previous work, adult mice from our breeding colony, which was originally obtained through the kindness of Dr. B. T. Simpson and Mr. M. C. Marsh, of the State Institute for the Study of Malignant Disease, in Buffalo. Female mice showing small spontaneous mammary carcinomas were put into individual cages and fed on the deficient diet for a sufficiently long time to permit a fair estimate of the tumor-growth rate. The latter was estimated by carefully measuring the two greatest diameters of the tumors twice weekly and plotting the tumor areas (product of the two dimensions) as ordinates against time in days as abscissas. The animals were given the diet *ad libitum*, and a careful record of the food consumption was kept, except in the experiments illustrated by chart 2. The animals were weighed every time that the tumor size was measured. The experiments were terminated in all cases when the tumors ulcerated, because ulceration introduces uncontrollable factors. At the conclusion of each experiment the tumors were submitted for histological examination to Passed Assistant Surgeon L. L. Ashburn for verification of their malignant nature. We are indebted to Dr. Ashburn for his kind assistance.

The vast majority of tumor animals placed on the deficient diet showed a greatly reduced rate of tumor growth as compared with the high tumor-growth rate in animals maintained on the stock diet, which is composed essentially of 30 percent whole milk powder and 70 percent ground whole wheat. It is well known that considerable

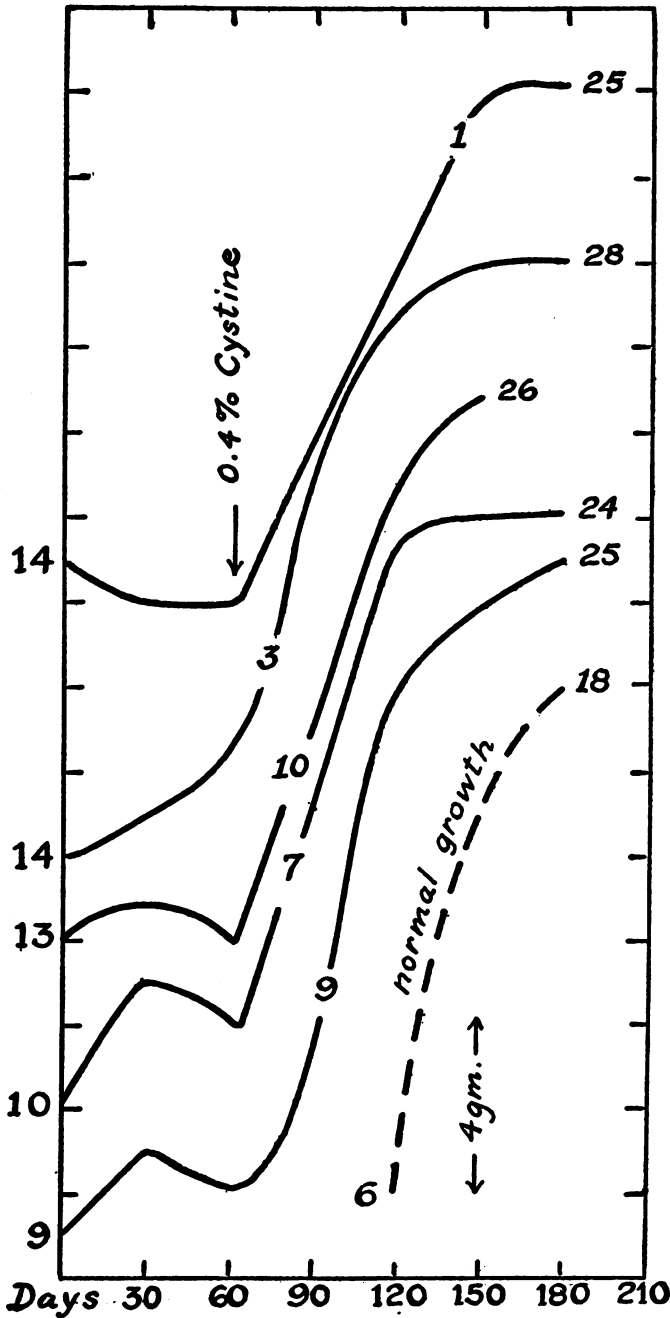


CHART 1.—Growth of young mice. Shows failure of normal growth on the deficient diet and the prompt resumption of growth following the administration of the cystine supplement. The figures at the beginning and end of the curves represent the corresponding body weights in grams. (Numbers in broken sections of the graphs in the charts accompanying this article represent the numbers of experimental animals.)

differences occur in the individual growth rate of healthy young animals maintained on partially deficient diets, even under the best controlled conditions. Similar differences were encountered in the tumor growth in the animals included in this report. These differences are clearly brought out in the first part of the curves presented in charts 2 to 6. Some of the tumors become stationary as soon as the animal is placed on the deficient diet; others grow for some time and then fail to grow; still others grow at a constant moderate rate until the supplement is given; and a few tumors were eliminated because they showed a relatively high growth rate and were therefore unsuited for testing the stimulating action of a supplement.

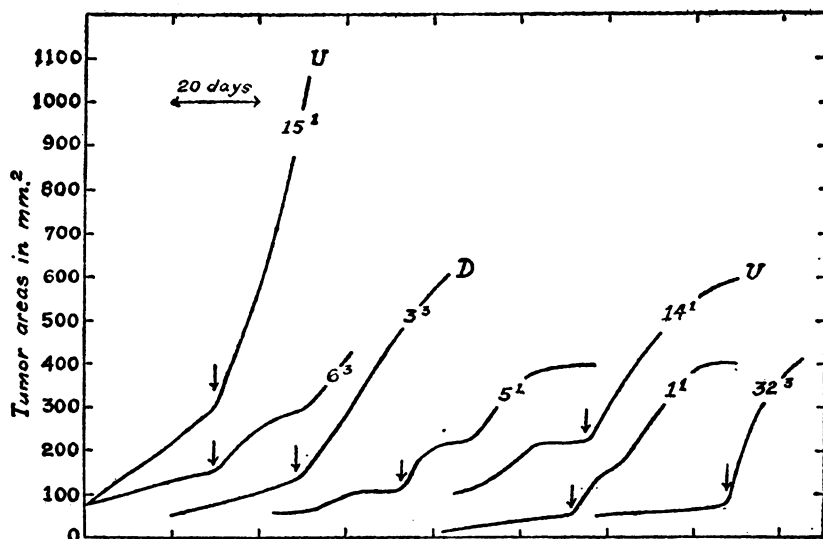


CHART 2.—Tumor growth. The first part of the curves shows the slow tumor growth on the deficient diet. The addition of 0.6 percent cystine to the diet (indicated by the arrow) shows the prompt stimulating action of this supplement on tumor growth. (U=ulcerated; D=died. Superior figures identify the animals in the several groups for record and for use in future studies.)

In two instances the tumors apparently regressed. One of these, which was of fairly large original size (150 mm<sup>2</sup>), ulcerated on the twelfth day of the experiment and disappeared on the sixteenth day. From the thirtieth day on, the diet of this animal was supplemented with 0.4 percent cystine. About 48 days later a small tumor had reappeared in the same location as that of the first tumor. This tumor grew rapidly and the animal died 25 days later. A tumor in another animal apparently completely regressed on the 19th day, but reappeared on about the one hundred and tenth day. These two instances of apparent regression are mentioned only incidentally, because we have never observed regression so far in many hundred tumor animals maintained on the stock diet.

*Action of cystine supplement on tumor growth.*—As has been mentioned previously, growth is strikingly stimulated in young mice maintained on the deficient diet, if the latter is supplemented with cystine. A group of tumor animals was therefore kept on the deficient diet for about 1 month. Thereafter the diet was supplemented with 0.6 percent of *l*-cystine. All of the 23 tumors of this series showed an abrupt stimulation of growth following the administration of the supplement. Chart 2 includes seven representative tumor growth curves of this series. The vertical arrows on the curves indicate the time at which the diet was supplemented with cystine. Table 1 gives the corresponding average body weights of each tumor animal on the basal diet and on this diet supplemented with cystine. It will be noted that there was a slight increase in weight during the period when the supplement was given.

TABLE 1.—Average body weights of tumor animals on basal diet and on basal diet supplemented with 0.6 percent cystine. (Corresponding tumor growth plotted in chart 2)

No. of animal *	Average weight on basal diet	Average weight on basal diet +0.6 percent cystine
	<i>Grams</i>	<i>Grams</i>
15 <sup>1</sup> .....	28	30
6 <sup>1</sup> .....	26	29
31 <sup>1</sup> .....	30	33
5 <sup>1</sup> .....	25	27
14 <sup>1</sup> .....	27	28
1 <sup>1</sup> .....	25	27
32 <sup>1</sup> .....	28	29

\*The superior figures in the first column of the tables differentiate the animals in the several groups and are retained for the identification of these animals in the original records and in connection with future studies.

*The action of glutathione on tumor growth.*—Pure crystalline reduced glutathione was prepared from bakers' yeast according to the method of Pirie (1930). Analysis showed that it had the correct nitrogen content. As it is not definitely known whether part or all of the glutathione incorporated in the diet is hydrolyzed before absorption from the gastrointestinal tract, it was deemed advisable to administer it subcutaneously. It was found that a 10 percent solution of glutathione, injected subcutaneously, produces considerable local tissue injury. Therefore, the substance was dissolved in sterile glass-distilled water, neutralized with NaOH, and brought up to volume with distilled water so as to yield a 10 percent solution. This solution was freshly prepared as needed. The subcutaneous injections were made daily except Sundays. No local or systemic reactions were observed. The results are illustrated by charts 3 to 6. The vertical arrows on

the curves indicate the beginning of glutathione injections. A single arrow implies that the dose was 15 mg per animal, a double arrow 30 mg, and a triple arrow 45 mg per mouse.

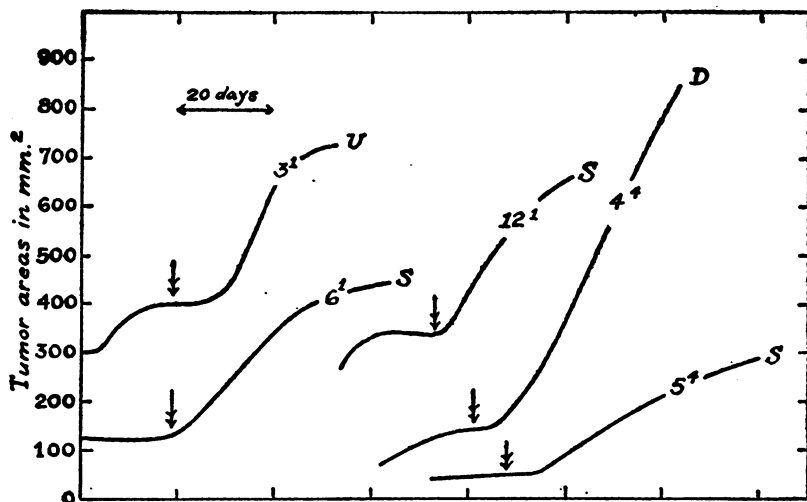


CHART 3.—Tumor growth. The first part of the curves shows the inhibition of tumor growth on the deficient diet. The subsequent administration of glutathione (as indicated by arrows) stimulates tumor growth. (U=ulcerated; D=died; S=killed.)

With very few exceptions the administration of glutathione produced a marked stimulation of tumor growth. The dose necessary to cause this effect apparently varies in different animals. For in-

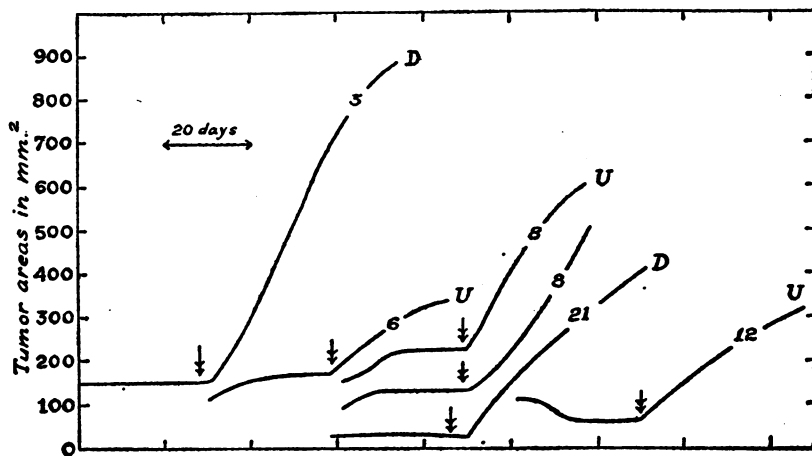


CHART 4.—Tumor growth. Inhibition of tumor growth and subsequent stimulating action of glutathione.

stance, in chart 5, 15 mg of glutathione increased the growth rate of the two tumors (7) in one animal. Tumor 24, however, on the same dosage was stimulated only temporarily, but again began to increase in size when the dose was increased to 30 mg. A similar situation is

met with in the case of tumor 17, where 45 mg were required to produce a prolonged and rapid increase in tumor size. In chart 6 curves of 4 multiple tumors (9) are plotted, two of which responded only

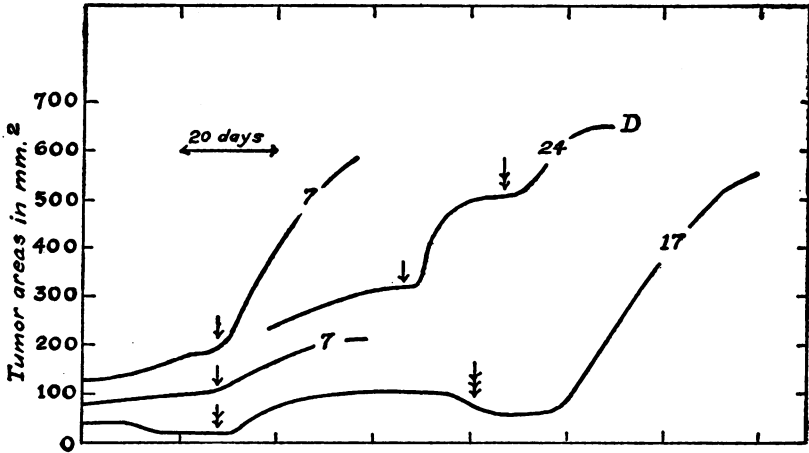


CHART 5.—Tumor growth. Confirms results illustrated by Charts 3 and 4 and in addition shows that the stimulating action of glutathione depends on dosage.

feebly to 30 mg and the other two not at all. It is quite possible that this failure of response may have been due to a too rapid excretion of the injected glutathione.

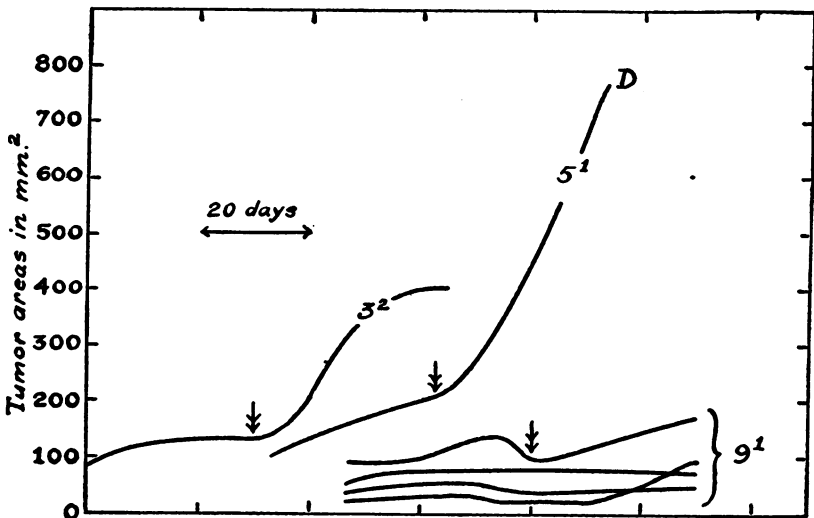


CHART 6.—Tumor growth. Confirms results illustrated by previous charts and also shows an exceptional case of lack of response to the administration of glutathione (curves 9¹).

The data on the average daily food consumption included in tables 2 and 3 indicate that the increase in the tumor growth rate following the administration of glutathione cannot be attributed to an increased food consumption.

TABLE 2.—*The average body weights of tumor animals and the average daily food consumption calculated for 25 grams of body weight. (Corresponding tumor growth plotted in chart 5)*

No. of animal	Basal diet		Basal diet + glutathione	
	Average weight	Average food consumption	Average weight	Average food consumption
3 <sup>1</sup> .....	Grams 33	Grams 2.88	Grams 32	Grams 2.73
6 <sup>1</sup> .....	28	2.79	31	2.89
12 <sup>1</sup> .....	29	3.62	29	2.90
4 <sup>1</sup> .....	31	2.74	33	2.82
5 <sup>1</sup> .....	28	2.52	31	2.77

TABLE 3.—*The average body weights of tumor animals and the average daily food consumption calculated for 25 grams of body weight. (Corresponding tumor growth plotted in charts 4, 5, and 6)*

No. of mouse	Basal diet		Basal diet + glutathione	
	Average weight	Average food consumption	Average weight	Average food consumption
3.....	Grams 29	Grams 2.67	Grams 30	Grams 2.81
6.....	24	2.43	26	2.67
8.....	31	2.70	32	2.15
21.....	28	2.70	27	2.73
12.....	29	2.84	27	3.11
7.....	35	2.15	34	1.89
24.....	24	1.92	• 23	• 2.53
17.....	23	3.18	• 24	• 2.36
			• 24	• 2.74
			• 25	• 3.35
3 <sup>2</sup> .....	30	2.91	29	2.91
5 <sup>1</sup> .....	20	3.80	24	3.56
9 <sup>1</sup> .....	29	3.01	31	3.48

\* The average weight and the average food consumption of mouse no. 24 and mouse no. 17 on the basal diet + glutathione are given in each case for two periods, corresponding to the two different doses of glutathione used (see chart 5).

#### DISCUSSION OF RESULTS

The results of the present investigation clearly show that it is possible by means of a diet deficient in cystine (and presumably methionine) to cause a marked slowing or even a cessation of the growth of a typical neoplasm. This same diet inhibits normal growth of young mice. Moreover, it is quite clear that, following a period of inhibited tumor growth, the administration of either cystine or glutathione causes a marked stimulation of tumor growth. A similar increase in the growth rate of young mice is produced by the cystine supplement. A paper has just appeared in which Dyer and du Vigneaud (1936) report that the growth of normal rats on a cystine deficient diet is accelerated by the oral or subcutaneous administration of glutathione. It would seem, therefore, that with respect to the growth-stimulating response to cystine or glutathione, respectively, there is no essential difference between normal growth of young mice and rats on the one hand, and the growth of the spontaneous mammary carcinoma on the other hand.

What is the explanation of the mechanism responsible for the stimulating effect of glutathione on malignant growth? It would be prema-

ture to offer an explanation in view of the complex and incompletely understood metabolic relationship between glutathione, cystine, cysteine and methionine (see Lewis, 1935). However, it can be said, at least, that progressive neoplastic growth requires a sufficient supply of cystine (or cysteine) for the synthesis of tumor proteins. Since glutathione occurs not only in normal but also in malignant tissues, it would seem also that the growing tumor must be supplied with glutathione or its constituent amino acids, particularly cystine (or cysteine). We reserve further comments on these questions until an investigation dealing with the action of methionine on tumor growth is completed.

One point needs emphasis, namely, that the growth of this mammary carcinoma can be inhibited by a diet deficient in cystine and methionine. In previous work (Voegtlin and Thompson, and Voegtlin and Maver, 1936) it was shown that a lysine-deficient diet also inhibits tumor growth. Thus evidence is accumulating which indicates that the proliferation of this typical malignant tumor can be inhibited by diets deficient in certain essential amino acids or peptides. It remains to be seen whether other types of malignant tumors, especially those induced by carcinogenic substances, behave similarly. Work along this line is in progress.

#### CONCLUSIONS

The growth rate of a spontaneous mammary carcinoma can be controlled by a diet deficient in cystine and methionine.

Following a period of growth inhibition, the administration of either cystine or glutathione exerts a striking stimulating action upon tumor growth.

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### DEATHS DURING WEEK ENDED NOV. 14, 1936

[From the Weekly Health Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended Nov. 14, 1936	Correspond- ing week, 1935
Data from 86 large cities of the United States:		
Total deaths.....	8,134	7,725
Deaths per 1,000 population, annual basis.....	11.4	10.8
Deaths under 1 year of age.....	553	496
Deaths under 1 year of age per 1,000 estimated live births.....	50	45
Deaths per 1,000 population, annual basis, first 46 weeks of year.....	12.1	11.3
Data from industrial insurance companies:		
Policies in force.....	68,609,080	67,721,419
Number of death claims.....	11,369	10,254
Death claims per 1,000 policies in force, annual rate.....	8.7	7.9
Death claims per 1,000 policies, first 46 weeks of year, annual rate.....	9.8	9.5

# PREVALENCE OF DISEASE

*No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring*

## UNITED STATES

### CURRENT WEEKLY STATE REPORTS

These reports are preliminary, and the figures are subject to change when later returns are received by the State health officers

Reports for Weeks Ended Nov. 21, 1936, and Nov. 23, 1937

*Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended Nov. 21, 1936, and Nov. 23, 1935*

Division and State	Diphtheria		Influenza		Measles		Meningococcus meningitis	
	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935
New England States:								
Maine.....	3				26	121	0	0
New Hampshire.....		1			4		0	0
Vermont.....	1				3	41	0	0
Massachusetts.....	6	7			75	62	2	2
Rhode Island.....					65	32	0	0
Connecticut.....	6	1	4	2	75	55	0	1
Middle Atlantic States:								
New York.....	29	32	113	14	104	481	8	8
New Jersey.....	11	25	17	8	28	23	0	0
Pennsylvania.....	30	60			50	133	8	8
East North Central States:								
Ohio.....	51	90	6	11	6	115	4	1
Indiana.....	49	89	12	15	7	7	3	0
Illinois.....	37	87	12	14	7	22	7	4
Michigan.....	32	23	1	2	31	37	2	6
Wisconsin.....	7	5	23	40	40	76	1	0
West North Central States:								
Minnesota.....	24	7		1	17	41	0	1
Iowa.....	3	28	3		1	7	3	1
Missouri.....	28	68	46	86	3	17	2	3
North Dakota.....	1	2	9	13	4	8	0	0
South Dakota.....	1	2		1	2	9	0	0
Nebraska.....	2	7			3	3	1	2
Kansas.....	17	16	1	12	4	11	1	0
South Atlantic States:								
Delaware.....		2			12	64	0	0
Maryland.....	11	16	7	9	42	6	9	3
District of Columbia.....	8	23		2	3	2	0	2
Virginia.....	92	68			23	23	4	6
West Virginia.....	22	48	20	25		18	2	0
North Carolina.....	100	78	9	10	18	37	1	0
South Carolina.....	19	8	324	163	6	5	0	0
Georgia.....	55	27		7		2	2	1
Florida.....	7	12	4	2	1	1	0	0
East South Central States:								
Kentucky.....	27	61	16	17	11	5	6	2
Tennessee.....	45	60	40	38	1	7	6	3
Alabama.....	44	37	40	15	2	12	2	1
Mississippi.....	25	23					1	0

See footnotes at end of table.

*Cases of certain communicable diseases reported by telegraph by State health officers.  
for weeks ended Nov. 21, 1936, and Nov. 23, 1935—Continued*

Division and State	Diphtheria		Influenza		Measles		Meningococcus meningitis	
	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935
<b>West South Central States:</b>								
Arkansas.....	6	28	23	44			0	0
Louisiana.....	27	24	24	4	1	8	1	4
Oklahoma.....	7	23	61	51	3	2	0	5
Texas.....	45	153	83	147	9	3	1	0
<b>Mountain States:</b>								
Montana.....	2	4	1	11	1	19	1	0
Idaho.....			5	2	73	14	1	0
Wyoming.....					2	3	0	0
Colorado.....	1	10			4	5	2	1
New Mexico.....	7	5	3	4	24		0	3
Arizona.....	1	5	22	36	18		0	1
Utah.....	1				17	1	3	0
<b>Pacific States:</b>								
Washington.....			1		10	87	3	1
Oregon.....		2	37	23	5	264	0	0
California.....	67	62	45	44	34	204	7	4
<b>Total</b> .....	<b>947</b>	<b>1,329</b>	<b>913</b>	<b>864</b>	<b>875</b>	<b>2,094</b>	<b>94</b>	<b>74</b>
<b>First 47 weeks of year</b> .....	<b>24,896</b>	<b>33,031</b>	<b>148,788</b>	<b>111,757</b>	<b>277,005</b>	<b>709,423</b>	<b>6,863</b>	<b>5,075</b>

Division and State	Poliomyelitis		Scarlet fever		Smallpox		Typhoid fever	
	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935
<b>New England States:</b>								
Maine.....	1	0	11	24	0	0	1	2
New Hampshire.....	0	0	2	6	0	0	0	1
Vermont.....	1	0	6	5	0	0	1	1
Massachusetts.....	1	10	105	192	0	0	1	1
Rhode Island.....	0	2	23	9	0	0	0	0
Connecticut.....	2	6	35	54	0	0	3	1
<b>Middle Atlantic States:</b>								
New York.....	4	28	334	395	0	0	8	13
New Jersey.....	0	4	51	79	0	0	2	11
Pennsylvania.....	4	13	391	397	0	0	21	15
<b>East North Central States:</b>								
Ohio.....	9	1	242	252	0	0	5	4
Indiana.....	0	0	124	189	2	2	3	3
Illinois.....	9	7	306	485	1	2	11	12
Michigan.....	2	8	291	222	1	0	3	4
Wisconsin.....	0	2	225	352	14	6	1	3
<b>West North Central States:</b>								
Minnesota.....	2	4	145	257	5	0	0	3
Iowa.....	3	2	80	116	2	2	3	3
Missouri.....	4	1	74	150	4	2	13	8
North Dakota.....	1	0	35	31	16	6	0	0
South Dakota.....	2	0	36	73	6	8	0	1
Nebraska.....	2	0	27	85	0	48	0	0
Kansas.....	2	0	231	127	10	11	3	6
<b>South Atlantic States:</b>								
Delaware.....	0	0	5	10	0	0	0	0
Maryland.....	0	5	62	71	0	0	10	15
District of Columbia.....	0	1	12	2	0	0	1	0
Virginia.....	0	1	75	51	0	0	13	13
West Virginia.....	0	0	77	119	0	2	14	5
North Carolina.....	0	7	105	76	0	0	10	4
South Carolina.....	1	1	11	2	0	0	10	2
Georgia.....	6	0	84	23	0	0	12	2
Florida.....	2	0	3	7	0	0	0	2

See footnotes at end of table.

*Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended Nov. 21, 1936, and Nov. 23, 1935—Continued*

Division and State	Poliomyelitis		Scarlet fever		Smallpox		Typhoid fever	
	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935	Week ended Nov. 21, 1935	Week ended Nov. 23, 1935	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935	Week ended Nov. 21, 1936	Week ended Nov. 23, 1935
<b>East South Central States:</b>								
Kentucky.....	5	4	68	75	0	0	14	7
Tennessee.....	6	6	70	74	0	5	11	4
Alabama <sup>1</sup> .....	4	0	28	12	0	0	3	2
Mississippi <sup>2</sup> .....	2	0	23	28	0	1	3	8
<b>West South Central States:</b>								
Arkansas.....	5	0	5	13	0	2	4	2
Louisiana.....	1	0	17	15	0	0	15	9
Oklahoma <sup>3</sup> .....	17	1	21	20	0	0	19	11
Texas <sup>4</sup> .....	1	0	42	66	2	0	20	31
<b>Mountain States:</b>								
Montana.....	0	1	69	116	23	40	0	0
Idaho.....	0	0	31	34	1	0	3	2
Wyoming.....	0	0	9	76	2	0	0	0
Colorado.....	2	0	39	85	3	1	2	1
New Mexico.....	1	1	27	25	1	0	4	11
Arizona.....	1	1	14	32	0	0	3	1
Utah <sup>5</sup> .....	0	0	17	105	0	0	0	0
<b>Pacific States:</b>								
Washington.....	0	0	59	80	2	37	2	0
Oregon.....	0	6	27	64	13	0	4	4
California.....	11	14	265	245	1	7	7	7
<b>Total.....</b>	<b>114</b>	<b>137</b>	<b>3,979</b>	<b>5,026</b>	<b>109</b>	<b>182</b>	<b>263</b>	<b>230</b>
<b>First 47 weeks of year.....</b>	<b>4,189</b>	<b>10,405</b>	<b>212,418</b>	<b>221,889</b>	<b>6,688</b>	<b>6,495</b>	<b>13,611</b>	<b>16,501</b>

<sup>1</sup> New York City only.

<sup>2</sup> Week ended earlier than Saturday.

<sup>3</sup> Rocky Mountain spotted fever, week ended Nov. 21, 1936, North Carolina, 1 case.

<sup>4</sup> Typhus fever, week ended Nov. 21, 1936, 34 cases, as follows: South Carolina, 2; Georgia, 20; Alabama, 7; Texas, 5.

<sup>5</sup> Exclusive of Oklahoma City and Tulsa.

## SUMMARY OF MONTHLY REPORTS FROM STATES

The following summary of cases reported monthly by States is published weekly and covers only those States from which reports are received during the current week:

State	Menin- gococ- cus menin- gitis	Diph- theria	Influ- enza	Mala- ria	Meas- les	Pel- lagra	Polio- mye- litis	Scarlet fever	Small- pox	Ty- phoid fever
<i>October 1936</i>										
California.....	12	191	106	38	169	13	35	715	2	83
Georgia.....	6	203	148	2,486	10	29	38	124	1	132
Illinois.....	17	134	39	17	50	1	256	832	11	93
Maryland.....	13	60	25	5	33	1	8	189	0	51
Michigan.....	4	71	6	11	80		58	729	1	49
Minnesota.....	6	68	4	1	67		5	292	22	3
Mississippi.....	3	96	2,172	5,598	62	266	15	65	0	42
Nevada.....			16				0	15	0	2
New York.....	33	70		12	236		33	878	0	121
Ohio.....	20	163	58	8	37		128	758	1	95
Pennsylvania.....	15	134		3	130	1	32	887	0	164
Rhode Island.....	1	3	1		128		0	70	0	3
Vermont.....		3			6		0	21	0	1
Wisconsin.....		17	82		74		13	652	9	14

## October 1936

Actinomycosis:	Cases	German measles—Contd.	Cases	Septic sore throat—Contd.	Cases
California.....	8	Maryland.....	16	Minnesota.....	5
Illinois.....	1	Michigan.....	35	New York.....	24
Michigan.....	2	New York.....	54	Ohio.....	68
Pennsylvania.....	1	Ohio.....	11	Wisconsin.....	10
Anthrax:		Pennsylvania.....	42	Tetanus:	
California.....	1	Rhode Island.....	2	California.....	11
New York.....	1	Wisconsin.....	21	Illinois.....	6
Chicken pox:		Granuloma, coccidioides:		Maryland.....	1
California.....	454	California.....	1	Michigan.....	2
Georgia.....	17	Hookworm disease:		New York.....	11
Illinois.....	383	Georgia.....	1, 175	Ohio.....	2
Maryland.....	96	Michigan.....	1	Pennsylvania.....	1
Michigan.....	682	Mississippi.....	239	Trachoma:	
Minnesota.....	273	Impetigo contagiosa:		California.....	25
Mississippi.....	107	Maryland.....	35	Georgia.....	1
Nevada.....	53	Jaundice, epidemic:		Illinois.....	51
New York.....	832	California.....	7	Mississippi.....	6
Ohio.....	681	Lead poisoning:		Ohio.....	3
Pennsylvania.....	1, 213	Maryland.....	3	Pennsylvania.....	3
Rhode Island.....	75	Ohio.....	10	Trichinosis:	
Vermont.....	78	Mumps:		California.....	12
Wisconsin.....	713	California.....	1, 335	New York.....	6
Conjunctivitis, infectious:		Georgia.....	82	Tularaemia:	
Georgia.....	13	Illinois.....	128	California.....	12
Dengue:		Maryland.....	128	Georgia.....	3
Georgia.....	6	Michigan.....	272	Illinois.....	8
Diarrhea:		Mississippi.....	141	Minnesota.....	2
Maryland.....	82	Nevada.....	4	Ohio.....	1
Ohio (under 2 years, enteritis included).....	37	Ohio.....	54	Typhus fever:	
Dysentery:		Pennsylvania.....	428	Georgia.....	108
California (amoebic).....	13	Rhode Island.....	25	Mississippi.....	1
California (bacillary).....	51	Vermont.....	25	New York.....	4
Georgia (amoebic).....	4	Wisconsin.....	217	Undulant fever:	
Georgia (bacillary).....	9	Ophthalmia neonatorum:		California.....	14
Illinois (amoebic).....	14	California.....	3	Georgia.....	3
Illinois (amoebic car- riers).....	27	Illinois.....	5	Illinois.....	8
Illinois (bacillary).....	35	Maryland.....	1	Maryland.....	2
Maryland.....	90	Mississippi.....	7	Michigan.....	8
Michigan (amoebic).....	4	New York.....	9	Minnesota.....	4
Michigan (bacillary).....	15	Ohio.....	63	Mississippi.....	3
Minnesota (amoebic).....	1	Pennsylvania.....	15	New York.....	17
Minnesota (bacillary).....	16	Wisconsin.....	1	Ohio.....	3
Mississippi (amoebic).....	79	Paratyphoid fever:		Pennsylvania.....	9
Mississippi (bacillary).....	474	California.....	3	Rhode Island.....	2
New York (amoebic).....	12	Georgia.....	3	Vermont.....	5
New York (bacillary).....	135	Illinois.....	2	Wisconsin.....	5
Ohio (amoebic).....	1	Minnesota.....	1	Vincent's infection:	
Ohio (bacillary).....	14	New York.....	11	Illinois.....	25
Pennsylvania (bacil- lary).....	11	Ohio.....	1	Maryland.....	16
Epidemic encephalitis:		Plague:		Michigan.....	36
California.....	5	California.....	1	New York.....	80
Georgia.....	1	Puerperal septicemia:		Whooping cough:	
Illinois.....	11	Mississippi.....	11	California.....	699
Maryland.....	1	Rabies in animals:		Georgia.....	60
Michigan.....	1	California.....	85	Illinois.....	502
New York.....	8	Illinois.....	20	Maryland.....	493
Ohio.....	1	Mississippi.....	9	Michigan.....	799
Pennsylvania.....	6	New York.....	6	Minnesota.....	153
Wisconsin.....	4	Relapsing fever:		Mississippi.....	174
Food poisoning:		California.....	1	Nevada.....	26
California.....	66	Septic sore throat:		New York.....	1, 000
German measles:		California.....	3	Ohio.....	580
California.....	52	Georgia.....	38	Pennsylvania.....	1, 682
Illinois.....	27	Illinois.....	2	Rhode Island.....	53
		Maryland.....	11	Vermont.....	42
		Michigan.....	17	Wisconsin.....	478

<sup>1</sup> Exclusive of New York City.

## RODENT PLAGUE IN ELDORADO COUNTY, CALIF.

A chipmunk, *Eutamias speciosus frater* Allen, trapped 3 miles south of Meyers, Eldorado County, Calif., on October 9, 1936, was reported under date of November 11 to have been proved plague infected.

## WEEKLY REPORTS FROM CITIES

*City reports for week ended Nov. 14, 1936*

This table summarizes the reports received weekly from a selected list of 140 cities for the purpose of showing a cross section of the current urban incidence of the communicable diseases listed in the table. Weekly reports are received from about 700 cities, from which the data are tabulated and filed for reference.

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Small-pox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
<b>Maine:</b>											
Portland	0		0	0	3	0	0	0	0	4	26
<b>New Hampshire:</b>											
Concord	0		0	0	1	0	0	1	0	0	13
Manchester	0		0	0	2	0	0	0	0	0	12
Nashua	0			0		0	0		0	0	
<b>Vermont:</b>											
Barre											
Burlington	0		0	1	0	1	0	0	0	0	9
Rutland	0		0	0	0	1	0	0	1	0	9
<b>Massachusetts:</b>											
Boston	3		0	6	16	31	0	9	0	127	203
Fall River	1		0	0	1	4	0	1	0	3	29
Springfield	0		0	0	3	0	0	1	0	11	32
Worcester	0		0	3	1	3	0	1	0	25	43
<b>Rhode Island:</b>											
Pawtucket	0		0	0	0	0	0	0	0	0	17
Providence	2		1	0	4	10	0	1	0	15	64
<b>Connecticut:</b>											
Bridgeport	0		0	4	4	2	0	1	0	8	34
Hartford	0		0	1	2	9	0	2	0	10	
New Haven	0		0	2	1	2	0	0	0	4	41
<b>New York:</b>											
Buffalo	0		0	11	12	18	0	3	1	13	121
New York	21	7	3	30	96	78	0	77	6	100	1,398
Rochester	0		0	0	4	3	1	0	0	5	71
Syracuse	2		0	0	4	6	0	0	1	13	47
<b>New Jersey:</b>											
Camden	1		0	0	1	1	0	2	0	2	34
Newark	0	1	0	1	16	4	0	9	0	32	123
Trenton	0		0	0	2	4	0	1	0	2	32
<b>Pennsylvania:</b>											
Philadelphia	5	6	2	5	27	35	0	21	9	118	424
Pittsburgh	1	2	2	5	24	41	0	4	1	25	174
Reading	0		0	0	1	3	0	1	2	39	25
Scranton	1			0		4	0		0	0	
<b>Ohio:</b>											
Cincinnati	8		1	0	13	9	0	4	0	0	130
Cleveland	4	10	2	2	12	37	0	12	3	39	172
Columbus	3	1	1	0	5	12	0	3	0	6	72
Toledo	0	1	1	1	2	5	0	4	0	12	74
<b>Indiana:</b>											
Anderson	0		0	0	1	1	0	0	0	1	9
Fort Wayne	2		0	0	0	15	0	0	0	0	15
Indianapolis	4		1	2	10	21	0	1	0	11	111
Muncie	0		0	0	2	6	0	0	0	0	13
South Bend	0		0	1	2	3	0	0	0	2	23
Terre Haute	1		0	0	0	3	0	0	0	0	24
<b>Illinois:</b>											
Alton	1		0	0	1	1	0	0	0	1	7
Chicago	9	6	3	2	42	139	0	32	3	73	672
Elgin	0		0	0	0	0	0	0	0	7	3
Moline	0		0	1	0	2	0	0	0	5	4
Springfield	0		0	0	3	1	0	0	0	3	21
<b>Michigan:</b>											
Detroit	22	1	0	5	14	61	0	16	0	65	256
Flint	7		0	2	2	7	0	0	0	2	31
Grand Rapids	0		0	0	1	10	0	0	0	11	35
<b>Wisconsin:</b>											
Kenosha	0		0	1	0	7	0	0	0	4	2
Madison	0		0	1	0	3	0	0	0	4	22
Milwaukee	0		0	3	6	20	0	1	0	45	94
Racine	0		0	1	1	20	0	1	0	5	11
Superior	0		0	0	1	2	0	0	0	3	10
<b>Minnesota:</b>											
Duluth	0		0	1	2	5	0	2	1	2	23
Minneapolis	7		1	1	5	9	0	0	0	12	101
St. Paul	0	1	1	4	10	11	0	1	0	15	
<b>Iowa:</b>											
Cedar Rapids	0			0		1	0		0	1	
Davenport	0			0		2	0		0	0	

## City reports for week ended Nov. 14, 1936—Continued

State and city	Diph- theria cases	Influenza		Mea- sles cases	Pneu- monia deaths	Scar- let fever cases	Small- pox cases	Tuber- culosis deaths	Ty- phoid fever cases	Whoop- ing cough cases	Deaths, all causes
		Cases	Deaths								
Iowa—Continued.											
Des Moines	1			0		7	0		0	0	28
Sioux City	0			1		8	0		0	1	
Waterloo	0			0		4	0		0	6	
Missouri:											
Kansas City	1		0	1	8	16	0	3	4	1	93
St. Joseph											
St. Louis	7	1	0	1	20	27	0	9	3	12	207
North Dakota:											
Fargo	0		0	0	0	5	0	0	0	0	11
Grand Forks	0			0		0	0		0	0	
Minot	0		0	0	0	0	0	0	0	0	7
South Dakota:											
Aberdeen	0			0		3	0		0	0	
Sioux Falls	0		0	0	0	5	0	0	0	0	12
Nebraska:											
Omaha	4		1	0	5	14	0	3	0	5	56
Kansas:											
Topeka											
Wichita	0		0	0	1	2	0	0	0	9	18
Delaware:											
Wilmington	0		0	4	2	1	0	1	0	2	25
Maryland:											
Baltimore	7	1	0	20	24	16	0	15	1	110	223
Cumberland	0		0	0	1	3	0	0	0	0	15
Frederick	0		0	0	2	0	0	0	1	0	5
Dist. of Col.:											
Washington	11		0	0	7	12	0	12	0	18	143
Virginia:											
Lynchburg	1		0	0	1	1	0	0	0	0	11
Norfolk	0		0	0	2	3	0	1	0	2	25
Richmond	1		0	0	7	3	0	2	0	0	57
Roanoke	3		0	0	0	4	0	0	0	0	13
West Virginia:											
Charleston	1		0	0	2	1	0	1	1	0	17
Huntington	0			0		4	0		1	0	
Wheeling	0		0	0	1	3	0	0	0	0	19
North Carolina:											
Gastonia	0		0	0	0	2	0	0	0	0	
Raleigh	0		0	0	1	0	0	0	1	0	15
Wilmington	1		0	0	1	1	0	1	2	0	9
Winston-Salem	1		0	1	0	4	0	1	0	0	14
South Carolina:											
Charleston	5	3	1	0	5	3	0	0	0	0	32
Columbia	0		0	0	6	0	0	1	0	0	40
Florence	0		0	0	2	0	0	0	0	0	10
Greenville	2		0	0	1	0	0	0	0	0	15
Georgia:											
Atlanta	15	12	0	0	6	12	0	4	0	0	76
Brunswick	0		0	0	0	1	0	0	0	0	4
Savannah	8	4	0	0	1	0	0	2	0	7	30
Florida:											
Miami	0	2	1	0	1	0	0	1	0	0	29
Tampa	1	1	1	1	0	0	0	0	0	3	20
Kentucky											
Ashland	1			0		2	0		0	0	0
Covington	0		0	0	5	2	0	1	0	0	23
Lexington	0		0	0	1	0	0	1	0	0	24
Tennessee:											
Knoxville	0		0	0	2	3	0	3	0	0	24
Memphis	3		0	1	7	6	0	2	1	13	84
Nashville	6		1	0	7	0	0	2	0	4	45
Alabama:											
Birmingham	9	4	1	0	5	2	0	5	1	0	56
Mobile	1		0	0	1	1	0	0	0	2	24
Montgomery	2			0		0	0		0	0	
Arkansas:											
Fort Smith											
Little Rock	0		0	0	5	2	0	3	0	0	9
Louisiana:											
Lake Charles	0		0	0	0	0	0	0	0	0	3
New Orleans	9	6	0	0	16	4	0	9	4	0	138
Shreveport	0		0	0	4	1	1	0	0	0	50
Oklahoma:											
Muskogee	6		0	0	0	0	0	0	0	0	
Tulsa	1			0		5	0		0	0	

## City reports for week ended Nov. 14, 1936—Continued

State and city	Diph- theria cases	Influenza		Meas- les cases	Pneu- monia deaths	Scar- let fever cases	Small- pox cases	Tuber- culosis deaths	Ty- phoid fever cases	Whoop- ing cough cases	Deaths, all causes
		Cases	Deaths								
Texas:											
Dallas.....	1	1	1	0	6	6	0	1	1	0	66
Fort Worth.....	4		1	0	5	6	0	1	1	4	32
Galveston.....	1		0	0	3	0	0	0	0	0	15
Houston.....	9		0	0	10	2	0	5	0	0	81
San Antonio.....	1		1	0	7	1	0	3	0	0	53
Montana:											
Billings.....	0		0	1	5	3	0	1	0	0	18
Great Falls.....	0		0	0	0	0	1	0	0	4	7
Helena.....	0		0	0	4	2	0	0	0	0	7
Missoula.....	0		0	0	1	0	0	0	0	0	10
Idaho:											
Boise.....	0		0	0	1	1	0	0	0	0	6
Colorado:											
Colorado Springs.....	4		0	0	2	3	0	2	0	0	13
Denver.....	3		1	1	8	9	0	3	0	50	74
Pueblo.....	0		0	0	3	0	0	0	1	2	7
New Mexico:											
Albuquerque.....	0		1	0	5	9	0	1	0	2	14
Utah:											
Salt Lake City.....	0		0	1	2	11	0	2	0	6	47
Nevada:											
Reno.....											
Washington:											
Seattle.....	0		0	6	6	4	0	5	0	1	99
Spokane.....	0		0	0	1	9	0	0	1	1	26
Tacoma.....	0		0	0	2	3	0	1	0	0	36
Oregon:											
Portland.....	0		0	2	6	8	0	1	0	4	88
Salem.....	0	1		0		2	0		0	4	
California:											
Los Angeles.....	16	19	1	2	21	18	0	20	1	74	354
Sacramento.....	4		0	1	5	16	0	3	0	10	40
San Francisco.....	1	2	0	3	8	16	0	11	0	24	174

State and city	Meningococcus meningitis		Polio- mye- litis cases	State and city	Meningococcus meningitis		Polio- mye- litis cases
	Cases	Deaths			Cases	Deaths	
Massachusetts:				Virginia:			
Boston.....	2	0	0	Norfolk.....	0	1	0
Rhode Island:				West Virginia:			
Pawtucket.....	2	1	0	Huntington.....	1	0	0
Providence.....	0	1	0	Wheeling.....	0	1	0
New York:				South Carolina:			
Buffalo.....	1	0	1	Charleston.....	0	0	1
New York.....	9	2	2	Georgia:			
Syracuse.....	0	0	1	Atlanta.....	2	0	0
Pennsylvania:				Florida:			
Philadelphia.....	0	1	1	Miami.....	1	1	0
Ohio:				Kentucky:			
Cincinnati.....	1	1	0	Ashland.....	1	0	0
Cleveland.....	1	0	2	Covington.....	1	1	0
Columbus.....	2	1	0	Tennessee:			
Toledo.....	0	0	1	Knoxville.....	0	0	1
Indiana:				Nashville.....	1	0	0
Fort Wayne.....	0	0	1	Alabama:			
Illinois:				Birmingham.....	1	0	0
Chicago.....	3	2	5	Oklahoma:			
Springfield.....	0	0	1	Tulsa.....	2	1	12
Michigan:				Colorado:			
Detroit.....	1	0	0	Pueblo.....	0	0	1
Minnesota:				Utah:			
St. Paul.....	1	1	0	Salt Lake City.....	1	1	0
Iowa:				Washington:			
Cedar Rapids.....	0	0	1	Spokane.....	0	0	1
Missouri:				California:			
St. Louis.....	0	0	3	Los Angeles.....	0	0	3
Maryland:				San Francisco.....	1	1	0
Baltimore.....	3	0	0				
District of Columbia:							
Washington.....	3	2	0				

Epidemic encephalitis.—Cases: San Francisco, 1.

Pellagra.—Cases: Philadelphia, 1; Winston-Salem, 1; Charleston, S. C. 2; Savannah, 3; Montgomery, 1; New Orleans, 1; Dallas, 1; Los Angeles, 1.

Rabies in man.—Deaths: Memphis, 1.

Typhus fever.—Cases: Charleston, S. C., 1; Montgomery, 1.

## FOREIGN AND INSULAR

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### CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER

NOTE.—A table giving current information of the world prevalence of quarantinable diseases appeared in the PUBLIC HEALTH REPORTS for November 27, 1936, pages 1659-1673. A similar cumulative table will appear in the PUBLIC HEALTH REPORTS to be issued December 25, 1936, and thereafter, at least for the time being, in the issue published on the last Friday of each month.

#### Cholera

*India*.—During the week ended November 14, 1936, cholera was reported in India as follows: Northwest Frontier Province, 2 fatal cases; Tuticorin, 5 cases, 3 deaths.

#### Plague

*Ecuador—Babahoyo*.—During the period November 13 to 18, 1936, 5 cases of plague with 2 deaths and 6 plague-infected rats were reported in Babahoyo, Ecuador.

*United States—California*.—A report of rodent plague in California appears on page 1701 of this issue of PUBLIC HEALTH REPORTS.

#### Smallpox

*Ceylon—Colombo*.—For the week ended October 10, 1936, 1 case of smallpox with 1 death was reported in Colombo, Ceylon.

*Egypt—Alexandria*.—During the week ended November 14, 1936, 1 fatal imported case of smallpox was reported in Alexandria, Egypt.

*Ethiopia*.—Up to October 31, 1936, 116 cases of smallpox were reported in Ethiopia. During the week ended November 14, 1936, 13 cases of smallpox were also reported.

#### Typhus fever

*Correction*.—An error appears in the table on page 1530 of the PUBLIC HEALTH REPORTS of October 30, 1936. The figure columns on the right-hand side of the page are all one line too high, which makes all the figures erroneous when read horizontally across the page. Attention has been called to the fact that the figures on the Panama Canal Zone line are erroneous, but this is true of each line in the right-hand half of the table. The right-hand half of the table showing typhus fever cases and deaths is published here as corrected.

## TYPHUS FEVER

[C indicates cases; D, deaths; P, present]

Place	March 1936	April 1936	May 1936	June 1936	July 1936	August 1936
Mexico:						
Puebla State: Puebla..... C	3	3	3	-----	-----	-----
Queretaro State..... C	-----	-----	1	-----	-----	-----
San Luis Potosi State: San Luis Potosi..... C	6	3	3	-----	3	-----
Sinaloa State..... D	-----	-----	-----	-----	1	-----
Tlaxcala State..... C	1	-----	-----	-----	-----	-----
Morocco (see also table above)..... C	7	45	26	9	6	-----
Panama Canal Zone..... C	1	-----	-----	2	-----	-----
Peru..... C	118	103	81	-----	-----	-----
Portugal (see also table above)..... C	1	1	-----	1	-----	-----
Rumania..... C	1,581	1,587	1,143	427	168	-----
Turkey..... C	33	79	39	25	39	-----
Istanbul..... C	4	1	1	1	2	-----
Union of South Africa:						
Cape Province..... C	39	48	71	60	58	-----
Natal..... C	8	1	2	1	-----	-----
Orange Free State..... C	5	18	10	24	2	-----
Transvaal..... C	3	3	-----	1	-----	-----
Yugoslavia..... C	113	106	125	78	53	16

## Yellow Fever

*Dahomey—Kandi.*—On November 9, 1936, 1 suspected case of yellow fever was reported in Kandi, Dahomey.

*Nigeria—Maiduguri.*—On October 27, 1936, 1 case of yellow fever was reported in Maiduguri, Nigeria.

*Senegal.*—Yellow fever has been reported in Senegal as follows: On November 15, 1936, 1 case in Bambey and during the week ended October 31, 1936, 1 suspected case was reported in Thies.

X