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## THE PREVALENCE OF INFLUENZA

*United States.*—For the week ended March 14, 1931, 8,165 cases of influenza (see pages 732 and 733) were reported to the Public Health Service by State health officers, as compared with 7,811 cases for the preceding week. However, later information may show that the apparent increase is due to irregularities in the reports, which are preliminary, rather than to an actual increase in the prevalence of the disease.

*England and Wales.*—For the week ended February 28, 1931, 546 deaths from influenza were registered in 107 great towns of England and Wales, as compared with 509 influenza deaths for the preceding week.

*Europe.*—Reports indicate that the prevalence of influenza and other respiratory diseases is decreasing generally in Europe. The disease has been very mild.

## ANTIGENIC VALUE OF SCARLET FEVER STREPTOCOCCUS TOXIN MODIFIED BY THE ACTION OF FORMALIN

By M. V. VELDEE, *Surgeon, United States Public Health Service*

The justification for the use of scarlet fever streptococcus toxin for the production of active immunization is founded on data presented by various independent workers.

Dick and Dick (1929) report no cases of scarlet fever among 1,191 susceptible nurses and internes who were immunized before they began work in hospitals for contagious diseases. As a control they report 37 cases of scarlet fever occurring among an unstated number of nurses and internes who entered before they had been tested for susceptibility, or who were known to have positive skin reactions and had not been immunized.

Toyoda (1930), writing from Dairen, Manchuria, reports an attack rate of 23.8 per 1,000 among the untested Japanese elementary school population; 1.3 per 1,000 among those with negative Dick reactions; 106.4 per 1,000 among those with positive Dick reactions but not treated, and only 2.6 per 1,000 among those with positive Dick reactions but who had been actively immunized with scarlet fever streptococcus toxin.

The injection of such toxin however, is not without unpleasant reactions, which, while not in themselves dangerous to life, are of

sufficient moment to make the clinician reluctant to use the toxin and more often to cause the parents to refuse further treatment. The need for five immunizing doses makes its use expensive, whether administered by the private physician or en masse as a public-health measure. In order to receive general favor, preventive measures of this nature must be relatively free from discomfort, require a minimum of injections, and be inexpensive. There is, therefore, a real need for a nontoxic, highly antigenic scarlet fever streptococcus product which will be no less effective against scarlet fever than the present raw toxin, yet be more like diphtheria toxoid in its freedom from reactions and in the number of doses required.

The success attained with the Ramon technique in detoxifying diphtheria toxin has naturally stimulated similar work with the toxin of the scarlet fever streptococcus.

Zoeller (1925) formalinized scarlet fever streptococcus toxin and found that by so doing the individual could tolerate much larger doses of the antigen.

Sparrow and Celarek (1927) added 0.5 per cent formalin to raw toxin having a titer of 20,000 skin-test doses per c. c., and incubated the mixture for six weeks at 38° C. They found that only very susceptible individuals suffered reactions when an initial dose of 2.0 c. c. was given (such persons showed exanthema, vomiting, and fever). They administered to a group of 143 Dick-positive children a first dose of 1.0 c. c. After an interval of 15 days all were retested, 79 per cent being found to have negative skin reactions and 9 per cent to have the intensity of their reactions reduced. Those children still positive in the fourth week received second injections (2 c. c. each). By the eighth week 88 per cent gave a negative skin reaction and 6 per cent gave slight reactions.

Smith (1928) experimented with varying strengths of formalinized toxin. He concluded that 0.5 per cent formalin is a practical amount. His raw toxin contained 10,000 skin-test doses per cubic centimeter. Incubation was at 37° C., though he does not make clear the optimum incubation period. One hundred and fourteen children and 44 medical students were each given a 1-c. c. dose of this undiluted toxoid, at weekly intervals, for three doses. Upon retest three and two months later, respectively, he found 52 per cent and 56 per cent of the reactions to have changed to negative.

Ramon and Debre (1929) treated scarlet fever streptococcus toxin with formalin according to the senior author's method for diphtheria toxoid. The titer of the raw toxin used is not stated. Three injections were given as follows: First dose 0.5 c. c., second dose 1.0 c. c., three weeks later, and finally, after a lapse of 15 days, a third injection of 1.5 c. c. to 2.0 c. c. Of the 86 persons treated, 88.4 per cent later gave negative skin reactions.

McMahon (1930) reports that 72 per cent of 176 children between the ages of 4 and 16 years were rendered negative to the Dick test following three doses of 0.5 c. c., 1.0 c. c., and 1.5 c. c., respectively, of scarlet fever streptococcus "toxoid." The interval between doses was 21 and 25 days, respectively, and the retest was made 76 days following the last dose. He does not state the titer of the product before detoxification, nor does he state the method used for detoxification.

Toyoda (1930) treated scarlet fever streptococcus toxin with 0.4 per cent formalin and stored one portion for one month at 40° C. and the other portion for two months. To 153 susceptible children he gave a total of 26,000 skin-test doses of raw toxin; to 36 children he gave a total of 37,000 skin-test doses of raw toxin detoxified for one month, and to 65 children he gave a total of 38,000 skin-test doses of raw toxin detoxified for two months. He does not state the number of doses given. Upon retest 84.8, 61.2, and 66.6 per cent, respectively, gave negative skin reactions. He observed that the reactions were much milder in those children receiving toxoid.

Futagi (1930) and Ando and Ozaki (1930) have extended the work in Dairen to larger groups of children and with variations in the method of detoxifying the toxin. The results which they obtained confirm the work of Toyada and his colleagues.

#### EXPERIMENTAL WORK

On January 28, 1930, 2 liters of scarlet fever streptococcus toxin (which had been prepared on January 8 by growing Dochez NY 5 strain of streptococcus in blood and sugar-free broth for three days) were treated with 0.3 per cent of commercial formalin. At this time the raw toxin showed a titer of about 60,000 skin-test doses per cubic centimeter, and had a pH reaction of 7.6. The toxin was then stored at a temperature varying between 37° C. and 38° C. On February 13, 1930, 0.1 per cent additional formalin was added. After eight weeks of continuous storage at the above temperature the material was removed from the warm room and tested for toxicity on several susceptible individuals. The reaction produced by injecting intradermally 0.1 cubic centimeter of a 1:100 dilution was of no greater intensity than that produced by 0.1 cubic centimeter of a 1:6000 dilution of the original raw toxin. Thus all but 1.7 per cent of the skin-reacting factor had been eliminated. This is actually less than the amount of skin-reacting factor remaining after the original scarlet fever streptococcus toxin had been heated at 80° to 85° C. for one hour. The residual skin-reacting factor in the detoxified material is also heat stable. There is some evidence at hand which strongly suggests that the skin-reacting factor remaining in both the detoxified and the heated toxin is not neutralized by antitoxin and is, therefore, not a true toxin.

This greatly detoxified antigen has now been employed for the active immunization of 115 Dick-positive individuals. These were divided into four groups: (I) 31 children of elementary school age, and coming from good homes; (II) 50 young men and women attending a State normal school; (III) 18 children living in two well-managed orphan homes; and (IV) 16 first-year nurses in a general hospital. Immunization of the first three groups was begun in April, 1930, and of the last group in November. The following protocols give the essential details surrounding the immunization of each group (the antigenic value of each dose is reported in terms of skin-test doses of the antigen before detoxification):

#### GROUP I

Number of doses given: 4.

Size of doses given: 5,000, 10,000, 20,000, and 30,000 skin-test doses, respectively.

Time interval between doses: 7 days.

Number of children completing treatment: 17 boys and 14 girls.

Ages of children treated: 5 to 13, both inclusive; average 8 years.

Reactions resulting from injections: None.

Time elapsing before retesting: 12 days.

Number of children retested: 30.

Number giving a positive Dick reaction on retest: 0.

#### GROUP II

Number of doses given: 3.

Size of doses given: 10,000, 20,000, and 25,000 skin-test doses, respectively.

Time interval between doses: 21 days.

Number of persons completing treatment: 4 boys and 46 girls.

Ages of persons treated: 17 to 26, both inclusive; average 19 years.

Reactions resulting from injections: Symptoms were limited to swelling and soreness at site of injection, and headache. These occurred in a considerable number following the first dose and grew progressively fewer with succeeding doses.

Time elapsing before retesting: 12 days.

Number of persons retested: 34.

Number giving a positive Dick reaction on retest: 0.

#### GROUP III

Number of doses given: 3.

Size of doses given: 10,000, 20,000, and 40,000 skin-test doses, respectively.

Time interval between doses: 21 days.

Number of children completing treatment: 10 boys and 8 girls.

Ages of children treated: 6 to 13 years, both inclusive; average 8 years.

Reactions resulting from injections: 1 child had swelling and tenderness at the site of needle insertion following the first dose. This had disappeared by morning. Another had headache after the first dose; gone by morning. The other 16 children remained free from symptoms.

Time elapsing before retesting: 27 days.

Number of children retested: 18.

Number giving a positive Dick reaction on retest: 1. The initial skin test on this child measured 22 by 30 mm. with a pink color and slight swelling. The retest reaction measured 14 by 18 mm., very faint pink and no swelling.

## GROUP IV

Number of doses given: 3.

Size of doses given: 10,000, 30,000, and 60,000 skin-test doses, respectively.

Time interval between doses: 21 days.

Number of persons completing treatment: 16 pupil nurses.

Age of persons treated: One was 34 years of age, all others were between 18 and 20.

Reactions resulting from injections: 1 nurse had a moderate reaction with headache, nausea and slight temperature following the first dose only.

Another had a moderate local reaction with severe general reactions after each dose. The remaining 14 continued essentially symptomless.

Time elapsing before retesting: 43 days.

Number of nurses retested: 14.

Number giving a positive Dick reaction on retest: 2. The initial skin reactions were 23 by 35 mm. faint pink with swelling and 16 by 25 mm. very faint pink, respectively. Upon retest the corresponding reactions were 14 by 22 very faint pink and 15 by 15 very faint pink.

## DISCUSSION

Out of the 115 persons tested with the detoxified toxin, 96 were retested following treatment, with only three giving a positive reaction. Thus 93, or 96.9 per cent, had their skin reactions rendered negative by the injections given, and this was accomplished without significant reactions except in one person, a nurse 34 years of age, who also reacted rather severely following immunizing injections against other diseases.

Parallel with Group II a second group of 65 susceptible normal school students (average age 18 years) were treated at weekly intervals with graduated doses of the original raw toxin from which the detoxified product had been prepared. The antigenic values of these doses were 500, 2,000, 8,000, 15,000, and 25,000 skin-test doses, respectively. It was originally intended to give as the fourth dose 25,000 and as the fifth 80,000 skin-test doses. However, because of the severity of both the local and general reactions following the first three doses, so much objection was raised by the school authorities that subsequent doses were reduced. Even with this precaution 11 out of the 65 students had dropped out before the fourth dose was given. Group II at the outset contained 55 students, but 5 discontinued after the first dose because of local reactions.

The point has been raised that the immunity produced with this detoxified product is the result of that skin-reacting factor which still remains. In actual measurement this is not more than the equivalent of 1,000 skin-test doses per cubic centimeter, and it is composed entirely of the heat-stable factor in the toxin. There is evidence to show that this heat-stable factor is not antigenic. Assuming that this remaining factor is antigenic, the total quantity given per person was less than the equivalent of 2,000 skin-test doses.

The experimental work here presented confirms the findings of other workers that scarlet fever streptococcus toxin can be rendered

much less toxic by subjecting it to heat and formalin. The antigenic value of the toxin apparently is not destroyed either by the action of the formalin or by the prolonged exposure to 37° to 38° C. The amount of antigen tolerated by susceptible individuals in each injection is greatly increased by this method of detoxification, so that the number of doses required for active immunization may be reduced. At the same time the reactions following the injections occur much less frequently and their severity is markedly diminished. Further experimentation may, it is hoped, develop a technique for removing the remaining toxic factor, thereby eliminating all disagreeable reactions and permitting the use of greater quantities of antigen.

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### EXPERIMENTAL ADDICTION OF ANIMALS TO OPIATES

By LAWRENCE KOLB, *Surgeon*, and A. G. DUMEZ, *Formerly Pharmacologist, United States Public Health Service*

The experiments described in this paper deal with the effects of morphine, heroin, and codeine upon monkeys. They were undertaken as another phase of the studies in drug addiction being carried out by the United States Public Health Service.<sup>1</sup>

The main objectives of the work were to compare the effects of these three alkaloids upon the test animals, to determine what degree of tolerance, if any, could be acquired for them, and to determine whether the administration of these drugs over comparatively

<sup>1</sup> The experiments were started in March, 1923, and continued without interruption until December, 1926. Observations were made on two of the surviving animals as late as September, 1927.

long periods of time would cause the animals to become dependent upon them to maintain equilibrium of certain body functions. As a basis for determining tolerance an attempt was also made to establish the approximate fatal dose.

The monkey was selected as the test animal for these experiments, as it was believed that it would portray human conditions more nearly than the animals, such as the dog, used by other investigators. That this belief was correct is borne out by the results obtained, and is corroborated by the work of Tatum, Seevers, and Collins, (1) reported last year. The work done on dogs by Plant and Pierce (2) and by Barbour, Hunter, and Richey (3), and also that which has been reported since these investigations were started, still further confirms the opinion that the monkey reacts more nearly like man than the dog and is therefore the better test animal to use. This is clearly demonstrated by the difference in the effects of addiction and withdrawal on weight and temperature and by the difference in the manifestation of discomfort by the two animals.

#### OPIATES USED

The drugs used in these experiments were morphine sulphate and codeine phosphate, conforming to the standards set by the United States Pharmacopœia X, and heroin, conforming to the standards laid down by the United States Pharmacopœia IX for diacetyl-morphine hydrochloride. Wherever reference is made in this paper to morphine, codeine, or heroin, the foregoing salts are meant.

#### APPROXIMATE FATAL DOSE

For the determination of the approximate fatal dose and in all other experiments, sufficient quantities of the respective alkaloidal salts were dissolved in distilled water to make a solution 1 cubic centimeter of which contained 50 milligrams of drug. In all cases the injection was made in the subcutaneous tissue of the abdomen. Tables 1 to 4 show the results of these experiments.

#### MORPHINE

Tables 1 and 2 show the effect of large doses of morphine sulphate on monkeys that had not been given the drug before or had been receiving it regularly. All of the animals were *Macacus rhesus*, except the one marked "long tail," which belonged to a closely related group. Only one, X, had been used for experimental purposes before, except the one that had previously been given a toxic dose of heroin. All were in good condition at the time the experiment was begun, and all had lived under the same conditions as regards environment and food, with the exception that those listed in Table 2 had been received from the dealer only a short time previous to making the tests, while those listed in Table 1 had lived at the laboratory for some months. The injections were given in all cases between 9 and 10 a. m.

TABLE 1.—Effect of large doses of morphine sulphate on monkeys (approximate fatal dose)

Date	Monkey		Dose of morphine sulphate		Effect			Observations
	Number and sex	Weight in kilos	Total number milli-grams	Milli-grams per kilo	Unconscious	Effect		
						Convulsions	Died	
Mar. 30, 1923	X f	2.75	27.5	10	No	No	No	Became quiet.
Apr. 10, 1923	X f	2.76	69.5	25	No	No	No	Became very sleepy; breathed as though snoring while sitting up; tremors of hind legs.
Apr. 23, 1923	X f	2.84	128.0	45	Yes	No	No	Still asleep on 24th; lying down on 25th; quiet 26th and 27th; blood in urine; pupils widely dilated 28th to 30th. In good condition May 1, but occasional twitching of muscles until May 4.
June 7, 1924	X f	2.75	275.0	100	Yes	No	No	Ten minutes after injection mouth hung open and looked very sick; asleep in 30 minutes much better on 8th, but twitching of muscles still frequent; well on 9th.
Apr. 2, 1923	2X m	2.88	26.0	10	No	No	No	Became quiet.
Apr. 11, 1923	2X m	2.90	87.0	30	No	No	No	Still very sleepy 6½ hours after injection; nodded almost to extent of falling; muscles still twitched on the 12th.
May 1, 1923	2X m	2.90	145.0	50	No	No	No	Very sleepy 6½ hours after injection; apparently normal on 2d.
May 18, 1923	2X m	2.87	186.5	65	No	No	No	Very sleepy all day but did not lie down, quiet next day but almost wholly recovered.
June 6, 1923	2X m	2.98	293.2	90	Yes	No	No	Very sleepy; mouth hung open one hour after injection, lay down sick in afternoon; sick and legs weak on 7th. No spasticity; handled without resistance; legs weak on 8th but fought when touched; dragged himself around on haunches on 9th; well but less active than normal on 11th.
Apr. 3, 1923	3X m	2.55	38.0	15	No	No	No	Sleepy during day but no other effect.
Apr. 17, 1923	3X m	2.54	88.0	35	No	No	No	Very sleepy during the day; asleep sitting up 6 hours after injection; normal on 18th.
May 2, 1923	3X m	2.58	126.0	50	No	No	No	About as above.
May 21, 1923	3X m	2.55	191.0	75	Yes	No	No	Very sick; became unconscious 3 hours after injection; could not be aroused; awakes, but quiet on 22d.
June 26, 1923	3X m	2.62	222.7	85	Yes	No	Yes	Drowsy; mouth hung open one-half hour after injection; asleep 2¼ hours later; could not be aroused; died without regaining consciousness.
Apr. 9, 1923	4X m	2.06	41.0	20	No	No	No	Sleepy; still quiet on 10th.
Apr. 16, 1923	4X m	2.14	83.6	40	No	No	No	Very sleepy; quiet on 16th.
May 26, 1923	4X m	2.11	169.0	80	No	No	No	Very sleepy; did not draw away when touched or held; still sleepy 5 hours after injection; quiet on 28th.
June 26, 1923	4X m	2.14	235.0	110	Yes	No	Yes	Still awake 6 hours after injection but very quiet and could be handled without resistance; died during night.
May 16, 1923	5X	2.715	150.0	55	No	No	No	Sleepy but did not lie down; pupils widely dilated shortly after injection; apparently normal but quiet on 17th.
May 31, 1923	5X	2.66	226.0	85	No	No	No	Pupils widely dilated 15 minutes after injection; quiet during day but did not sleep; spastic paralysis of digits on June 1; could not grasp things, had to be fed; quiet and not doubled up on 2d, gradually grew more active and was normal on 3 June 6.
July 6, 1923	6X m	2.92	204.0	70	No	No	No	Very quiet; mouth hung open, pale and very sick 1 hour after injection; held on to cage to keep from falling. On 7th digits of fore and hind limbs spastic and had difficulty moving around; some fibrillary twitching of muscles. Still somewhat spastic on 8th.



Unconscious in 10 minutes; breathing very shallow, hardly observable; slight twitching regained consciousness 5 minutes later; breathing 8 per minute 1 hour after injection; about 8 gasps per minute 6 hours after injection; died 6½ hours after injection.  
 Became sick within a few minutes after receiving injection but not unconscious until 5 hours later. Spastic paralysis of all four limbs on 18th, but apparently not sleepy.  
 Very sick 10 minutes after injection; mouth hung open; quiet, pale, 6 hours later, but still able to move around; loud mucous sound with respiration; July 27 spastic paralysis fore and hind limbs; breathing 60 per minute; tremors. July 28 quiet but otherwise normal.

TABLE 2.—Effect of large doses of morphine sulphate on monkeys (approximate fatal dose)

Date	Monkey		Dose of morphine sulphate		Effect			Observations
	Number and sex	Weight in kilos	Total number milligrams	Milligrams per kilo	Unconscious	Convulsions	Died	
July 3, 1923	7X m...	3.90	351.0		Yes	No	Yes	Unconscious in 10 minutes; breathing very shallow, hardly observable; slight twitching regained consciousness 5 minutes later; breathing 8 per minute 1 hour after injection; about 8 gasps per minute 6 hours after injection; died 6½ hours after injection. Became sick within a few minutes after receiving injection but not unconscious until 5 hours later. Spastic paralysis of all four limbs on 18th, but apparently not sleepy. Very sick 10 minutes after injection; mouth hung open; quiet, pale, 6 hours later, but still able to move around; loud mucous sound with respiration; July 27 spastic paralysis fore and hind limbs; breathing 60 per minute; tremors. July 28 quiet but otherwise normal.
July 17, 1923	8X m...	1.98	159.0		Yes	No	No	
July 26, 1923	9X m...	2.32	209.0		No	No	No	
Feb. 24, 1926	30 m...	2.01	231.0	115	No	No	No	Received toxic dose of heroin Jan. 26. Very quiet after morphine and looked ill during the day; sleepy. Much better on Feb. 25; well as ever on 26th. Quiet in few minutes after injection; held on to cage to keep from falling; could be touched without resistance; appeared worried and confused. Much better on 30th; normal on Feb. 1. Received toxic dose of heroin Feb. 24; effect of morphine about as above, but not quite so severe. Very quiet; could be handled without resistance, but not asleep until 4 hours after injection; spastic; convulsive jerks of fore and hind limbs about every 5 minutes in afternoon; grew gradually worse, but no convulsions. Died night of 2d. Unconscious in 45 minutes; awake 2 hours after injection, but fore and hind limbs and neck spastic; Jan. 29 noted the paralysis was not all due to spasticity; marked incoordination of fore and hind limbs; gradually improved, but did not disappear entirely until Mar. 30. Unconscious 25 minutes after injection, awake, but died during the night. Quiet and sleepy during the day, but did not fall over; apparently as well as ever on 11th. Markedly affected in 25 minutes; held on to cage to keep from falling; better 5 hours after injection; normal on 26th.
Jan. 29, 1926	31 m...	1.64	180.4	110	No	No	No	
Apr. 5, 1926	31 m...	1.94	242.5	125	No	No	No	
Jan. 22, 1926	Long tail, f.	1.89	207.9	110	Yes	No	Yes	
Jan. 28, 1926	32 m...	3.38	338.0	100	Yes	No	No	
Apr. 5, 1926	32 m...	3.21	353.0	110	Yes	No	Yes	
Mar. 10, 1926	33 m...	2.45	267.3	110	No	No	No	
Mar. 24, 1926	33 m...	2.50	278.0	110	No	No	No	

The animals listed in Table 1 were, on the average, older and heavier than those listed in Table 2. The former were taken from the same lot as those upon which the addiction experiments described in subsequent pages were made. They, therefore, offer a more accurate basis of comparison with the experimental addiction animals than the younger group.

The dose of morphine sulphate that will surely kill the majority of monkeys was not accurately determined by this experiment. On the basis of the results shown in Table 1 the minimum fatal dose could be said to lie between 85 milligrams and 110 milligrams per kilo of body weight, for deaths occurred with 85, 90, and 110 milligrams, and very severe symptoms, lasting in some instances for several days, resulted from doses ranging between 70 and 100 milligrams; but an examination of Table 2 shows that 110 milligrams could not be depended upon to kill younger and lighter animals. It is concluded, as a result of the experiment, that young monkeys are more resistant to morphine sulphate than older ones, and that a toxic dose based on weight does not form an accurate basis of comparison between animals of different weights.

Some of the animals were given toxic doses more than once. The question naturally arises whether the first dose did not create tolerance with increased resistance to subsequent doses. This is suggested by the case of X. This animal developed severe symptoms, from which it did not recover for 12 days following 45 milligrams per kilo, and 6 weeks later survived 100 milligrams per kilo. However, all the other animals, except No. 31, that were given increased toxic doses after a period of rest were more severely affected by the larger doses than were those given a large dose for the first time. It is, therefore, probable that some contributory factor, not observed at the time, was in part responsible for the severe symptoms developed by X after 45 milligrams.

The general effect of toxic doses of morphine sulphate, depending on the size of the dose and resistance of the animal, was to produce quiet, drowsiness, light sleep while sitting up, and then deep unconsciousness. Ten milligrams per kilo were sufficient to produce quiet, and 25 milligrams sometimes produced light sleep and cyanosis.

With unconsciousness, respiration became shallow and almost imperceptible, in extreme cases amounting to only a few gasps per minute. When consciousness was regained, the rate of respiration would increase to normal or above.

There was no constant effect upon the pupils; they were contracted or dilated, but never pin point, and were usually mobile even when the animals were unconscious. Unusual quietness, twitching of muscles, and spastic paralysis lasting one or two days were the common symptoms. Marked incoordination of fore and hind legs followed

profound unconsciousness and spasticity in one case (No. 32). The incoordination did not entirely disappear until two months after the toxic dose had been given.

The animals that received large doses but remained conscious became slightly cyanotic, looked sick and worried, held on to the cage to keep from falling, and, though normally very active and resistant to handling, could be touched without eliciting any evidence of resistance or fear. As soon as they had recovered sufficiently to do so, all severely affected animals would climb to a small water container attached to the cage and sit in it. This practice would continue for one or two days until the symptoms subsided. The relief obtained by sitting in water is not understood. No convulsions resulted from morphine. This is in striking contrast to the effect of heroin and codeine.

#### HEROIN

Table 3 shows the effect of large doses of heroin hydrochloride on animals that had not received the drug before. All of the animals were healthy, active *Macacus rhesus*; none had been used for any experimental purpose before, but three of them, as indicated by the table, had previously been given toxic doses of morphine, and two had previously been given toxic doses of codeine.

The results shown in Table 3 do not justify an accurate fixation of the minimum fatal doses of heroin for monkeys, but it seems probable that 7 milligrams per kilo of body weight will kill most monkeys that have not previously been given morphine, heroin, or codeine. Of the previously untreated animals, one of the three that received 6 milligrams per kilo died, and three of the four that received 7 milligrams per kilo died, and every animal, except one, that received as much as 6 milligrams per kilo became unconscious a few minutes later.

The survival of No. 30 after 7 milligrams per kilo, and of Nos. 30, 31, and 33 after 8 milligrams may have been due to a mild degree of tolerance established by the several toxic doses of morphine or heroin which these animals had already received. The fact that in only 2 of the 15 experiments did the animal involved fail to become unconscious also suggests a mild degree of tolerance from previous toxic doses. One of these, No. 26X, had received a toxic dose of codeine 8 days before, and the other, No. 31, had received a toxic dose of morphine 27 days before. No. 30 also was affected less severely by 8 milligrams than by 6 and 7 milligrams given on two former occasions.

In connection with tolerance, we have found that tolerance and cross tolerance can be induced by gradually increasing daily doses of morphine, heroin, and codeine, but that such tolerance is apparently completely lost after about two weeks of abstinence. However, the circumstances here are so different that the observation can not be

TABLE 3.—Effect of large doses of heroin hydrochloride on monkeys (approximate fatal dose)

Date	Monkey		Dose of heroin hydrochloride		Effect			Observations
	Number and sex	Weight in kilos	Total number milli-grams	Milli-grams per kilo	Uncon- scious	Convul- sions	Died	
Sept. 11, 1924	25X f.	3.45	14.0	4	Yes	No	No	Received toxic dose of cocaine June 25; unconscious 15 minutes after receiving the injection of heroin; could not be aroused by shaking; aroused by touching cage 1 hour later; apparently normal but sleepy 2½ hours after injection; complete recovery at end of 24 hours.
Sept. 12, 1924	26X f.	3.63	18.2	5	No	No	No	Received a toxic dose of cocaine September 4. Very quiet after the heroin; staring into space in 7 minutes; drowsy for 3½ hours; completely recovered at end of 24 hours.
Sept. 15, 1924	29X m.	3.69	22.2	6	Yes	No	Yes	Fell to floor of cage unconscious in 4 minutes; breathing 4 per minute; dead 10 minutes after injection.
Sept. 17, 1924	27X	2.50	4.0	1.6	Yes	Yes	No	Fell to floor of cage asleep 10 minutes after receiving heroin; convulsions lasting ¼ minute 10 minutes later; thereafter active when aroused but sleepy for 6 hours.
Feb. 24, 1926	31 m.	1.78	10.7	6	No	No	No	Received toxic dose of morphine on January 29. Became very quiet from heroin; could be touched without moving; as active as ever 6 hours after injection.
Apr. 23, 1926	31 m.	2.01	10.08	8	Yes	No	No	Received toxic dose of morphine April 5. Unconscious 5 minutes after heroin; breathed in gasps; awake at end of 1¼ hours; unable to get up; sat up six hours after injection and moved around but movements incoordinate; completely recovered in 24 hours.
Jan. 28, 1926	30 m.	2.14	12.84	6	Yes	Yes	No	Unconscious 5 minutes after the injection; breathing imperceptible, except few gasps every ¼ minute; convulsions 10 minutes after injection lasting 1¼ minutes; gasped for 15 minutes, regained consciousness; spastic and dazed; 6 hours after injection apparently as well as ever.
Mar. 24, 1926	30 m.	2.02	14.14	7	Yes	No	No	Received toxic dose of morphine February 24; unconscious 3 minutes after heroin, remained so for 6 hours; then unable to get up; spastic paralysis and movements incoordinate on 26th; apparently blind on 29th; did not recover completely until April 8.
Apr. 27, 1926	30 m.	2.16	17.28	8	Yes	No	No	Unconscious 5 minutes after the injection; respiration, 1 every 2 minutes; awake in 2 hours but weak; completely recovered on 26th.
Apr. 20, 1926	35 m.	2.90	17.4	6	Yes	No	No	Unconscious 4 minutes after the injection; remained in this state for 4¼ hours; muscular twitching 8 minutes after injection but no convulsion; dozed for 7 hours after injection; completely recovered in 24 hours.
May 28, 1926	do	3.06	21.42	7	Yes	No	Yes	Unconscious 5 minutes after receiving the drug; no breathing observable; 2 gasps and 7 short, jerky breaths per minute 7 minutes later; died without regaining consciousness 1 hour 20 minutes after injection.
Apr. 21, 1926	36 m.	2.83	19.8	7	Yes	No	Yes	Unconscious in 5 minutes after receiving the heroin; breathing imperceptible; dead in 1 hour.
Apr. 22, 1926	37 m.	2.88	20.16	7	Yes	No	Yes	Unconscious 8 minutes after the injection; gasped a few times; dead 10 minutes after injection.
Mar. 10, 1926	34 m.	2.62	18.3	7	Yes	No	No	Unconscious 7 minutes after the injection; breathed in gasps; conscious 1¼ hours after injection, but paralyzed and movements incoordinate; movements of hind and fore limbs and neck still incoordinate on 11th; incoordination did not completely disappear until Apr. 23.
Apr. 5, 1926	33 m.	2.46	19.68	8	Yes	Yes	No	Received toxic doses of morphine Mar. 10 and 24. Unconscious 9 minutes after heroin; generalized convulsions lasting 3¼ minutes 11 minutes after injection; awake but weak and incoordinate 1 hour and 10 minutes after injection; almost normal 6½ hours after injection; normal in 24 hours.

taken to prove that one large, nearly fatal, dose may not produce a mild tolerance that would protect against a slightly larger dose given several weeks later.

The effect of heroin in toxic doses differed from the effect of morphine chiefly in that the severe symptoms were more quickly established and more transitory than for morphine. Unconsciousness was the rule with heroin. It came on usually within 5 minutes and always within 9 minutes after the injection had been given, whereas with morphine unconsciousness was much less common and in some instances did not occur in animals that were otherwise seriously affected for 1 or 2 days. It seldom came on within 25 minutes and usually was not established for several hours after the morphine had been given.

Heroin caused convulsions, but morphine never did. Spastic paralysis, a very common after-effect of morphine, occurred in only one case after heroin. Except for incoordination in two cases, all of the heroin-treated animals that recovered were completely well within 24 hours after the injection, whereas some of the morphine-treated animals were obviously quite ill for several days. No. 30 was unconscious for 5 hours after the injection of heroin, and its movements were incoordinate for 15 days, and it was apparently blind one of these days. No. 34 was unconscious for approximately 1½ hours and its movements incoordinate for 43 days. These two cases are somewhat similar to No. 32, a morphine-treated monkey whose movements were incoordinate for two months after having been given 110 milligrams of morphine per kilo. The lesion in each case was more likely due to asphyxia resulting from the drug than to any direct destructive effect of the drug on the nervous tissue.

#### CODEINE

Table 4 shows the effect of large doses of codeine phosphate on monkeys. All were healthy active animals that had never been used for experimental purposes before.

From the results shown in Table 4 it is concluded that 80 milligrams of codeine phosphate per kilo of body weight will kill the majority of monkeys. No animal survived this amount and 1 died from 60 milligrams, while 3 of the 4 that survived 60 or 70 milligrams developed convulsions and became unconscious.

The effect of toxic doses of codeine differed from the effect of toxic doses of morphine and heroin in that the two latter drugs always produced quiet, whereas codeine sometimes caused moderate excitement; and convulsions were very common after codeine, being present in all the fatal cases and in 50 per cent of those that survived, whereas they were much less common after heroin and never occurred after morphine.

TABLE 4.—Effect of large doses of codeine phosphate on monkeys (approximate fatal dose)

Date	Monkey		Dose of codeine phosphate		Effect			Observations
	Number and sex	Weight in kilos	Total number milligrams	Milligrams per kilo	Unconscious	Convulsions	Died	
June 17, 1924	22X f	3.58	294	110	Yes	Yes	Yes	8 minutes after injection fell to floor of cage in clonic convulsions, respiration slow and irregular; 30 minutes later respiration 5 per minute. Died without regaining consciousness 2 hours and 30 minutes after the injection.
June 20, 1924	23X m	3.58	304	85	Yes	Yes	Yes	5 minutes after injection very excited, running back and forth in cage; 20 minutes later fell over with a clonic convulsion that lasted several minutes, followed by 3 other convulsions. The convulsive movement lasted a total of 20 minutes. Died without regaining consciousness 2 hours after injection.
June 23, 1924	24X m	3.42	205	60	Yes	Yes	Yes	Fell to floor of cage 15 minutes after injection; arose and fell again. This was followed by alternate stages of excitement and quiet. Had 2 severe convulsions 25 minutes after injection while unconscious. Breathing irregular and shallow. Died without regaining consciousness 1 hour and 10 minutes after injection.
June 25, 1924	25X f	3.80	153	40	No	No	No	Quiet and drowsy 30 minutes after injection. This continued for about 4 hours when animal began to regain its liveliness; apparently normal at end of 24 hours, although still somewhat quiet.
Aug. 21, 1924	25X f	3.33	167	50	Yes	No	No	Quiet and legs almost completely paralyzed 20 minutes after injection; unconscious 45 minutes after injection; awake but quiet 80 minutes later and paralysis nearly gone; normal at end of 24 hours.
June 26, 1924	19X f	2.43	122	50	No	No	No	Very excited 12 minutes after injection, running back and forth in cage. 20 minutes later quiet but not drowsy; normal at end of 24 hours.
Sept. 4, 1924	26X f	3.67	220	60	Yes	Yes	No	Convulsions 30 minutes after injection, followed by deep sleep; awoke 2 hours after injection but was drowsy for some time; somewhat quieter than usual the next day but otherwise normal.
Dec. 23, 1924	28X	2.14	150	70	No	No	No	Very quiet, lying down 30 minutes after injection; mouth hung open; still quiet 4 hours after injection; normal at end of 24 hours.
Mar. 5, 1928	38 f	3.10	217	70	Yes	Yes	No	19 minutes after injection fell to floor of cage with convulsions of irregular severity, lasting 10 minutes. Respiration 9 per minute at end of convulsions, pupils dilated, inactive. Awoke 45 minutes after injection; able to get up 2 hours after injection.
Do.....	39 m	2.41	169	70	Yes	Yes	No	16 minutes after injection fell to floor of cage in convulsions, lasting 9 minutes, then breathed quietly, 20 per minute. Awoke 40 minutes after injection, limbs doubled up. Moved around freely 2 hours after injection. Normal on 6th.
Mar. 6, 1928	40 m	2.63	210	80	Yes	Yes	Yes	Much affected 10 minutes after the injection; lay down at end of 20 minutes, but conscious until the onset of a severe convulsion 2 hours after the injection; another convulsion, but milder, 3¼ hours after injection. Breathing was shallow and the animal was unconscious after first convulsion until death, which occurred 8¼ hours after injection.
Do.....	41 m	3.70	296	80	Yes	Yes	Yes	Unconscious 19 minutes after the injection; convulsion 2 minutes later lasting 3 minutes; another convulsion 3 minutes later lasting 1 minute. Did not regain consciousness. Died 45 minutes after the injection.

## ADDICTION EXPERIMENTS

## MORPHINE

Six *Macacus rhesus* were used in the morphine addiction experiment. They were kept in well lighted rooms in cages (32 by 28 by 30 inches). In the back of each cage was a wooden shelf, and attached to the side, or door, was a small water container. Removable floors were covered with sawdust, which was changed at regular intervals. The animals were fed every day with bananas, potatoes, bread, and sunflower seed, and twice weekly with boiled eggs. Cabbage was given occasionally. None of the animals had been used for other experimental purposes. All were healthy and so active and resistant that it was necessary to catch them with a net for each treatment until after a month or two when they had become accustomed to handling.

Subcutaneous injections of an aqueous solution of morphine sulphate (1 cubic centimeter = 50 milligrams) were begun on March 28, 1923, and continued until the animals died as the result of one or another of the various experiments that were made upon them. One animal (No. 5) was experimented with for 52 months, but the drug was changed during this period from morphine to heroin and later on to morphine again. The animals were numbered 1 to 6.

*Dose.*—The beginning daily dose of morphine sulphate (7 or 8 milligrams per animal) was gradually increased until the doses reached 200, 190, 180, 200, 200, and 190 milligrams, respectively. The large doses were reached in from 8 to 10 months, and were then decreased in order to preserve the animals for other experiments. The drug was given in one daily dose at about 9 a. m. from March 28 to June 26, 1923, and in two daily doses at 9 a. m. and 4 p. m. from June 26 to October 28, 1923, Sundays and holidays excepted. By the latter date withdrawal symptoms were so severe following 40 hours of abstinence that a morning dose equal to one-half the total daily dose was given on Sundays and holidays.

*Effects.*—The first effect noted was quietness that would last for most of the day even when only a very small morning dose was given. In about six weeks, when the animals were receiving 40 milligrams daily, some of them began to have spells of illness, during which the dose was omitted for one or two days. A common symptom was spastic paralysis of the limbs. This effect is illustrated by the history of No. 6: No. 6 was spastic on May 8 (daily dose 40 milligrams); sick June 2 (daily dose 50 milligrams); sick June 28 (daily dose 70 milligrams); spastic July 26 (daily dose 90 milligrams). It was not necessary to omit the drug after July 26, although the dose was increased to 190 milligrams daily by January, when the animal died from the effects of abrupt withdrawal.

Spasticity affected every animal more than once. It quickly cleared up after an enema of soap and water and one or two days of abstinence, and it is believed to have been due in part to interference with elimination. In addition to spasticity there were other infrequent upsets during which the affected animal would be unusually quiet and seem uncomfortable. The omission of one or two doses, together with the administration of a purgative in some instances, was always sufficient to clear up the condition, after which the drug was given in equal or increasing doses.

The effect on weight varied slightly with the animal. No. 6 began to lose weight at the end of five months, when the daily dose had reached 90 milligrams. No. 2 showed no loss in weight for the first eight months, even though the dose had been increased to 180 milligrams; but the continued administration of such large doses as this was followed invariably by loss of weight. No. 5 lost weight slightly after the first two weeks, but the dose was increased in eight months from 7 to 190 milligrams, and the weight dropped only from 2.3 kilos to 2.19 kilos. In the animals that survived withdrawal, the weight usually decreased during the first few days; it then increased rapidly in all cases for the first two months of the period of abstinence, but decreased just as rapidly when the injections were started again.

All the animals began to show marked deterioration when the daily dose reached 190 milligrams. Nos. 3 and 5 grew dirty, the fur became thinner, and the appetite was not quite so good. No. 2 died shortly after this dose was reached. During eight months of treatment, it had been sick twice for one day with abdominal upsets and once for two days with spastic paralysis. This animal was sick when the last injection was given. It vomited at the time and was lying down, pale and quiet, before death, which occurred 20 hours later. There had been no loss of weight. At necropsy the organs were pale and there was evidence of early general pneumonia.

No. 1, while receiving 200 milligrams of morphine daily, was killed by 100 milligrams of cocaine. The other four animals lived many months longer. Each animal was subjected to repeated withdrawal of the drug for one or two days and to other debilitating experiments that affected their vitality; but it was obvious that even without these experiments they could not have survived for any great length of time the continued administration of as much as 190 milligrams of morphine daily.

Following withdrawal of morphine for three weeks or longer, tolerance was apparently completely lost in every instance and it was necessary to begin with small doses when the animals were put back on it. The dose was again gradually increased, but in no instance reached the previous high limit. The animals were apparently less resistant to the drug, and when they began to show deterioration the dose was



not pushed further. This is well illustrated in the case of No. 3. This animal was raised to 180 milligrams per day in eight months, held at this dose for two months, and then dropped to 100 milligrams and held to that dose during the next six months. At the end of this time it weighed 2.28 kilos, and the drug was withdrawn with the result that in two months of abstinence the weight increased to 2.84 and health was apparently as good as ever. A total of 50 milligrams in three days then brought on spastic paralysis. This cleared up with one day of abstinence, but 20 milligrams more brought on paralysis lasting two days. In a month the dose had been increased to 40 milligrams daily. The weight had fallen to 2.37 kilos, and the animal was growing dirty, looked emaciated, and was covered with lice. The decline continued, and in one month more (daily dose 60 milligrams) the weight was 2.28 kilos. Two months later (daily dose 70 milligrams) a stiffness of the hind limbs cleared up with only the omission of the afternoon dose; 14 days after this a cross tolerance to codeine phosphate was shown by failure of the animal to develop any unfavorable reaction whatever following a dose of codeine phosphate large enough to kill an untreated animal of the same weight. After this the daily dose of morphine was reduced to 40 milligrams, but decline continued and the animal died four and one-half months after the second addiction experiment had been started.

A symptom that affected four of the morphine-addicted animals was necrosis of the tip of the ears. The earliest appearance of the symptom was observed in No. 3 after nine months of treatment, and the latest in No. 5 after 22 months. The absence of the symptom in two of the animals is attributed to their death within 10 months. Necrosis first became evident as a brownish discoloration that progressed slightly until, in the most marked cases, it was a dry scaly area about 8 mm. in width. Only the outer margin of the ear would slough off. When the drug was stopped or heroin was substituted for morphine, progression stopped but the brownish area did not recede. There was no progression in No. 5 when codeine was substituted for morphine. Number 5 also began to show some discoloration of the tip of the nose.

*Withdrawal symptoms.*—During the latter part of June, 1923, it was observed that the animals were more restless on Monday mornings than on other mornings, but there was no definite evidence of discomfort. The animals began to receive two daily doses on June 26, but the Saturday afternoon doses were omitted during the summer. During the latter part of July, four months after the injections had been started, definite withdrawal symptoms were observed on all animals on Monday mornings following the 48-hour period of abstinence. They were hypersensitive to noise and more resistant to

handling. Some had occasional slight twitching of the muscles and all showed the peculiar grin indicative of discomfort. These symptoms disappeared in from 15 to 20 minutes after the dose of morphine had been given.

Withdrawal symptoms gradually became more evident. By the end of September some of the animals would be found doubled up with apparent abdominal discomfort on Monday mornings. About this time withdrawal symptoms were evident in some of them every morning due to the 17 hours of abstinence following the last dose given at 4 p. m. the day before. Beginning on October 28, one injection was given on Sundays in order to avoid the debilitating effect of repeated withdrawals. The animals were then receiving daily doses of 180, 180, 160, 180, 180, and 170 milligrams, respectively.

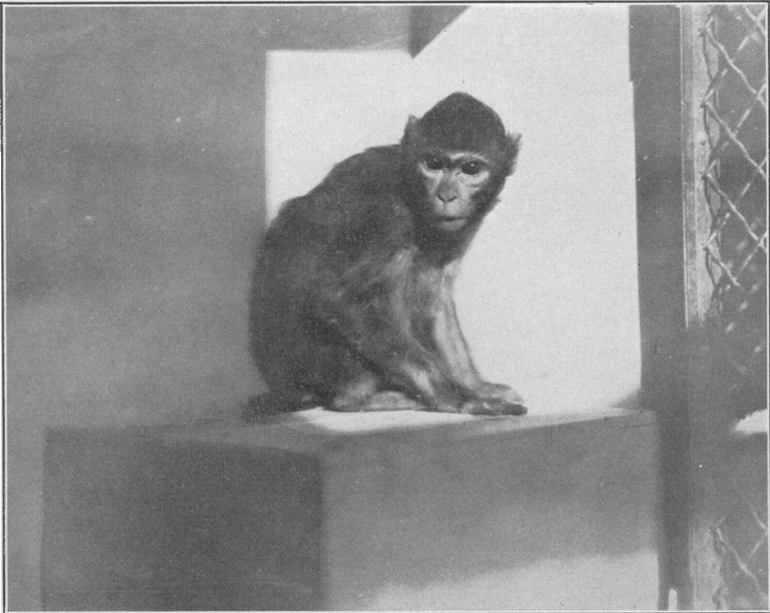
The depressing effect of withdrawal was most strikingly illustrated in No. 6; abrupt withdrawal was attempted when this animal was receiving 190 milligrams of morphine daily. It had been on the drug for 9½ months and was showing considerable evidence of hypersensitiveness and discomfort every morning until the morphine was given. The last dose (95 milligrams) was injected on the morning of January 13. The animal was then in good condition. The usual evidence of hypersensitiveness and discomfort occurred during the next few days, but the most striking effect was the depression of vital functions as shown by the fall in temperature, which is given in Table 5.

TABLE 5.—*Temperature record of No. 6 during withdrawal of morphine*

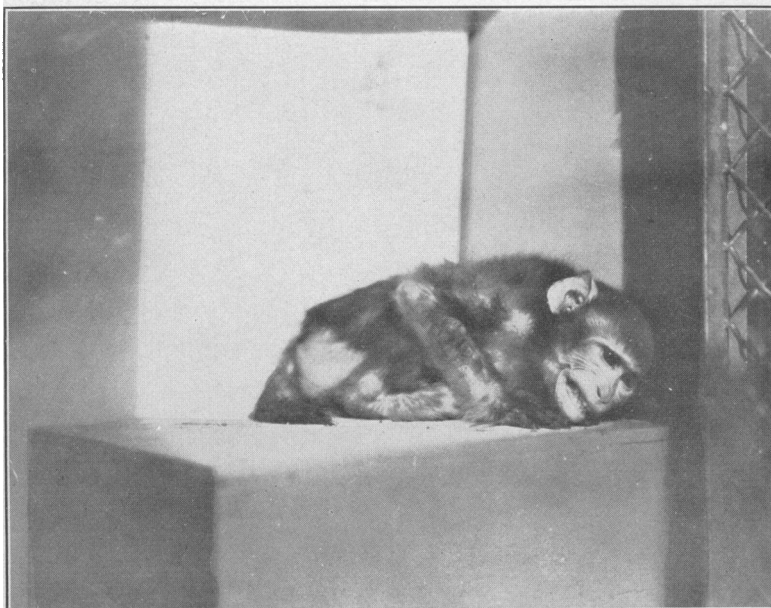
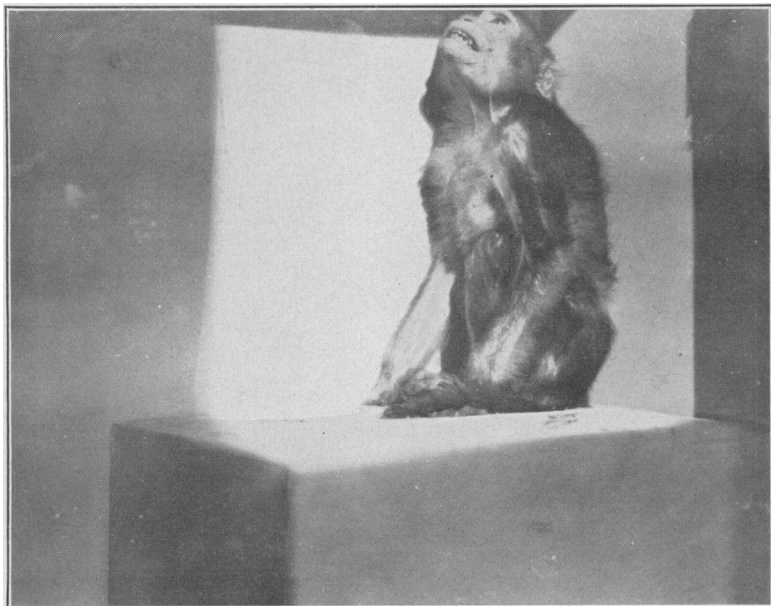
Date	Temperature at 9 a. m. (° C.)	Dose of morphine
1924		
Jan. 13.....	38.0	96 milligrams.
Jan. 14.....	37.6	None.
Jan. 15.....	36.0	Do.
Jan. 16.....	36.6	Do.
Jan. 17.....	36.2	Do.
Jan. 18.....	34.1	Do.
Jan. 19.....	32.0	25 milligrams (9 a. m.).
Do.....	32.0	50 milligrams (3.30 p. m.).

The morphine was given on the 19th in an effort to save the animal but it had no apparent effect, death occurring at 8 p. m. The necropsy showed beginning pneumonic process in the right lower lobe. In this case depression of vital functions rendered the animal susceptible to pneumonia, and it is of interest to note that there was no capacity for reaction with fever.

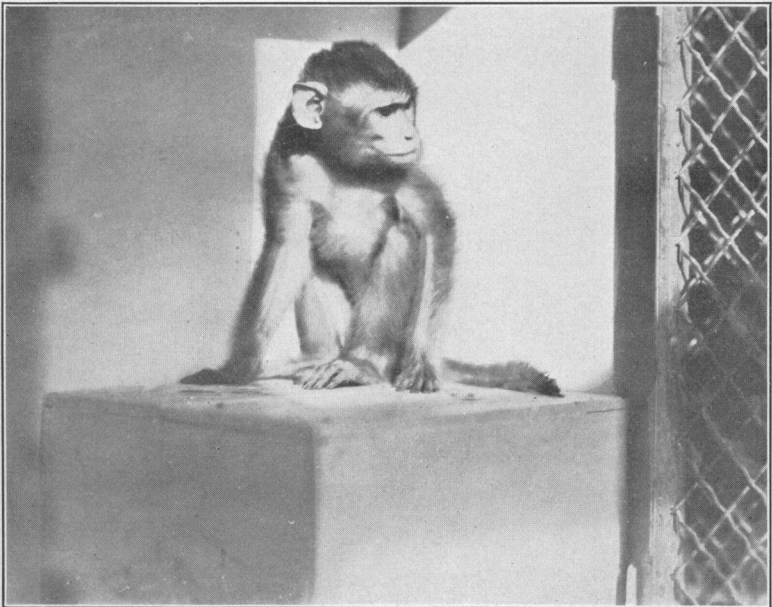
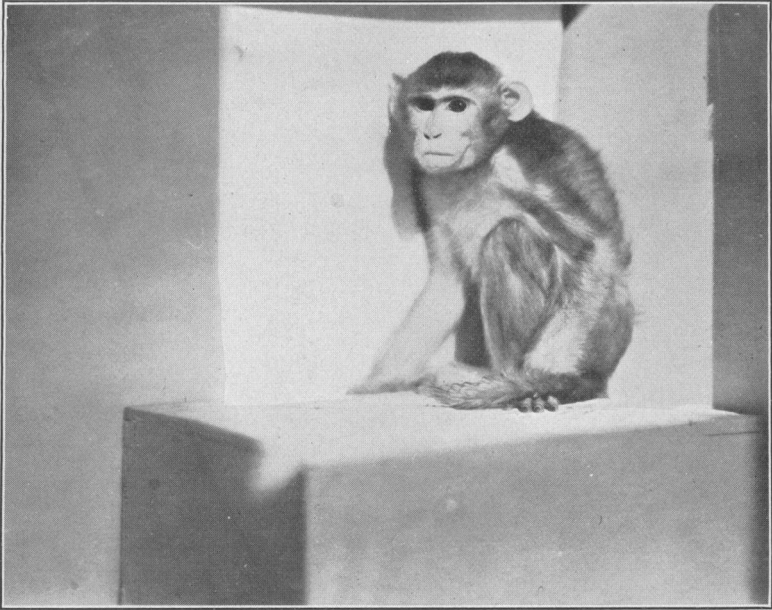
The accompanying photographs illustrate the facial expression and attitudes resulting from the discomfort of withdrawal and the comfort following injection of the usual dose. The animals were photographed immediately before the morning injection of morphine was given and 15 to 30 minutes following the injection.



Monkey No. 5. Upper: November 27, 1923—At the end of a 25-hour period of withdrawal.  
Lower: Same date, 30 minutes after an injection of 100 mg. of morphine sulphate



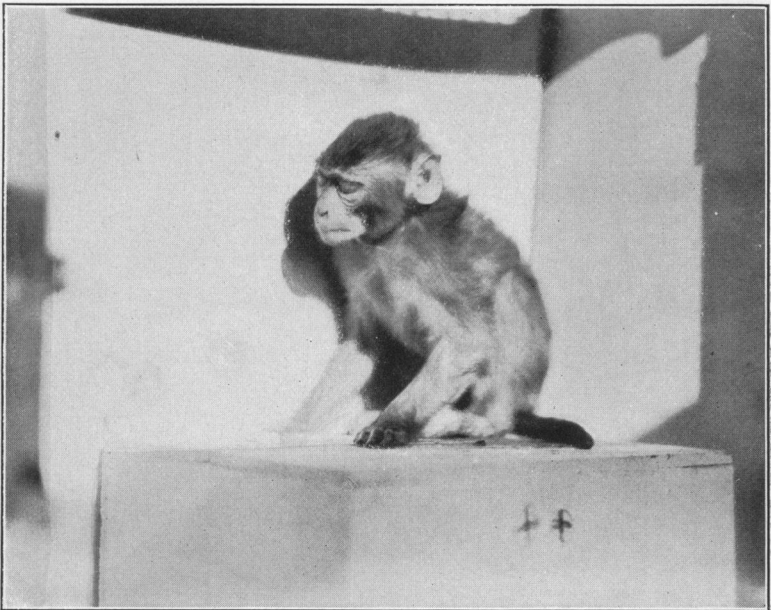
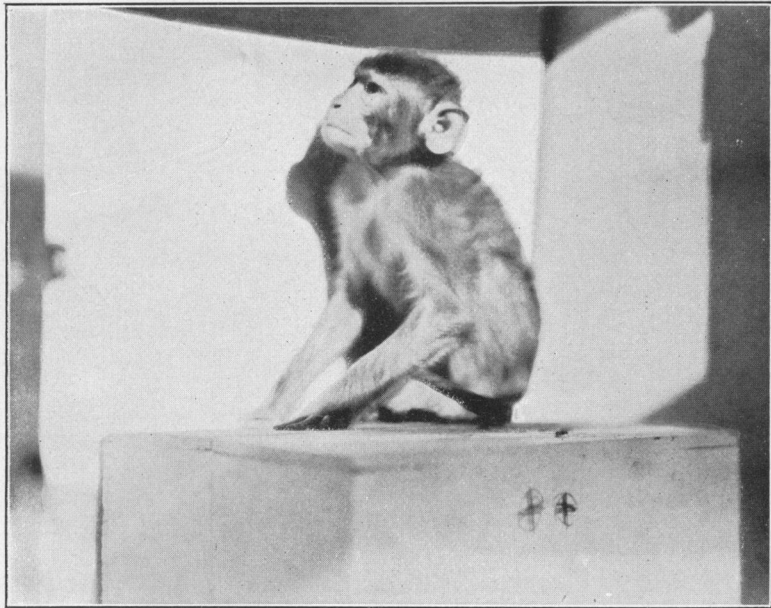
Monkey No. 6. November 27, 1923: At the end of a 25-hour period of withdrawal



Monkey No. 6. November 27, 1923: Thirty minutes after an injection of 95 mg. of morphine sulphate



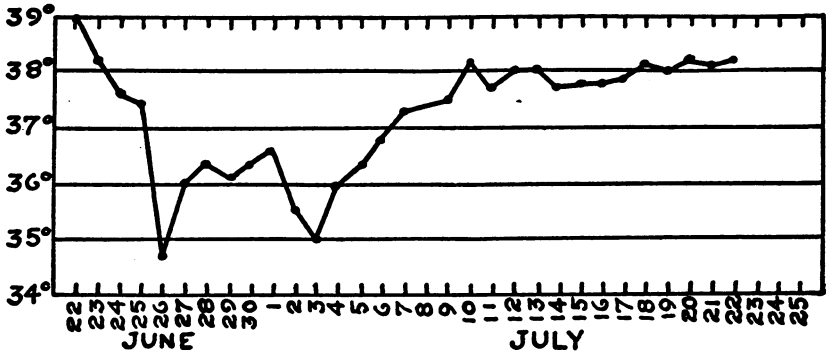
Monkey No. 3 December 11, 1923: At the end of a 23-hour period of withdrawal



Monkey No. 3. December 11, 1923: Fifteen minutes after an injection of 90 mg. of morphine sulphate

No. 3 had been on the drug  $8\frac{1}{2}$  months and was receiving 180 milligrams daily. Nos. 5 and 6 had been on the drug 8 months. No. 5 was receiving 200 milligrams and No. 6, 190 milligrams daily.

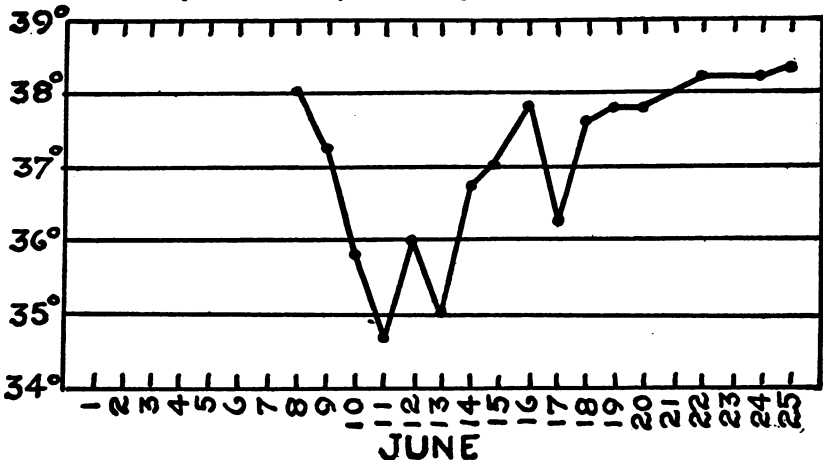
CHART 1.—Temperature of monkey No. 5 during withdrawal of morphine in June and July, 1924



This monkey had been receiving the drug for 15 months. The daily dose was reduced from 200 mg. on December 27, 1923, to 100 mg. on June 22, 1924. The last dose, 50 mg., was given at 3 p. m. on June 22.

The drug was abruptly withdrawn from Nos. 3, 4, and 5 after they had been on it for 15 months. The daily dose had been reduced during the previous six months from 180, 200, and 200 milligrams, respectively, to 100 milligrams in each case. None was receiving as

CHART 2.—Temperature of monkey No. 5 during withdrawal of heroin in June, 1925



The drug was changed from morphine to heroin on March 23, 1924. The daily dose was 14 mg. at the time of withdrawal, having been reduced from 20 mg. The last dose was given at 3:30 p. m. on June 8.

much as No. 6 (190 milligrams daily) when the drug was finally withdrawn, but each had been on daily doses six months longer, and withdrawal symptoms were very evident. The temperature of each animal while receiving the drug regularly was between 38° and 39°. On the day before withdrawal it was 38.4°, 38.7°, and 38.8°,



respectively. The effect of withdrawal varied in degree. The temperature of No. 3 was 37° on the third and sixth days. It went above 38° on the ninth day and did not fall again. In the case of No. 4 the lowest temperature, 36.8°, was reached on the third day. It gradually rose after the sixth day but did not rise above 38° until the twelfth day, and did not remain there until after the sixteenth day. No. 5 was affected more severely, as shown by the accompanying temperature chart.

Animal No. 5 had received opiates for a longer period than any of the other animals. Its history, given below, is illustrative of the history of all those that received morphine chiefly.

## NARCOTIC HISTORY OF MONKEY NO. 5

Adult male monkey in good condition; weight, 2.30 kilos; received a narcotic, chiefly morphine, daily, with the exceptions noted below, from March 28, 1923, to December 17, 1925. Died March 24, 1926, from the effect of a special experiment.

Total daily dose given at 9 a. m. until June 25, 1923; thereafter daily amount given in two equal doses, one at 9 a. m. and one at 4 p. m. Dose omitted on Sundays until October 28, 1923.

TABLE 6.—Narcotic record of monkey No. 5

Date	Daily dose (mgs.)	Observations
1923		
<i>Morphine</i>		
Mar. 28-30.....	6.9	Moderately quiet.
Mar. 30-Apr. 3.....	9.2	More quiet.
Apr. 4-5.....	None.	Sick from effect of drug.
Apr. 6-9.....	11.5	Moderately quiet.
Apr. 10-11.....	13.8	Do.
Apr. 12-16.....	16.0	Do.
Apr. 17-18.....	18.4	Do.
Apr. 19-23.....	20.7	Do.
Apr. 24-26.....	23.0	Do.
Apr. 27-30.....	25.3	Do.
May 1-3.....	32.6	Do.
May 4-7.....	36.5	Very quiet; drowsy; feet wet and cold on the 7th.
May 8.....	None.	Still very quiet and appears ill. Received a dose of castor oil
May 9.....	36.5	Quiet.
May 10-24.....	44.0	Do.
May 25-29.....	45.0	Do.
May 30-June 14.....	50.0	Do.
June 15-23.....	55.0	Do.
June 24-25.....	60.0	Do.
June 26-July 5.....	70.0	Apparently uncomfortable. Fibrillary tremors of fore and hind limbs on 28th.
July 6-11.....	80.0	Do.
July 12-30.....	90.0	Do.
July 31-Aug. 16.....	100.0	Marked discomfort in mornings before injections, restless, lips drawn back in a peculiar grin.
Aug. 17-27.....	110.0	Do.
Aug. 28-Sept. 13.....	120.0	Very sensitive; muscles twitched and exhibited the peculiar grin before receiving injections; calm afterwards.
Sept. 17-22.....	150.0	Do.
Sept. 23-Oct. 4.....	160.0	Do.
Oct. 5-27.....	170.0	Do.
Oct. 28-Nov. 5.....	180.0	On Oct. 28 began giving 1 dose on Sundays to avoid the effect of omission of drug from Saturday to Monday morning.
Nov. 6-21.....	190.0	Do.
Nov. 22-Dec. 27.....	200.0	Began to look emaciated and dirty, but its weight only fell off to 2.19 kilos.
Dec. 28-31.....	150.0	Emaciated and dirty; weight, 2.19 kilos.

TABLE 6.—Narcotic record of monkey No. 5—Continued

Date	Daily dose (mgs.)	Observations
<b>1924</b>		
Jan. 1-19	<i>Morphine</i>	Emaciated and dirty; weight, 2.19 kilos.
Jan. 20-Apr. 1	100.0	Necrosis of tips of ears first noted on Apr. 1.
Apr. 1-12	100.0	
Apr. 13	None.	Extremely hypersensitive next morning. Cried when cage was struck, etc. Calm after injection.
Apr. 14-June 4	100.0	Sick May 19, but drug not omitted until next day. Had regained lost weight.
June 5	50.0	Decreased dose because of tolerance test the next day.
June 6	229.0	Tolerance test, 100 milligrams per kilo, given in 1 dose at 9 a. m. No unusual effect, but somewhat quieter than usual the following 2 days.
June 7-13	100.0	Unusually quiet on 7th and 8th.
June 14	50.0	Given at 9 a. m.
June 15	None.	48 hours' withdrawal test. On 16th before injection doubled up with pain, etc.
June 16-22	100.0	
June 23-Sept. 29	None.	Withdrawal experiment. Became ill, dirty, and disheveled looking. Temperature fell; weight dropped from 2.30 to 2.05 kilos in 16 days. Improved gradually after the 5th day, gaining in weight.
Sept. 30	20.0	Began the administration of morphine again. Clean and healthy in appearance and very active. Weight, 2.64 kilos. Necrosis of ears had disappeared.
Oct. 1-6	20.0	Quiet.
Oct. 7-13	28.0	Twitching of abdominal muscles on the 8th.
Oct. 14	30.0	
Oct. 15-16	40.0	
Oct. 17-21	50.0	Weight had fallen to 2.34 kilos.
Oct. 18-27	60.0	
Oct. 28-Nov. 5	66.0	No drug given on Nov. 2. Hypersensitive and overactive on the 3d before receiving injection of morphine.
Nov. 6-24	70.0	Further reduction in weight noted.
Nov. 25	<i>Codeine phosphate</i> 165.0	Cross tolerance test, 75 milligrams per kilo of codeine phosphate were given in 1 dose. No unusual effect observed.
Nov. 26-27	None.	Hind limbs spastic on 26th.
Nov. 28-29	<i>Morphine</i> 70.0	Signs of distress before injection on morning of 28th.
Nov. 30	None.	
Dec. 1	40.0	Wheezing, apparently from bronchitis. Temperature, 36°. Had recovered from bronchitis by the 5th.
<b>1925</b>		
Jan. 2-6	40	Necrosis of tips of ears again noted.
Jan. 6-Feb. 11	40	No Sunday injections; very hypersensitive and doubled up with distress on Monday mornings before injections.
Feb. 12-Mar. 21	60	Spastic hind limbs on Feb. 18, but drug not omitted. Spastic hind limbs again Mar. 18; no omission of drug.
Mar. 22	None.	Has been growing dirty and disheveled in appearance.
Mar. 23	<i>Heroin</i> 10	Heroin given in 2 equal doses, 1 in the morning and 1 in the afternoon. No effect, except hypersensitiveness from 1 day's abstinence from morphine, which was quickly relieved by heroin.
Mar. 24-26	12	
Mar. 27-28	14	None on 29th. Very hypersensitive on 30th before injection.
Mar. 29	None.	
Mar. 30-Apr. 6	16	
Apr. 7	18	Had a cold; very sleepy and mouth hung open 10 minutes after injection in afternoon. Crawled around on haunches because of spasticity of legs. Necrosis of ears no longer evident.
May 14-29	20	Unable to straighten out hind limbs for several days during this period.
May 30-31	None.	
June 1	15	Very sensitive in the mornings. Doubled up, limbs spastic and apparently sick on 5th.
June 7	None.	
June 8	14	Limbs stiff; dirty and debilitated in appearance, but apparently growing less sensitive to withdrawal of drug.
June 9-Aug. 10	None.	Weight June 9, 2.15 kilos. Doubled up on 10th as if uncomfortable, but not much evidence of hypersensitiveness. Much improved by the 15th. Weight 2.45 kilos on July 25.
Aug. 11-12	4	Began the administration of heroin again on Aug. 11. Is much improved in appearance, but not in the best condition.
Aug. 13-15	3	Much more susceptible to drug than formerly—deep sleep from small doses. Sick, masturbated frequently, and penis and testicles became much swollen. Weight reduced to 2.00 kilos.

TABLE 6.—Narcotic record of monkey No. 5—Continued

Date	Daily dose (mgs.)	Observations
1925		
Aug. 16-17.....	<i>Heroin</i>	
Aug. 18-22.....	None.	
Aug. 23.....	6	
Aug. 24.....	None.	
Aug. 25-26.....	6	
Aug. 27-Nov. 29.....	3	
	None.	Recovered rapidly when drug was stopped, but continued to masturbate for several days. Clean by Sept. 14.
<i>Morphine</i>		
Nov. 30.....	10	Began the administration of morphine. Clean and active. Weight, 2.81 kilos.
Dec. 1-5.....	10	Doubled up. Quiet after first injection on Nov. 30. Appetite lost; masturbating; wheezing on the 5th.
Dec. 6-7.....	None.	Wheezed some, but ate.
Dec. 8.....	10	Temperature, 38.2°.
Dec. 9.....	None.	Rapid deterioration; poor appetite; masturbated frequently; licked body and limbs so that the anterior surfaces from the groin to the chin became moist and reddened from subcutaneous hemorrhages; wheezed at times. Temperature, 37.8° to 38.6°. Weight, 2.14 kilos.
Dec. 10-11.....	10	
Dec. 12-13.....	None.	
Dec. 14.....	10	
Dec. 15.....	None.	
Dec. 16-17.....	10	
Dec. 18, 1925-Mar. 24, 1926..	None.	Rapid improvement in appearance and weight. Temperature maintained between 38° and 39°. Some wheezing was noted for 3 weeks, after withdrawal of drug. At end of period clean, dry, and active. Weight, 2.53 kilos.
1926		
March.....	126.5	Sensitization test: 50 mg. per kilo of body weight were given in 1 dose. Very quiet in 10 minutes; asleep, but easily aroused in 45 minutes. Unable to move because of spasticity of limbs 1½ hours after injection; less spastic and able to sit up 1 hour later. Died 3¼ hours after injection.

At necropsy the bones of No. 5 were decidedly softer than normal. No other pathological conditions were discovered.

The effect of the drug and of withdrawal on weight is shown in the accompanying chart.

*Increased sensitiveness.*—A striking feature in the history of No. 5 is that after periods of abstinence the animal reacted more strongly to the opiates than when they were originally given. It fared well for more than a month on 200 milligrams of morphine daily, but two years later, after three months of abstinence, reacted strongly and very unfavorably to only 10 milligrams per day. It was finally killed by 50 milligrams per kilo of body weight, a dose which caused only mild symptoms in fresh untreated monkeys. Spasticity was a very prominent symptom following the last dose given previous to complete withdrawal.

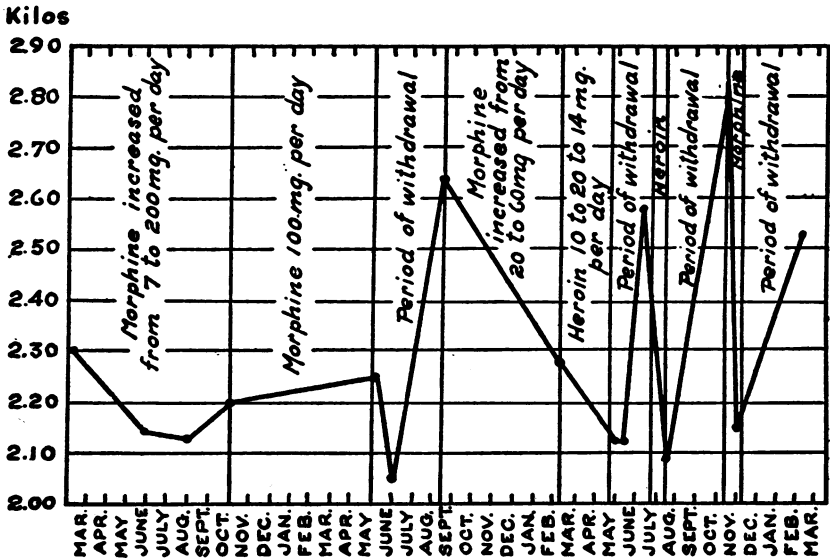
The same condition was observed in No. 4. This animal had received 200 milligrams of morphine for nearly two months with only slight symptoms of deterioration. It then received from 10 to 20 milligrams of heroin for two and one-half months without the appearance of any serious symptoms, after which time it was placed on codeine. Twenty-nine months after the experiment had been started and after a six weeks' period of abstinence the animal was in good condition and weighed more than ever before (3.20 kilos). It then

died from the effect of 6 milligrams of heroin given in two doses five hours apart. This dose, less than 2 milligrams per kilo, seldom caused more than transitory symptoms in fresh untreated monkeys. Spastic paralysis was a prominent symptom. The animal was alert and tried to fight when touched, but because of spasticity, was unable to get up for 30 hours before death. Spasticity is an uncommon symptom following heroin in previously untreated monkeys.

The necropsy of No. 4 revealed slight oedema of the brain, but no other pathological condition.

The decreased resistance of the monkeys to morphine and other opiates as time went on may have been due in part to their increased

CHART 3.—Weight of monkey No. 5



age, but age could not account for the increased sensitiveness evidenced by the marked spasticity.

#### HEROIN

Three healthy monkeys (23X, 27X, and 22X) were given subcutaneous injections of heroin hydrochloride daily, except Sundays and holidays, for 19 months, 22 months, and 25 months, respectively. A dose or two was occasionally omitted because of sickness, but there was less occasion for such omission than there was with the morphine-treated animals. The beginning dose was in each case 4 milligrams, given once daily. This apparently was too large, and in the case of 27X and 23X it was necessary to reduce the dose to 2 milligrams. Number 27X was more sensitive to the drug than either of the others, but tolerance gradually increased, and after 17 months the animal was doing well on 12 milligrams three times daily; after eight months 22X and 23X were receiving up to 12 milligrams and 13 milligrams, respectively, three times daily. No animal was given more than a

total of 39 milligrams daily. Numbers 22X and 23X received the daily amount in one dose for 16 days and in two doses for eight months, after which the daily amount was given in three doses, at 9 a. m., 12 noon, and 4 p. m. Number 27X received two doses daily, beginning on the third day, and three doses daily after six months.

Heroin was given three times a day in an effort to raise the daily amount up to the point where it would physically deplete the animals and also cause addiction. As contrasted with morphine, it was necessary to divide the daily dose further, because from single doses of heroin that caused striking toxic symptoms recovery was made within 15 to 20 minutes without apparent harm, whereas daily doses of morphine large enough to cause physical depletion in a few weeks would be tolerated at the time without toxic effect. In other words, it appeared that the daily amount of heroin could have been increased considerably beyond what was given if the doses had been spaced 4 hours apart and given over the 24 hours instead of from 9 to 4 only, but the daily amount of morphine could not have been increased by such spacing of the doses.

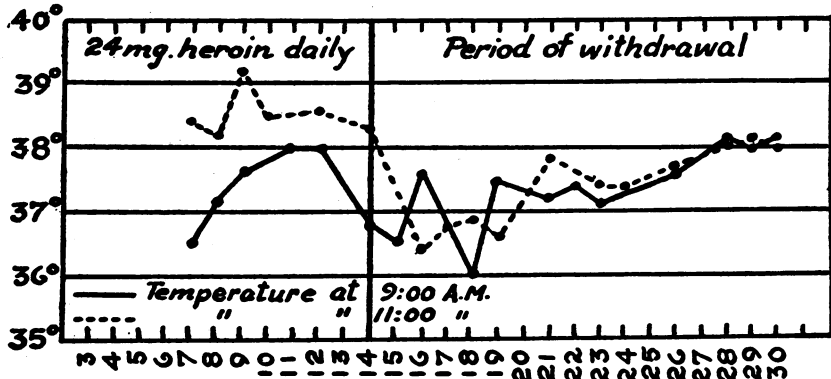
The effect of repeated doses of heroin was similar in most details to that already described for morphine, but different in degree. The quieting effect of each dose of heroin was more quickly established, more pronounced in degree, and more transitory than the quieting effect of morphine. The morphine-treated animals would become quiet and somewhat drowsy about 20 minutes after the dose had been given and be only a little less quiet three to five hours later, but they seldom went to sleep. During the first three months of treatment the heroin-dosed animals would often be so sound asleep in from five to ten minutes after the injection that moderate handling would not awaken them, but three hours later they would be more lively than the morphine-treated animals. Eighteen months after treatment had been started the heroin animals would often go to sleep after the injection and sometimes fall off the shelves in their cages. They would, however, awaken immediately on being touched and then sometimes go to sleep again. Sleeping and extreme drowsiness with nodding lasted from 15 to 30 minutes, but some degree of quietness continued throughout the day.

All the heroin-treated animals had convulsions on several occasions immediately following the injection of the drug. The convulsions were mild as compared with those produced by toxic doses in previously untreated animals. They were followed by sleep lasting from 10 to 20 minutes, from which the animals awakened apparently unharmed. Number 27X had three convulsions during the first three months of treatment and only two more during the following 16 months. As previously stated, no morphine-treated animal had convulsions.

Number 27X was the only one of the heroin-treated animals that lost weight during the course of treatment, and the loss was slight; the other two gained. Numbers 27X and 23X began to show some physical deterioration two weeks and two months, respectively, after the maximum dose had been reached. The maximum was reached in 27X after 18 months and in 23X after 11 months. Because of this deterioration, the dose was reduced. It was reduced in the case of 22X 10½ months after the treatment had been started, because of stiffness and weakness in the hind limbs.

Spastic paralysis was not so prominent a symptom as with the morphine-treated animals. It was an early symptom in the morphine-dosed animals, but was not observed in any of the heroin-treated animals until after 8 months of treatment, when 22X showed it for the first time. Number 23X developed it after a year, and 27X did not develop it at all. The paralysis was not an extreme spasticity with

CHART 4.—Temperature of monkey No. 23X before and after withdrawal of heroin



drawing up of limbs and clenching of the digits, but a weakness with some stiffening of the hind limbs and only occasional clenching of the digits. As with the paralysis due to morphine, it cleared up after the omission of a few doses. Number 23X developed a cyanotic condition of the tips of the ears suggesting beginning necrosis. The ears of the other two animals were not affected. After the animals had been under treatment for a year, vomiting was occasionally observed just before or after the usual morning dose. The vomiting was not accompanied by any observed distress or loss of appetite. The morphine-treated animals did not show this symptom. During the course of treatment the three heroin animals were subjected to withdrawal of the drug in order to study withdrawal symptoms.

*Withdrawal symptoms.*—Addiction, as expressed by symptoms of distress or depression following the withdrawal of the drug, was much less slowly established for heroin than for morphine and was decidedly less pronounced in degree. Following a day of abstinence, a slight

degree of sensitiveness was noted in 23X after a year's treatment. Following two days' abstinence there was twitching of muscles and the animal looked somewhat ill. The only effect observed in 23X during 7 days' abstinence after 8 months' treatment was increased appetite, but much of the tolerance to large doses was lost during this time. Four months later some hypersensitiveness was observed after one day's abstinence and, occasionally, from then on, there was in addition an apparent discomfort on Monday mornings following the abstinence over Sundays. The discomfort was evidenced by crouching until after the morning dose was given. No apparent discomfort resulted from two days' abstinence in 27X after one year's treatment. Slight sensitiveness was noted two months later following abstinence on Sundays, and four months later there was discomfort following two days' abstinence. From then on there was quite obvious hypersensitiveness on Monday mornings before the usual dose was given. No heroin-addicted animal showed at any time the marked symptoms of discomfort and distress repeatedly observed in morphine-addicted animals following one or more days of abstinence. The characteristic grin was never observed in the heroin-addicted animals and crouching was very infrequent.

The most obvious distress symptom following withdrawal of heroin appeared in 23X. When the drug was withdrawn from this animal after 17 months' treatment it became wet and dirty, due to excessive urination and bowel movements; it looked sick and would lie down occasionally, but there was no other evidence of discomfort, except a slight hypersensitiveness when handled. Improvement began on the fifth day after the withdrawal of the drug and was rapid thereafter.

Chart 4 shows the effect of withdrawal on temperature. The last dose was given at 4 p. m. December 14, 1925. Before that date the temperature was taken at 9 a. m., an injection of heroin was given, and the temperature was taken again at 11 a. m. The same routine, omitting the dose of heroin, was followed after the 14th. Note that after this date there was no 11 a. m. rise.

The chart shows clearly the drop in temperature due to the overnight abstinence and the rise following the usual injection in the morning. This occurred with all the animals treated. The low 9 a. m. temperatures on the 7th and 14th were due to 41 hours' abstinence over Sunday.

The average 11 a. m. temperature of 27X for one month before the withdrawal of heroin in May, 1926, was 38.41°. The animal was then receiving 30 milligrams daily and had been on the drug for 20 months. For 18 days after withdrawal the 11 a. m. temperature did not once reach 38.4° and the average for the period was 37.9°. During the next 15 days it was maintained at or above 38.4°; the

average 11 a. m. temperature of this same animal in September, 1927, after an abstinence from drugs for 13 months, was 38.85°.

It appears from a comparative study of the temperatures of morphine and heroin addicted monkeys and those of normal monkeys that the temperature is depressed a fraction of a degree below normal in those that have become tolerant and continue to receive the drug regularly; that sudden withdrawal results in a marked drop (more marked after withdrawal of morphine than of heroin), and that in from two weeks to a month the temperature reaches nearly normal again.

The history of 23X, given in Table 7, is illustrative of the narcotic history of all three heroin-treated animals.

TABLE 7.—Narcotic history of monkey No. 23X

Date	Daily dose	Weight	Effect
1924			
July 8-9	Mg. 4	2.48	Kg.
July 10-15	2		Very quiet; down after injection on 9th, but not asleep. Very quiet after injections; lively 4 hours afterwards.
July 16-20	3		Do.
July 21-26	6		Quiet after injections, but less than formerly.
July 27-29	8		Two injections of 3 milligrams each, beginning on 21st; quiet after injection, but effect less than on 8th and 9th.
July 30-31	10		Quiet after injections.
Aug. 1-3	12		Do.
Aug. 4-5	14		Do.
Aug. 6-10	16		Do.
Aug. 11-16	18		Convulsion 10 minutes after morning injection; lasted 5 minutes; normal 15 minutes later.
Aug. 15-21	18	2.65	Fell off shelf in sleep 10 minutes after morning injection on the 21st; no convulsion.
Aug. 22-Sept. 3	18		Lay quietly at door of cage in mornings; could be handled without resistance, but lively when aroused.
Sept. 4-8	20	2.61	Asleep on 4th and 8th, 5 minutes after morning injection; not awakened by handling. Respiration 9 per minute while asleep on the 4th. Awake and apparently unharmed 10 minutes later.
Sept. 9-Oct. 7	18	2.97 (9/30)	Very sleepy after injections.
Oct. 8-16	20		Do.
Oct. 17-Nov. 20	22	3.03 (9/17)	No unusual symptoms; apparently healthy as ever, but quiet.
Nov. 21-Dec. 31	24	3.19 (10/25), 3.20 (12/22)	Do.
1925			
Jan. 1-21	24	3.29 (1/19)	Do.
Jan. 22-Mar. 15	26	3.29 (2/13)	Fell unconscious Feb. 24, after morning injection. Slight convulsive movements; awake and apparently unharmed less than one-half hour after dose was given.
Mar. 16	30		Beginning Mar. 16, drug given in 3 daily doses, 9 a. m., 12 noon, and 4 p. m.
Mar. 17-June 1	30	3.19 (4/28), 3.29 (5/20)	Very sleepy after each dose; nodding; occasional vomiting in mornings; tip of left ear cyanotic.
June 2-July 3	30		Often weak in hind limbs during this period. Slight stiffness that cleared up after first injection in the mornings. Also began to show definite hypersensitiveness in the mornings before injections.
July 4-5	None.		
July 6-7	30		On morning of 6th sat doubled up as if uncomfortable; trembling, abdomen wet; hind legs stiff; quiet but salivated after injection.
July 8-16	21		Dose reduced because still salivated on the 8th; hind limbs stiff on 13th and 14th.
July 17	24		
July 18-19	None.		



TABLE 7.—*Narcotic history of monkey No. 23X—Continued*

Date	Daily dose	Weight		Effect
		Mg.	Kg.	
1925				
July 20.....	24	-----	-----	Not well on 20th; also hind limbs stiff. Spastic paralysis of hind legs on 21st; salivated. Hypersensitive in mornings; trembles and muscles twitch.
July 21-27.....	18	-----	-----	
July 28-Aug. 3.....	21	3.29 (8/3).....	-----	
Aug. 4-Dec. 14.....	24	3.29 (11/25).....	-----	Healthy, except appearance disheveled and dirty from Sept. 7 to 14; drowsy during entire period after injections, but not as much as formerly with larger dose; no spasticity or stiffness; quite active every morning and somewhat hypersensitive to noises on Mondays, but not markedly uncomfortable.
Dec. 15-31.....	None.	3.275 (12/15), 3.37 (12/23), 3.42 (12/31).	-----	No drug from Dec. 15 to Feb. 23; result, sick for a few days, followed by rapid improvement.
1926				
Jan. 1-Feb. 22.....	None.	3.58 (1/14), 3.52 (2/12).....	-----	In very good health; much more active than when taking narcotics.
Feb. 23.....	6	2.40.....	-----	Lively and in very good condition; 4 milligrams at 9 a. m., followed by unconsciousness in 5 minutes; gasping for breath; awake 10 a. m., quiet at 3 p. m.; 2 milligrams given at this time was followed by unconsciousness.
Feb. 24.....	2	-----	-----	Inactive, climbed on seat with difficulty at 9 a. m.; then injection of 2 milligrams was followed by unconsciousness in 8 minutes; respiration 6 per minute; died without regaining consciousness 1½ hours after injection.

At necropsy, 23X showed a dilated right heart and some congestion of the lungs.

*Increased sensitiveness.*—As was the case with the morphine-treated monkeys, 23X was much more sensitive to heroin after a period of abstinence than it was in the beginning. It was killed by a total of 8 milligrams given in 3 doses in a period of 24 hours. This dose is much smaller than the minimum fatal dose given in one injection to a previously untreated animal.

Numbers 22X and 27X were put back on heroin in July, 1926, after an abstinence of eight weeks; each animal had taken the drug for 20 months previous to this; both of them were less resistant to it than they had been in the beginning, but the difference was not so striking as in the case of 23X.

#### CODEINE

Nine animals were given daily subcutaneous injections of codeine phosphate.

The beginning dose was 10 milligrams once daily in 6 cases and 20 milligrams once daily in 3 cases. The daily amount was gradually increased. It was given in 1 dose at first, but in 2 equal doses in from 3 days to 2 months after the experiment was started.

The effect of the daily administration of codeine was rather striking in that it was decidedly more harmful than either morphine or heroin. Healthy, active animals rapidly became stooped and aged in appearance. Spasticity was an earlier and more common symptom throughout the experiment, and the general health was greatly impaired by doses much smaller than was observed to harm the animals

taking morphine. An early thinning of hair accentuated the disheveled appearance of the codeine-treated animals. Necrosis of the ears came on earlier and was more marked than in the morphine-treated animals.

Convulsions were common and occurred following doses of 40 milligrams, but some of the animals died before receiving a large enough dose to cause convulsions. Some showed increased activity, sometimes indicative of excitement or anxiety for 10 to 15 minutes after an injection of 25 milligrams or more of codeine, but the general effect was decreased activity and a moderate degree of quietness throughout the day. There was, however, no drowsiness comparable with that produced by morphine and heroin.

The harmful effect of codeine is indicated by the deaths that resulted from it as shown in Table 8.

TABLE 8.—*Effect of codeine phosphate given daily*

Animal	Weight	Injections started	Beginning daily dose	Maximum daily dose	Died	Remarks <sup>1</sup>
	<i>Kg.</i>		<i>Mg.</i>	<i>Mg.</i>		
5X.....	2.95	Jan. 3, 1924	20	50	June 1, 1924	Many doses omitted.
11X.....	2.01	do	20	25	Jan. 18	Dose omitted 5 of the 18 days.
14X.....	1.49	Jan. 26	10	10	Feb. 1	Only 3 doses given.
18X.....	2.78	Mar. 12	20	52	Aug. 15	Many doses omitted.
20X.....	2.63	June 11	10	90	Dec. 28	Do.

<sup>1</sup> The omission of doses was because of sickness, spasticity, weakness of limbs, etc.

In addition to the animals included in Table 8, one animal, weight 2.92 kilos, received codeine from January 3, 1924, to September 16, 1924. The maximum daily dose was 60 milligrams, but it was necessary to reduce this because of emaciation, paralysis, loss of hair, necrosis of tips of ears and a general run-down condition. The administration of the drug was finally stopped abruptly, but there were no withdrawal symptoms, and after a month of abstinence the animal was in good condition again.

The three animals listed in Table 9 were not so seriously affected by codeine.

TABLE 9.—*Effect of codeine phosphate given daily*

Animal	Weight	Injections started	Beginning daily dose	Maximum daily dose	Died	Remarks
	<i>Kg.</i>		<i>Mg.</i>	<i>Mg.</i>		
21X.....	2.61	June 11, 1924	10	110	July 7, 1925, from toxic dose of heroin.	The daily dose of codeine had been reduced to 40 milligrams.
25X.....	3.56	Sept. 17, 1924	10	110	do	The daily dose of codeine had been reduced to 80 milligrams.
13X.....	1.68	Jan. 26, 1924	10	70	July 24, 1925, from toxic dose of cocaine.	

The daily dose was reduced in the case of 21X and 25X because they were becoming emaciated, but the health of these two animals was not as seriously affected as was that of the first group, and it was not necessary to omit the daily dose so often. Their emaciation and consequent reduced resistance is in part shown by the effect of heroin given to them to test the cross tolerance of codeine-tolerant animals. Number 25X survived an injection of 50 milligrams of heroin hydrochloride in February, 1925, and died from an injection of 40 milligrams in July. Number 21X survived an injection of 30 milligrams of heroin on two different occasions in February, 1925, and died from 20 milligrams in July. Number 13X was harmed less than any other of the nine codeine-treated animals. The effect of codeine upon it was no more serious than the effect of morphine upon the morphine-treated animals. The resistance of 13X may have been due to the fact that it was the only monkey that did not belong to the *rhesus* species.

*Withdrawal symptoms.*—No noticeable symptoms of discomfort were observed upon withdrawal of the drug from any of the codeine-treated animals. The drug was repeatedly withheld for a day or two from 25X and 21X after they had been receiving it for six months. There was a suggestion of withdrawal symptoms in 21X after nine months of treatment. The animal appeared to be uneasy after 48 hours of abstinence and there was a slight twitching of muscles when the cage was struck but these symptoms were too mild to be regarded as any more than suggestive.

After six months of treatment the drug was withheld from 25X for 13 days. There was no suggestion of increased sensitiveness but the temperature registered 37.8° for four days after which it remained consistently above 38°. This drop is suggestive but not conclusive evidence of a depression of vital functions similar to but less in degree than that caused in other animals by the withdrawal of morphine or heroin.

Four of the codeine-treated animals became tolerant to daily doses that would have killed them in two or three days at the most if they had received such large doses in the beginning; but this tolerance to toxic doses does not prove dependence on the drug for the maintenance of comfort and vitality. There are apparently two factors involved in bringing about these two physiological adjustments to drugs, and one may act without the other.

The experiment with codeine does not prove that it produces dependence, since only one animal received the drug for as long as a year, and the heroin-treated animals showed very little dependence at the end of a year.

An experiment with codeine on a morphine-treated animal, No. 4, throws some light on whether or not codeine can produce dependence.

No. 4 became very much dependent on morphine. After one year heroin was substituted for morphine and used in its place for 75 days. The animal was comfortable under heroin, showing that this drug satisfied in some degree the dependence caused by morphine. It, however, gradually lost some of this dependence. This was shown by the exhibition of a degree of sensitiveness and discomfort in the mornings following overnight abstinence less than that which had been observed in the mornings when morphine was being injected. When codeine was substituted for heroin there was a striking change in the picture. Sensitiveness to interference and obvious discomfort increased during the day instead of disappearing after the injection, and by the third day the animal was doubled up, looked ill, and had the facial expression of pain characteristic when morphine is withdrawn from morphine-treated animals.

The inference from the above is that codeine injected daily into monkeys has very little dependence-producing properties as compared with that produced by morphine and heroin, for the power of an opiate to produce dependence should go along with its power to satisfy the dependence produced by another opiate.

#### TOLERANCE

A high degree of tolerance to morphine and heroin was brought about by the daily administration of these drugs in increasing doses. The dose in each case was gradually brought up to about twenty times the original dose without causing more severe symptoms than in the beginning. The animals receiving 180 to 200 milligrams of morphine daily showed less immediate effect than when they were receiving 40 milligrams. The large doses taken daily were equal to from 75 to 90 milligrams per kilo of body weight. Such doses given only once to similar untreated animals (Table 1) caused death or very severe symptoms, lasting in some cases for several days or a week. Also, the morphine-treated animals received, from time to time, from 90 to 125 milligrams per kilo of body weight in place of the regular morning dose. Increased drowsiness was the only unusual symptom, except that in several cases there was mild spastic paralysis the following day. One of the heroin-treated animals survived 40 milligrams of heroin (14 milligrams per kilo) given in place of the regular 4 p. m. dose.

The evidence of tolerance to increasing daily doses of codeine was not so striking. As previously stated, this drug was so debilitating that most of the animals died early in the experiment. Increased tolerance was, however, brought about in some cases.

#### CROSS TOLERANCE

*Codeine to morphine and heroin.*—Monkey No. 21X, while receiving 110 milligrams of codeine daily, was given in one dose 253 milligrams

of morphine (100 milligrams per kilo). The only effect was increased quietness. Four months later this same animal, while receiving 60 milligrams of codeine daily, survived on two occasions one week apart 12 milligrams per kilo of heroin given in place of the usual dose of codeine. The first dose caused unconsciousness and the second caused a convulsion. In both cases recovery was complete in one hour. Four months later, after the animal had become weakened from codeine, it was killed by 8 milligrams per kilo of heroin.

No. 25X, while receiving 120 milligrams of codeine daily, was only made a little more drowsy by 383 milligrams of morphine (110 milligrams per kilo) given in one injection in place of the morning dose of codeine. Two months later, 25X, while receiving 110 milligrams of codeine daily, survived 50 milligrams of heroin (14 milligrams per kilo) given in one injection in place of the 4 p. m. dose of codeine. The heroin produced unconsciousness. This same animal was killed by 40 milligrams of heroin (10 milligrams per kilo) four months later. It had been growing weak from the effect of codeine.

No. 20X, while receiving 30 milligrams of codeine daily (the dose having been reduced from 88 milligrams because of weakness and spasticity) survived 288 milligrams (100 milligrams per kilo) of morphine without any unusual symptoms. The injections of codeine were continued and the animal died five days later.

*Morphine to heroin and codeine.*—The most striking evidence of cross tolerance was observed in morphine-tolerant animals when the drug was changed to heroin or codeine. No. 4, after receiving daily doses of morphine for two years, was changed over to heroin, 10 milligrams per day, which was raised within seven days to 16 milligrams per day. No unusual effect was noted, although the animal had become somewhat weakened from the effects of morphine. After three months of heroin the injection of 40 milligrams of codeine per day was started and kept up for 21 days. There were no immediate ill effects from the change.

No. 3, while receiving 180 milligrams of morphine daily, was given in one injection 154.7 milligrams of codeine (70 milligrams per kilo) in place of the morning injection of morphine. There was no immediate ill effect observed.

No. 5, while receiving 70 milligrams of morphine daily, was given one injection, 165 milligrams of codeine (75 milligrams per kilo). There was some spasticity the next day, but no other effect. No. 5 at this time was weak and emaciated from the long-continued administration of morphine.

#### SUMMARY

Monkeys were killed by subcutaneous injections of morphine sulphate as low as 85 milligrams per kilo of body weight, and very severe symptoms with sickness lasting several days were caused by smaller

doses, but one animal survived 125 milligrams per kilo, and the minimum fatal dose was not accurately determined. Young and small monkeys survived larger doses per kilo than older and larger animals.

Seven milligrams of heroin per kilo of body weight killed the majority of monkeys that had not previously been given a toxic dose. Some that had previously received a toxic dose of an opiate survived 8 milligrams per kilo.

Some monkeys that survived a toxic dose of morphine, heroin, or codeine were less severely affected by slightly larger doses given from a week to a month afterwards.

No monkey survived as much as 80 milligrams of codeine phosphate per kilo of body weight, and one died from 60 milligrams per kilo.

Codeine caused convulsions frequently, heroin much less often, and morphine never.

By daily administration of morphine, heroin, and codeine, monkeys were made tolerant to increasingly large doses. After 8 or 9 months 200 milligrams per day of morphine caused less severe immediate symptoms than 10 to 40 milligrams did during the first six weeks; 39 milligrams of heroin caused less severe symptoms than did 4 milligrams at first; and 110 milligrams of codeine caused less severe symptoms than did 10 milligrams in the beginning. One animal that was started on morphine was kept on it or on heroin for 52 months.

Gradual deterioration in general health was caused by daily administration of codeine, morphine, and heroin. Codeine was decidedly the most harmful, and heroin the least.

Morphine caused marked dependence, shown by a crouching posture, facial distortion, hypersensitiveness, fall in temperature, and, in one case, death, on withdrawal of the drug. Heroin caused less dependence, and codeine was not definitely shown to produce dependence.

Monkeys made tolerant to large doses of morphine, heroin, or codeine were tolerant to large doses of all three drugs, but the dependence produced by morphine and heroin was not satisfied by codeine.

Tolerance was almost completely lost in about two weeks after withdrawal of the drugs, and the monkeys improved in health and general appearance during the remainder of the period of abstinence.

Monkeys abstinent for six weeks or two months after having received daily doses of morphine or heroin for 16 months or more were more sensitive and less resistant to the drugs when injections were started again than they had been in the beginning. Some of these cases reacted with marked spasticity.

The relative effects in the order of their severity of the three drugs given to monkeys in one toxic dose or in smaller daily doses are as follows:

*Toxicity:* Heroin decidedly most toxic; morphine least toxic.

*General health:* Codeine decidedly most harmful; heroin least harmful.

*Dependence-producing properties:* Morphine most potent; potency of codeine very slight or nonexistent.

#### REFERENCES

- (1) Tatum, Seevers, and Collins: *J. Pharmacol. & Exper. Therap.* (1929), vol. 36, pp. 453-461.
- (2) Plant and Pierce: *J. Pharmacol. & Exper. Therap.* (1928), vol. 33, pp. 229-357.
- (3) Barbour, Hunter, and Richey: *J. Pharmacol. & Exper. Therap.* (1929), vol. 36, pp. 260, 274.

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### ACT EXTENDING THE HOURS OF QUARANTINE INSPECTION

The Congress of the United States, toward the close of the Seventy-first Session, passed legislation which was approved by the President on March 3, 1931, to enable quarantine inspection services to be provided after the hour of sunset in those United States ports of entry in which the need therefor exists. Up to the present, the performance of quarantine inspections has been confined to daylight hours, between sunrise and sunset, at all ports, with the exception of vessels arriving in distress and requiring immediate emergency passage through quarantine.

This new legislation provides that the Secretary of the Treasury shall establish by regulation, following a determination of the commercial needs of the port for such services, definite hours for the performance of quarantine inspection at each quarantine station during the 24 hours each day or any fraction thereof. In those ports in which an extension of the present sunrise to sunset hours for the performance of quarantine inspections seems desirable, the port authorities and/or shipping interests in such ports are required to make an application for such extended quarantine services to the Secretary of the Treasury. Such applications should set forth definitely the period for which it is desired that quarantine services be made available during each 24 hours and should be supported by data showing the commercial necessity therefor. The Secretary of the Treasury, upon receipt of such application, will give the matter consideration and will prescribe the hours during which quarantine services may be performed in such ports.

Ultimately it is anticipated that quarantine services will be made available in units of 8 hours, or multiples thereof, in the various

maritime ports of entry, totaling 126 in number. Where circumstances so warrant, quarantine services may be made available in some of the largest ports during the entire 24 hours of each day, and in other ports during 16 hours out of every 24 hours, and in the smaller ports during 8 hours out of each 24 hours. Providing quarantine services in units of 8 hours, or multiples thereof, is the most economical arrangement, as it permits full 8 hours of duty for each group of personnel.

However, the quarantine inspection of vessels arriving from ports infected with quarantinable diseases will be restricted to hours of daylight in all ports and vessels which are not equipped with adequate artificial lighting facilities to permit of proper quarantine inspection during hours of darkness also will be inspected only during hours of daylight. Vessels arriving during hours of darkness may anchor in the quarantine anchorage and may elect to undergo quarantine inspection the following morning.

The legislation also modifies the charges made for quarantine services rendered at the port of New York, which heretofore have been higher, to conform with the charges made at other United States ports.

Another purpose of the act is to correct a discrimination that heretofore obtained under existing laws respecting officers and employees engaged in the navigation and care of the quarantine vessels operated by the Public Health Service in the various maritime ports of entry. Heretofore, personnel of the Public Health Service employed in the care and navigation of some 70 vessels of the Public Health Service were the only persons so engaged on American vessels, either privately owned or Government owned, who were not entitled to free medical care and hospital treatment in case of sickness or injury. The employees of other Government vessels and of the American merchant marine were already beneficiaries of the Public Health Service, and this feature of the bill now permits the Public Health Service to take care of its own seamen on a basis of equality with the care it is required to furnish seamen employed on other Government vessels or on the American merchant marine.

In addition, officers and employees of the Public Health Service who are assigned to quarantine duty at any of the national quarantine stations, or at infected foreign ports, are necessarily exposed from time to time to direct infection with quarantinable diseases (plague, cholera, yellow fever, smallpox, typhus fever) and other infectious and contagious diseases (such as leprosy, anthrax, etc.) and to injury in the course of their performance of duty incident to exposure to dangerous gases used in fumigation and disinfection procedures and to boarding vessels in rough weather, which this legislation recognizes. The act provides that such officers and employees who become sick



or injured in line of duty shall be furnished medical care, hospital treatment, and similar benefits as beneficiaries of the Public Health Service.

Following is the text of the act:

[Public, No. 796, 71st Congress]

[S. 5743]

AN ACT To authorize twenty-four-hour quarantine inspection service in certain ports of the United States, and for other purposes

*Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,* That the act entitled "An act granting additional quarantine powers and imposing additional duties upon the Marine Hospital Service," approved February 15, 1893, as amended, is further amended by adding at the end thereof the following new sections:

"SEC. 13. The original bills of health required to be obtained in duplicate in foreign ports under the provisions of section 2 of this act shall be presented to the collector of customs in accordance with the provisions of section 5 of this act, and the duplicate copies of such bills of health shall be presented to the quarantine officer at the time quarantine inspection is performed by him.

"SEC. 14. The Secretary of the Treasury shall establish by regulation the hours during which quarantine service shall be performed at each quarantine station, and, upon application by any interested party, may establish quarantine inspection during the twenty-four hours of the day, or any fraction thereof, at such quarantine stations as, in his judgment, require such extended service; but the Secretary may restrict the performance of quarantine inspection to hours of daylight for such arriving vessels as can not, in his opinion, be satisfactorily inspected during hours of darkness. Nothing herein contained, however, shall be construed to require a vessel upon arriving at the quarantine anchorage to undergo quarantine inspection during the hours of darkness, unless the quarantine officer at such quarantine station shall deem an immediate inspection necessary to protect the public health; nor shall any provision of this act be construed to require uniformity in the regulations governing the hours during which quarantine inspection may be obtained at the various ports of the United States.

"SEC. 15. The certificate of health required by section 5 of this act, shall, upon the arrival of any vessel from foreign ports at the anchorage or place established for quarantine inspection purposes in any port of the United States, be procurable at any time within which quarantine services are performed at such station from the quarantine health officer, following satisfactory inspection.

"SEC. 16. The Secretary of the Treasury is authorized and directed to prescribe a schedule of charges for quarantine services rendered to vessels at each of the national quarantine stations, which charges shall be reasonable and uniform for all ports, including the port of New York. The quarantine officer in each port of entry shall promptly forward to the collector of customs at such port an itemized statement of the quarantine services rendered to each vessel at the prescribed charges, which charges shall be paid to the collector of customs by said vessel prior to clearance or departure from such port. All such collections shall be accounted for by the collector of customs and shall be covered into the Treasury as miscellaneous receipts.

"The provisions of the act of June 5, 1920 (41 Stat. 875), relating to the schedule of fees and rates of charges to be adopted and promulgated by the Secretary of the Treasury at the New York Quarantine Station are hereby repealed.

"**SEC. 17.** Any officer or employee of the Public Health Service on duty at any national quarantine station or on a national quarantine vessel, or detailed for duty in foreign ports, under the provisions of sections 2 and 5 of this act, who is suffering from sickness or injury incurred in line of duty, shall be a beneficiary of the Public Health Service and shall be entitled to receive all necessary medical treatment and other benefits authorized to be furnished to beneficiaries."

**SEC. 2.** There is hereby authorized to be appropriated the sum of \$100,000, or so much thereof as may be necessary, to carry out the provisions of this amendatory act.

**SEC. 3.** Whenever steamship companies desiring the benefits of such extended quarantine service at any port shall offer to advance funds in order to permit the immediate institution of such service at such port, the Secretary of the Treasury may, in his discretion, receive such funds and expend the same for such purpose; and the moneys so contributed shall be repaid by the Secretary, without interest, from any funds appropriated under authority of section 2 of this act.

Approved, March 3, 1931.

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## COURT DECISION RELATING TO PUBLIC HEALTH

*Statute providing for sterilization of feeble-minded inmates of State institution as a prerequisite to parole upheld.*—(Nebraska Supreme Court; *In re Clayton*; *Clayton v. Board of Examiners of Defectives*, 234 N. W. 630; decided Feb. 11, 1931.) Acting under authority of chapter 163 of the laws of 1929, the board of examiners of defectives ordered that the petitioner, an inmate of the State institution for the feeble-minded, be sterilized as a condition prerequisite to his parole from the said institution. It appeared that the petitioner's mentality was that of a 6 or 7 year old child, that he had reached his greatest capacity of mentality, that his feeble-minded condition was congenital and not acquired, that his condition would be transmitted to his offspring, and that in the opinion of the examining physicians his sterilization was unquestionably advisable. One of the objections raised to the statute in question was that it violated the constitutional provision prohibiting cruel and unusual punishment. Concerning this the supreme court stated: "From the record before us, we conclude that the operation under discussion, as applied to a feeble-minded person, does not come within the meaning of the constitutional inhibition against cruel and unusual punishment." Another point urged was that the subject matter of the act was not clearly expressed in the title, but the court rejected this contention. Regarding the validity of the statute, the court said:

The legislative act before us is in the interest of the public welfare in that its prime object is to prevent the procreation of mentally and physically abnormal human beings. We think it is within the police power of the State to provide for the sterilization of feeble-minded persons as a condition prerequisite to release from a State institution.

**DEATHS DURING WEEK ENDED MARCH 7, 1931**

Summary of information received by telegraph from industrial insurance companies for the week ended March 7, 1931, and corresponding week of 1930. (From the Weekly Health Index, issued by the Bureau of the Census, Department of Commerce)

	Week ended March 7, 1931	Corresponding week, 1930
Policies in force.....	75, 123, 813	75, 538, 052
Number of death claims.....	16, 589	16, 292
Death claims per 1,000 policies in force, annual rate.....	11. 5	11. 2

Deaths <sup>1</sup> from all causes in certain large cities of the United States during the week ended March 7, 1931, infant mortality, annual death rate, and comparison with corresponding week of 1930. (From the Weekly Health Index, issued by the Bureau of the Census, Department of Commerce)

[The rates published in this summary are based upon mid-year population estimates derived from the 1930 census]

City	Week ended Mar. 7, 1931				Corresponding week, 1930		Death rate <sup>2</sup> for the first 10 weeks	
	Total deaths	Death rate <sup>1</sup>	Deaths under 1 year	Infant mortality rate <sup>1</sup>	Death rate <sup>1</sup>	Deaths under 1 year	1931	1930
Total (81 cities).....	9, 447	13. 8	857	67	13. 3	846	14. 2	13. 4
Akron.....	29	7. 9	8	79	9. 2	7	8. 3	8. 8
Albany <sup>1</sup> .....	36	14. 5	6	119	15. 5	3	15. 4	16. 8
Atlanta.....	92	17. 3	9	92	18. 2	11	16. 8	17. 8
White.....	54	( <sup>1</sup> )	5	79	( <sup>1</sup> )	6	( <sup>1</sup> )	( <sup>1</sup> )
Colored.....	38	( <sup>1</sup> )	4	115	( <sup>1</sup> )	5	( <sup>1</sup> )	( <sup>1</sup> )
Baltimore <sup>1</sup> .....	269	17. 2	22	75	17. 8	21	17. 5	15. 6
White.....	207	( <sup>1</sup> )	15	65	( <sup>1</sup> )	12	( <sup>1</sup> )	( <sup>1</sup> )
Colored.....	62	( <sup>1</sup> )	7	109	( <sup>1</sup> )	9	( <sup>1</sup> )	( <sup>1</sup> )
Birmingham.....	77	14. 9	7	70	13. 3	8	15. 0	14. 4
White.....	35	( <sup>1</sup> )	3	51	( <sup>1</sup> )	4	( <sup>1</sup> )	( <sup>1</sup> )
Colored.....	42	( <sup>1</sup> )	4	97	( <sup>1</sup> )	4	( <sup>1</sup> )	( <sup>1</sup> )
Boston.....	229	15. 2	23	66	15. 3	28	17. 5	15. 8
Bridgeport.....	28	9. 9	3	50	15. 6	8	13. 7	14. 4
Buffalo.....	171	15. 3	23	90	14. 3	15	15. 3	14. 5
Cambridge.....	35	16. 0	3	60	15. 1	4	14. 5	14. 0
Camden.....	33	14. 5	1	17	14. 5	3	13. 7	14. 5
Canton.....	17	8. 8	2	46	8. 4	3	10. 9	12. 0
Chicago <sup>1</sup> .....	750	11. 3	72	64	11. 8	71	12. 3	11. 8
Cincinnati.....	153	17. 4	17	102	16. 9	15	18. 1	17. 6
Cleveland.....	261	14. 9	26	76	13. 4	28	12. 8	12. 4
Columbus.....	91	16. 1	4	39	15. 0	3	14. 7	15. 3
Dallas.....	50	9. 6	8	( <sup>1</sup> )	10. 3	7	12. 4	13. 3
White.....	29	( <sup>1</sup> )	4	( <sup>1</sup> )	( <sup>1</sup> )	7	( <sup>1</sup> )	( <sup>1</sup> )
Colored.....	21	( <sup>1</sup> )	4	( <sup>1</sup> )	( <sup>1</sup> )	0	( <sup>1</sup> )	( <sup>1</sup> )
Dayton.....	65	16. 6	10	140	6. 7	2	14. 1	10. 4
Denver.....	87	15. 6	10	97	17. 7	6	16. 1	15. 8
Des Moines.....	27	9. 7	1	15	15. 3	1	12. 2	13. 0
Detroit.....	331	10. 4	37	59	8. 1	48	9. 7	10. 5
Duluth.....	33	16. 9	4	96	11. 3	1	12. 8	11. 5
El Paso.....	31	15. 4	4	( <sup>1</sup> )	18. 2	6	19. 9	19. 1
Erle.....	22	9. 7	1	19	11. 7	4	11. 4	11. 4
Fall River <sup>1</sup> .....	34	15. 4	1	23	14. 0	1	13. 7	14. 1
Flint.....	34	10. 8	6	77	12. 2	6	8. 0	10. 3
Fort Worth.....	38	11. 8	1	( <sup>1</sup> )	11. 1	2	11. 4	12. 9
White.....	31	( <sup>1</sup> )	1	( <sup>1</sup> )	( <sup>1</sup> )	1	( <sup>1</sup> )	( <sup>1</sup> )
Colored.....	7	( <sup>1</sup> )	0	( <sup>1</sup> )	( <sup>1</sup> )	1	( <sup>1</sup> )	( <sup>1</sup> )
Grand Rapids.....	26	10. 9	4	59	13. 9	6	9. 6	11. 4
Houston.....	78	13. 1	13	( <sup>1</sup> )	12. 4	10	12. 3	13. 6
White.....	51	( <sup>1</sup> )	7	( <sup>1</sup> )	( <sup>1</sup> )	8	( <sup>1</sup> )	( <sup>1</sup> )
Colored.....	27	( <sup>1</sup> )	6	( <sup>1</sup> )	( <sup>1</sup> )	2	( <sup>1</sup> )	( <sup>1</sup> )
Indianapolis.....	105	14. 8	4	33	16. 1	9	15. 5	16. 7
White.....	89	( <sup>1</sup> )	4	38	( <sup>1</sup> )	9	( <sup>1</sup> )	( <sup>1</sup> )
Colored.....	16	( <sup>1</sup> )	0	( <sup>1</sup> )	( <sup>1</sup> )	0	( <sup>1</sup> )	( <sup>1</sup> )
Jersey City.....	75	12. 3	13	115	12. 5	7	14. 0	12. 8
Kansas City, Kans.....	32	13. 6	1	21	9. 8	0	16. 7	12. 9
White.....	20	( <sup>1</sup> )	0	( <sup>1</sup> )	( <sup>1</sup> )	0	( <sup>1</sup> )	( <sup>1</sup> )
Colored.....	12	( <sup>1</sup> )	1	127	( <sup>1</sup> )	0	( <sup>1</sup> )	( <sup>1</sup> )
Kansas City, Mo.....	128	16. 3	12	91	13. 8	14	15. 6	14. 4
Knoxville.....	22	10. 5	4	85	14. 7	2	14. 1	14. 9
White.....	15	( <sup>1</sup> )	4	95	( <sup>1</sup> )	1	( <sup>1</sup> )	( <sup>1</sup> )
Colored.....	7	( <sup>1</sup> )	0	( <sup>1</sup> )	( <sup>1</sup> )	1	( <sup>1</sup> )	( <sup>1</sup> )
Long Beach.....	28	9. 6	2	48	14. 1	2	10. 7	10. 6
Los Angeles.....	253	10. 0	14	41	11. 3	20	12. 2	12. 4
Louisville.....	107	18. 1	5	43	13. 2	4	17. 1	14. 6
White.....	81	( <sup>1</sup> )	4	39	( <sup>1</sup> )	3	( <sup>1</sup> )	( <sup>1</sup> )
Colored.....	26	( <sup>1</sup> )	1	66	( <sup>1</sup> )	1	( <sup>1</sup> )	( <sup>1</sup> )

See footnotes at end of table.

Deaths <sup>1</sup> from all causes in certain large cities of the United States during the week ended March 7, 1931, infant mortality, annual death rate, and comparison with corresponding week of 1930.—Continued

City	Week ended Mar. 7, 1931				Corresponding week, 1930		Death rate for the first 10 weeks	
	Total deaths	Death rate	Deaths under 1 year	Infant mortality rate	Death rate	Deaths under 1 year	1931	1930
Lowell <sup>2</sup> .....	32	16.6	2	51	16.6	5	14.8	15.6
Lynn.....	23	11.7	1	26	12.2	0	12.7	12.9
Memphis.....	91	18.3	9	95	20.5	5	17.7	17.6
White.....	56		6	100		1		
Colored.....	35	( <sup>3</sup> )	3	87	( <sup>3</sup> )	4	( <sup>3</sup> )	( <sup>3</sup> )
Miami.....	30	13.9	2	51	17.4	3	14.4	13.5
White.....	20		1	35		0		
Colored.....	10	( <sup>3</sup> )	1	88	( <sup>3</sup> )	3	( <sup>3</sup> )	( <sup>3</sup> )
Milwaukee.....	123	10.9	12	52	11.9	18	10.7	11.0
Minneapolis.....	110	12.1	14	90	11.6	6	12.5	11.9
Nashville.....	57	22.5	5	74	17.3	7	18.5	16.8
White.....	36		1	20		4		
Colored.....	31	( <sup>3</sup> )	4	226	( <sup>3</sup> )	3	( <sup>3</sup> )	( <sup>3</sup> )
New Bedford <sup>2</sup> .....	23	10.7	1	27	12.5	2	13.8	12.2
New Haven.....	39	12.5	1	19	14.4	2	13.3	15.2
New Orleans.....	124	13.8	7	38	20.6	12	20.1	20.1
White.....	67		1	8		4		
Colored.....	57	( <sup>3</sup> )	6	98	( <sup>3</sup> )	8	( <sup>3</sup> )	( <sup>3</sup> )
New York.....	1,764	13.0	169	71	12.1	160	13.9	12.1
Bronx borough.....	252	9.9	24	54	8.7	15	10.1	8.6
Brooklyn borough.....	582	11.6	57	60	10.8	66	12.9	11.2
Manhattan borough.....	692	19.9	67	114	18.4	63	21.1	17.9
Queens borough.....	188	8.5	14	38	8.0	14	9.2	7.8
Richmond borough.....	50	10.0	7	126	14.1	2	14.5	15.2
Newark, N. J.....	114	13.3	13	68	13.7	8	14.2	14.6
Oakland.....	87	15.5	9	115	13.0	4	12.4	12.4
Oklahoma City.....	46	12.2	8	110	10.3	5	11.6	10.7
Omaha.....	60	14.4	4	45	14.6	3	15.4	14.7
Paterson.....	44	16.5	3	52	12.8	1	15.8	13.6
Philadelphia.....	598	15.9	72	105	13.9	57	13.4	13.9
Pittsburgh.....	222	17.1	15	52	16.7	25	18.0	15.7
Portland, Oreg.....	80	13.6	1	12	11.7	3	13.0	13.9
Providence.....	79	16.2	8	74	18.7	9	16.0	15.9
Richmond.....	57	16.1	8	117	17.9	4	18.0	16.8
White.....	30		4	88		1		
Colored.....	27	( <sup>3</sup> )	4	174	( <sup>3</sup> )	3	( <sup>3</sup> )	( <sup>3</sup> )
Rochester.....	84	13.2	7	64	13.6	5	14.1	12.8
St. Louis.....	292	18.4	12	40	15.8	8	18.8	15.8
St. Paul.....	72	13.6	1	10	11.1	3	11.1	11.6
Salt Lake City <sup>4</sup> .....	35	12.8	2	30	11.9	3	12.9	14.4
San Antonio.....	73	15.9	8		20.3	13	15.5	19.5
San Diego.....	51	17.0	4	81	15.7	3	16.5	16.1
San Francisco.....	237	19.0	7	46	13.8	10	15.2	14.4
Schenectady.....	27	14.6	3	88	16.9	8	11.9	11.1
Seattle.....	110	15.4	7	66	11.2	4	12.9	11.8
Somerville.....	17	8.4	2	74	10.5	3	11.9	12.8
South Bend.....	31	15.0	2	50	11.4	1	9.4	10.8
Spokane.....	28	12.6	2	52	14.0	2	13.1	13.7
Springfield, Mass.....	47	16.1	6	92	12.1	3	14.5	14.6
Syracuse.....	49	12.0	1	12	12.7	5	13.4	13.4
Tacoma.....	42	20.3	0	0	19.0	1	15.5	13.1
Toledo.....	84	14.8	7	64	12.7	9	13.4	14.3
Trenton.....	61	25.7	6	104	16.5	8	20.3	18.8
Utica.....	41	20.9	2	52	18.9	6	16.7	15.8
Washington, D. C.....	161	17.0	19	105	16.1	11	18.8	16.2
White.....	101		11	90		8		
Colored.....	60	( <sup>3</sup> )	8	138	( <sup>3</sup> )	3	( <sup>3</sup> )	( <sup>3</sup> )
Waterbury.....	22	11.4	1	30	13.0	3	11.3	10.9
Wilmington, Del. <sup>5</sup> .....	38	18.6	2	43	17.1	5	16.7	16.1
Worcester.....	61	16.1	5	69	20.3	8	15.5	15.9
Yonkers.....	25	9.4	0	0	8.1	1	10.9	9.2
Youngstown.....	48	14.5	7	98	13.1	3	11.7	11.2

<sup>1</sup> Deaths of nonresidents are included. Stillbirths are excluded.

<sup>2</sup> These rates represent annual rates per 1,000 population, as estimated for 1931 and 1930 by the arithmetical method.

<sup>3</sup> Deaths under 1 year of age per 1,000 live births. Cities left blank are not in the registration area for births.

<sup>4</sup> Data for 76 cities.

<sup>5</sup> Deaths for week ended Friday.

<sup>6</sup> For the cities for which deaths are shown by color, the percentage of colored population in 1920 was as follows: Atlanta, 31; Baltimore, 15; Birmingham, 39; Dallas, 15; Forth Worth, 14; Houston, 25; Indianapolis, 11; Kansas City, Kans., 14; Knoxville, 15; Louisville, 17; Memphis, 33; Miami, 31; Nashville, 30; New Orleans, 26; Richmond, 32; and Washington, D. C., 25.

<sup>7</sup> Population Apr. 1, 1930; decreased 1920 to 1930, no estimate made.

# 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 March 14, 1931, and March 15, 1930

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended March 14, 1931, and March 15, 1930

Division and State	Diphtheria		Influenza		Measles		Meningococcus meningitis	
	Week ended Mar. 14, 1931	Week ended Mar. 15, 1930	Week ended Mar. 14, 1931	Week ended Mar. 15, 1930	Week ended Mar. 14, 1931	Week ended Mar. 15, 1930	Week ended Mar. 14, 1931	Week ended Mar. 15, 1930
<b>New England States:</b>								
Maine.....	5	1	63	7	49	73	1	0
New Hampshire.....	1	4	1	9	59	10	0	0
Vermont.....	2	4				38	0	0
Massachusetts.....	46	71	18	8	419	915	0	7
Rhode Island.....	3	25		2	12	1	0	0
Connecticut.....	15	15	24	14	766	16	2	0
<b>Middle Atlantic States:</b>								
New York.....	126	171	142	120	1,835	648	21	12
New Jersey.....	76	132	70	21	633	591	3	8
Pennsylvania.....	93	150			3,633	1,176	32	10
<b>East North Central States:</b>								
Ohio.....	55	78	872	61	680	626	11	15
Indiana.....	28	24	53		757	61	15	22
Illinois.....	63	172	125	59	1,711	614	1	10
Michigan.....	32	72	223	5	543	864	13	41
Wisconsin.....	19	18	113	44	449	947	3	2
<b>West North Central States:</b>								
Minnesota.....	16	17	1	2	82	249	4	6
Iowa.....	7	15			16	624	1	6
Missouri.....	38	46	47	19	331	75	9	18
North Dakota.....	7	4			17	32	1	3
South Dakota.....	8	1	1		30	112	1	1
Nebraska.....	7	28			2	490	1	3
Kansas.....	12	15	77	5	40	522	1	4
<b>South Atlantic States:</b>								
Delaware.....	3	2	6	2	97	11	0	0
Maryland <sup>1</sup> .....	13	30	140	45	889	41	0	2
District of Columbia.....	7	17	2	2	153	14	4	0
Virginia.....							1	
West Virginia.....	8	15	162	33	110	90	1	1
North Carolina.....	24	37	86	17	501	28	6	6
South Carolina.....	16	18	2,320	914	127		4	2
Georgia <sup>2</sup> .....	6	9	1,072	103	114	202	4	0
Florida.....	8	7	87	9	134	301	0	1
<b>East South Central States:</b>								
Kentucky.....					403	99	9	2
Tennessee.....	7	2	393	96	169	265	2	4
Alabama <sup>3</sup> .....	31	21	627	93	349	156	9	4
Mississippi.....	13	9					2	21
<b>West South Central States:</b>								
Arkansas.....	6	7	242	127	24	28	4	5
Louisiana.....	27	17	39	24	2	151	4	0
Oklahoma <sup>4</sup> .....	9	14	167	119	20	469	1	3
Texas.....	74	49	263	124	276	106	0	2
<b>Mountain States:</b>								
Montana.....	2				1	32	0	3
Idaho.....					3	24	0	3
Wyoming.....			3	1		6	0	0
Colorado.....	9	6		3	669	170	0	0
New Mexico.....	5	6	29	8	53	83	2	1
Arizona.....	1	9	19	8	120	7	5	3
Utah <sup>4</sup> .....	1					244	3	6

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

<sup>2</sup> Week ended Friday.

<sup>3</sup> Typhus fever, 1931, 2 cases; 1 case in Georgia and 1 case in Alabama.

<sup>4</sup> Figures for 1931 are exclusive of Oklahoma City and Tulsa.

*Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended March 14, 1931, and March 15, 1930—Continued*

Division and State	Diphtheria		Influenza		Measles		Meningococcus meningitis	
	Week ended Mar. 14, 1931	Week ended Mar. 15, 1930	Week ended Mar. 14, 1931	Week ended Mar. 15, 1930	Week ended Mar. 14, 1931	Week ended Mar. 15, 1930	Week ended Mar. 14, 1931	Week ended Mar. 15, 1930
Pacific States:								
Washington.....	6	9	1	2	51	252	2	2
Oregon.....	5	5	299	55	80	54	0	0
California.....	58	71	508	35	1,256	1,805	7	7
Division and State	Pollomyelitis		Scarlet fever		Smallpox		Typhoid fever	
	Week ended Mar. 14, 1931	Week ended Mar. 15, 1930	Week ended Mar. 14, 1931	Week ended Mar. 15, 1930	Week ended Mar. 14, 1931	Week ended Mar. 15, 1930	Week ended Mar. 14, 1931	Week ended Mar. 15, 1930
New England States:								
Maine.....	0	0	47	32	0	0	2	0
New Hampshire.....	1	0	16	18	0	0	0	0
Vermont.....	0	0	9	8	0	1	0	0
Massachusetts.....	2	1	357	274	0	0	3	5
Rhode Island.....	0	0	67	82	0	0	0	0
Connecticut.....	0	1	59	123	0	0	1	3
Middle Atlantic States:								
New York.....	0	4	1,237	650	11	19	13	12
New Jersey.....	2	1	317	271	0	0	0	3
Pennsylvania.....	0	0	562	501	0	1	9	3
East North Central States:								
Ohio.....	0	0	627	525	42	232	5	6
Indiana.....	0	0	289	199	104	114	6	3
Illinois.....	4	2	352	593	26	164	0	0
Michigan.....	1	0	402	364	22	39	5	2
Wisconsin.....	3	0	162	180	4	34	2	1
West North Central States:								
Minnesota.....	0	0	114	176	7	3	0	3
Iowa.....	1	0	132	99	73	93	1	0
Missouri.....	0	1	301	102	45	69	5	1
North Dakota.....	0	0	89	36	11	13	0	3
South Dakota.....	0	0	14	22	32	34	1	1
Nebraska.....	0	2	62	140	33	44	0	0
Kansas.....	3	0	71	153	116	63	1	1
South Atlantic States:								
Delaware.....	0	0	25	9	0	0	1	0
Maryland <sup>1</sup> .....	0	0	85	89	0	0	1	3
District of Columbia.....	0	0	33	19	0	0	0	0
Virginia.....	0	0	40	35	10	32	1	18
West Virginia.....	0	0	51	38	1	13	1	2
North Carolina.....	0	0	4	3	3	6	6	10
South Carolina.....	0	0	82	18	0	0	7	1
Georgia <sup>2</sup> .....	0	0	7	2	1	0	3	2
Florida.....	0	0						
East South Central States:								
Kentucky.....	0	1	94	60	15	4	1	4
Tennessee.....	0	1	29	51	0	12	0	2
Alabama <sup>1</sup> .....	0	0	24	15	33	3	3	2
Mississippi.....	0	0	16	12	15	1	2	5
West South Central States:								
Arkansas.....	0	0	31	16	18	26	1	0
Louisiana.....	0	0	25	27	26	3	6	17
Oklahoma <sup>4</sup> .....	0	0	38	34	74	94	2	9
Texas.....	0	1	38	85	56	125	1	6
Mountain States:								
Montana.....	0	1	32	49	2	13	0	2
Idaho.....	0	0	9	28	0	9	0	0
Wyoming.....	0	0	23	22	5	12	0	0
Colorado.....	0	0	54	15	1	26	2	0
New Mexico.....	0	0	9	11	3	8	0	2
Arizona.....	0	0	3	9	0	32	0	2
Utah <sup>3</sup> .....	0	0	19	11	4	0	0	0
Pacific States:								
Washington.....	0	0	50	80	37	86	0	3
Oregon.....	0	0	19	29	18	31	0	0
California.....	2	3	139	214	46	92	4	8

<sup>1</sup> Week ended Friday.

<sup>2</sup> Typhus fever: 1931, 2 cases; 1 case in Georgia and 1 case in Alabama.

<sup>4</sup> Figures for 1931 are 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	Malaria	Measles	Pella- gra	Polio- myelitis	Scarlet fever	Small- pox	Ty- phoid fever
<i>January, 1931</i>										
Michigan.....	21	219	24	1	582		4	1,365	226	19
Mississippi.....	10	89	9,380	1,051	116	393	6	122	77	21
<i>February, 1931</i>										
Alabama.....	18	111	1,319	65	2,063	23	6	129	27	28
Connecticut.....	4	45	684		1,338		0	224	0	1
District of Columbia.....	8	53	83		270	1	1	94	0	1
Georgia.....	10	32	5,630	70	500	32	1	260	4	20
Indiana.....	20	174	460		2,720		0	1,407	432	6
Massachusetts.....	12	208	534	1	2,196		4	1,510	0	12
Nebraska.....	9	48	46		15		2	212	222	5
New Jersey.....	19	213	842		2,879		0	1,084	0	10
North Dakota.....	4	42	32		37		1	132	38	5
Tennessee.....	63	57	2,357	15	1,268	27	0	477	39	20
Vermont.....		1			62		0	31	1	
Wyoming.....	4	3	6		9		0	131	9	1

<i>January, 1931</i>		Cases	<i>January, 1931</i>		Cases
Chicken pox:			Chicken pox—Continued.		
Michigan.....		1,862	Georgia.....		266
Mississippi.....		905	Indiana.....		497
Dengue:			Massachusetts.....		1,296
Mississippi.....		2	Nebraska.....		323
Dysentery:			New Jersey.....		1557
Mississippi (amebic).....		27	North Dakota.....		119
Mississippi (bacillary).....		205	Tennessee.....		526
Hookworm disease:			Vermont.....		90
Mississippi.....		153	Wyoming.....		120
Lethargic encephalitis:			Conjunctivitis:		
Michigan.....		3	Connecticut.....		10
Mumps:			Georgia.....		6
Michigan.....		381	Dysentery:		
Mississippi.....		629	Georgia.....		9
Ophthalmia neonatorum:			Massachusetts.....		1
Mississippi.....		6	Tennessee.....		1
Puerperal septicemia:			German measles:		
Mississippi.....		34	Connecticut.....		20
Rabies in man:			Massachusetts.....		226
Michigan.....		1	New Jersey.....		53
Septic sore throat:			Tennessee.....		5
Michigan.....		33	Hookworm disease:		
Trachoma:			Georgia.....		16
Mississippi.....		7	Impetigo contagiosa:		
Tularaemia:			Tennessee.....		3
Michigan.....		1	Lead poisoning:		
Undulant fever:			Connecticut.....		2
Michigan.....		2	Massachusetts.....		3
Whooping cough:			Lethargic encephalitis:		
Michigan.....		810	Alabama.....		5
Mississippi.....		517	Connecticut.....		2
			Indiana.....		1
			Massachusetts.....		2
			New Jersey.....		3
			Tennessee.....		2
<i>February, 1931</i>			Mumps:		
Anthrax:			Alabama.....		156
Connecticut.....		1	Connecticut.....		281
Massachusetts.....		4	Georgia.....		171
Chicken pox:			Indiana.....		57
Alabama.....		38			
Connecticut.....		384			

Mumps—Continued.	Cases	Tularaemia:	Cases
Massachusetts.....	525	Georgia.....	4
Nebraska.....	285	Tennessee.....	5
New Jersey.....	177	Typhus fever:	
North Dakota.....	59	Alabama.....	2
Tennessee.....	179	Georgia.....	24
Vermont.....	136	Tennessee.....	1
Wyoming.....	28	Undulant fever:	
Ophthalmia neonatorum:		Connecticut.....	3
Massachusetts.....	75	Indiana.....	2
New Jersey.....	2	Nebraska.....	1
Tennessee.....	1	New Jersey.....	3
Paratyphoid fever:		North Dakota.....	1
New Jersey.....	1	Vermont.....	2
Rabies in animals:		Vincent's angina:	
Connecticut.....	6	North Dakota.....	42
Septic sore throat:		Tennessee.....	2
Connecticut.....	17	Wyoming.....	2
Georgia.....	77	Whooping cough:	
Indiana.....	17	Alabama.....	54
Massachusetts.....	11	Connecticut.....	201
Nebraska.....	9	District of Columbia.....	18
Tennessee.....	9	Georgia.....	47
Vermont.....	7	Indiana.....	200
Wyoming.....	5	Massachusetts.....	553
Trachoma:		Nebraska.....	84
Georgia.....	3	New Jersey.....	639
Indiana.....	5	North Dakota.....	58
Massachusetts.....	6	Tennessee.....	104
New Jersey.....	2	Vermont.....	75
North Dakota.....	1	Wyoming.....	61
Tennessee.....	3		
Trichinosis:			
Massachusetts.....	1		



**Cases of Certain Communicable Diseases Reported for the Month of December, 1930, by State Health Officers**

State	Chicken pox	Diphtheria	Measles	Mumps	Scarlet fever	Small-pox	Tuberculosis	Typhoid and paratyphoid fever	Whooping cough
Maine.....	314	22	84	198	77	0	46	21	248
New Hampshire.....		8			18	0		5	
Vermont.....	219	15	30	7	29	2	10	5	57
Massachusetts.....	1,842	348	1,250	263	1,022	0	417	25	488
Rhode Island.....	159	55	6	12	160	0	58	1	39
Connecticut.....	337	68	483	201	293	0	117	21	221
New York.....	3,179	547	746	921	2,275	27	1,468	85	1,769
New Jersey.....	1,422	338	694	98	774	0	373	20	548
Pennsylvania.....	4,685	597	1,911	1,040	2,004	0	527	96	731
Ohio.....	2,914	324	317	445	2,234	271	563	95	327
Indiana.....	578	203	543	46	776	242	197	24	70
Illinois.....	1,811	684	1,152	1,154	1,591	199	755	91	511
Michigan.....	1,938	302	299	289	1,121	149	461	68	562
Wisconsin.....	2,274	72	729	715	492	37	113	13	446
Minnesota.....	687	78	49		285	50	156	7	102
Iowa.....	447	54	15	42	338	106	15	7	42
Missouri.....	413	212	2,625	63	530	41	153	34	72
North Dakota.....	176	20	12	61	79	22	91	9	72
South Dakota.....	75	46	12	9	55	96	10	3	54
Nebraska.....	217	54	6	67	180	173	14	5	36
Kansas.....	717	112	26	78	222	226	76	15	118
Delaware.....	18	12	3	13	59	0	17	1	6
Maryland.....	725	166	107	76	392	0	177	40	57
Dist. of Columbia.....	83	56	43		110	0	62	4	17
Virginia.....	651	303	446		409	3	158	49	321
West Virginia.....	206	89	88		214	54	45	58	101
North Carolina.....	843	337	241		318	5		15	208
South Carolina.....	202	319	9	70	83	5	92	52	81
Georgia.....	61	102	130	14	181	1	62	27	61
Florida.....	57	76	143	23	53	1	24	7	32
Kentucky <sup>1</sup> .....									
Tennessee.....	283	143	136	62	282	15	<sup>1</sup> 168	35	47
Alabama.....	206	232	390	57	274	7	225	44	79
Mississippi.....	579	134	142	161	133	30	162	46	624
Arkansas.....	109	52	6	26	62	17	<sup>1</sup> 14	70	14
Louisiana.....	27	134	8	5	72	38	<sup>2</sup> 114	82	41
Oklahoma <sup>3</sup> .....	59	157	124	5	171	112	25	60	55
Texas.....		264			188			34	
Montana.....	237	8	9	88	144	85	30	3	122
Idaho.....		8			63			1	
Wyoming.....	149	4	2	28	63	3		3	92
Colorado.....	249	44	147	122	178	25	72	2	131
New Mexico.....	101	46	293	46	41	4	51	27	30
Arizona.....	26	17	151	35	19	2	116	7	7
Utah <sup>1</sup> .....									
Nevada.....	1	2		2	3		7		
Washington.....	467	73	99	154	230	107	148	9	124
Oregon.....	165	34	159	316	47	57	30	2	53
California.....	1,566	305	1,052	779	487	257	1,013	53	442

<sup>1</sup> Reports received weekly.

<sup>2</sup> Pulmonary.

<sup>3</sup> Exclusive of Oklahoma City and Tulsa.

**Case Rates per 1,000 Population (Annual Basis) for the Month of December, 1930, Based on Provisional Populations**

State	Chicken pox	Diph- theria	Measles	Mumps	Scarlet fever	Small- pox	Tuber- culosis	Typhoid and para- typhoid fever	Whoop- ing cough
Maine.....	4.62	0.32	1.23	2.91	1.13	0.00	0.68	0.31	3.65
New Hampshire.....		.20			.45	.00		.13	
Vermont.....	7.18	.49	.98	.23	.95	.07	.33	.16	1.87
Massachusetts.....	5.09	.96	3.54	.73	2.82	.00	1.15	.07	1.35
Rhode Island.....	2.72	.94	.10	.20	2.73	.00	.99	.02	.67
Connecticut.....	2.46	.50	3.53	1.47	2.14	.00	.86	.15	1.62
New York.....	2.95	.51	.69	.66	2.11	.03	1.36	.06	1.64
New Jersey.....	4.14	.98	2.02	.28	2.25	.00	1.06	.06	1.69
Pennsylvania.....	5.71	.73	2.33	1.27	2.44	.00	.64	.12	.89
Ohio.....	5.15	.57	.56	.79	3.95	.48	1.00	.17	.68
Indiana.....	2.11	.74	1.98	.17	2.83	.88	.72	.09	.25
Illinois.....	2.79	1.05	1.78	1.78	2.45	.31	1.16	.14	.79
Michigan.....	4.68	.73	.72	.70	2.71	.96	1.11	.14	1.36
Wisconsin.....	9.11	.29	2.92	2.87	1.97	.15	.45	.05	1.79
Minnesota.....	3.15	.86	.22		1.31	.23	.71	.03	.47
Iowa.....	2.13	.26	.07	.20	1.61	.61	.07	.03	.20
Missouri.....	1.34	.69	8.52	.20	1.72	.13	.50	.11	.23
North Dakota.....	3.03	.84	.21	1.05	1.36	.38	1.57	.16	1.24
South Dakota.....	1.28	.78	.20	.15	.94	1.67	.17	.05	.92
Nebraska.....	1.85	.46	.05	.57	1.53	1.47	.12	.04	.81
Kansas.....	4.48	.70	.16	.49	1.39	1.41	.48	.09	.74
Delaware.....	.89	.59	.15	.64	2.91	.00	.84	.05	.30
Maryland.....	5.23	1.20	.77	.55	2.83	.00	1.28	.29	.71
District of Columbia.....	2.00	1.35	1.04		2.65	.00	1.50	.10	.41
Virginia.....	3.16	1.47	2.17		1.99	.01	.77	.24	1.56
West Virginia.....	1.40	.60	.60		1.45	.37	.31	.39	.69
North Carolina.....	3.12	1.25	.89		1.18	.02		.06	.77
South Carolina.....	1.37	2.17	.06	.48	.66	.03	.62	.35	.65
Georgia.....	.25	.41	.53	.06	.73	.00	.25	.11	.25
Florida.....	.45	.61	1.14	.18	.42	.01	.19	.06	.25
Kentucky <sup>1</sup> .....									
Tennessee.....	1.27	.64	.61	.23	1.27	.07	1.76	.16	.21
Alabama.....	.91	1.03	1.73	.25	1.22	.03	1.00	.20	.35
Mississippi.....	3.39	.78	.83	.94	.78	.18	.95	.27	3.65
Arkansas.....	.69	.33	.04	.16	.39	.11	1.09	.44	.09
Louisiana.....	.15	.75	.04	.08	.40	.21	1.64	.46	.23
Oklahoma <sup>2</sup> .....	.34	.89	.71	.03	.97	.64	.14	.34	.31
Texas.....		.53			.38			.07	
Montana.....	5.20	.18	.20	1.93	3.16	1.87	.66	.07	2.68
Idaho.....		.21			1.66			.03	
Wyoming.....	7.79	.21	.10	1.46	3.29	.16		.16	4.81
Colorado.....	2.83	.50	1.67	1.38	2.02	.28	.82	.02	1.49
New Mexico.....	2.77	1.26	8.04	1.26	1.13	.11	1.40	.74	.52
Arizona.....	.70	.46	4.06	.94	.51	.05	3.12	.19	.19
Utah <sup>1</sup> .....									
Nevada.....	.13	.26		.26	.89		.90		
Washington.....	3.51	.55	.74	1.16	1.73	.80	1.11	.07	.93
Oregon.....	2.03	.42	1.95	3.89	.68	.70	.37	.02	.65
California.....	3.22	.63	2.16	1.60	1.00	.53	2.08	.11	.91

<sup>1</sup> Reports received weekly.<sup>2</sup> Pulmonary.<sup>3</sup> Exclusive of Oklahoma City and Tulsa.

**GENERAL CURRENT SUMMARY AND WEEKLY REPORTS FROM CITIES**

The 97 cities reporting cases used in the following table are situated in all parts of the country and have an estimated aggregate population of more than 33,405,000. The estimated population of the 90 cities reporting deaths is more than 31,860,000. The estimated expectancy is based on the experience of the last nine years, excluding epidemics.

Weeks ended March 7, 1931, and March 8, 1930

	1931	1930	Estimated expectancy
<i>Cases reported</i>			
Diphtheria:			
46 States.....	1,096	1,296	
97 cities.....	465	553	841
Measles:			
45 States.....	15,274	12,814	
97 cities.....	4,795	3,914	
Meningococcus meningitis:			
46 States.....	172	311	
97 cities.....	79	128	
Poliomyelitis:			
46 States.....	34	19	
Scarlet fever:			
46 States.....	6,117	5,349	
97 cities.....	2,209	2,025	1,580
Smallpox:			
46 States.....	960	1,833	
97 cities.....	81	154	61
Typhoid fever:			
46 States.....	130	207	
97 cities.....	26	52	30
<i>Deaths reported</i>			
Influenza and pneumonia:			
90 cities.....	1,445	1,094	
Smallpox:			
90 cities.....	0	0	

City reports for week ended March 7, 1931

The "estimated expectancy" given for diphtheria, poliomyelitis, scarlet fever, smallpox, and typhoid fever is the result of an attempt to ascertain from previous occurrence the number of cases of the disease under consideration that may be expected to occur during a certain week in the absence of epidemics. It is based on reports to the Public Health Service during the past nine years. It is in most instances the median number of cases reported in the corresponding weeks of the preceding years. When the reports include several epidemics, or when for other reasons the median is unsatisfactory, the epidemic periods are excluded, and the estimated expectancy is the mean number of cases reported for the week during nonepidemic years.

If the reports have not been received for the full nine years, data are used for as many years as possible, but no year earlier than 1922 is included. In obtaining the estimated expectancy, the figures are smoothed when necessary to avoid abrupt deviation from the usual trend. For some of the diseases given in the table the available data were not sufficient to make it practicable to compute the estimated expectancy.

Division, State, and city	Chicken pox, cases reported	Diphtheria		Influenza		Measles, cases reported	Mumps, cases reported	Pneumonia, deaths reported
		Cases, estimated expectancy	Cases reported	Cases reported	Deaths reported			
NEW ENGLAND								
Maine:								
Portland.....	7	1	1		0	0	23	4
New Hampshire:								
Concord.....	0	0	0		0	0	0	1
Manchester.....	0	0	0		4	1	0	2
Vermont:								
Barre.....	1	0	0		0	0	0	2
Massachusetts:								
Boston.....	74	35	28	16	2	122	17	29
Fall River.....	0	3	1	1	1	0	15	8
Springfield.....	9	4	0	1	1	1	14	0
Worcester.....	4	3	2		0	1	1	1
Rhode Island:								
Pawtucket.....	5	2	2		0	0	2	4
Providence.....	13	8	7	3	1	0	0	11
Connecticut:								
Bridgeport.....	2	6	2		1	0	2	4
Hartford.....	5	6	1	2	0	70	1	10
New Haven.....	8	0	0		2	184	8	3

## City reports for week ended March 7, 1931—Continued

Division, State, and city	Chicken pox, cases reported	Diphtheria		Influenza		Measles, cases reported	Mumps, cases reported	Pneumonia, deaths reported
		Cases, estimated expectancy	Cases reported	Cases reported	Deaths reported			
<b>MIDDLE ATLANTIC</b>								
New York:								
Buffalo.....	23	13	14	2	3	195	66	35
New York.....	293	207	87	49	30	845	52	291
Rochester.....	11	6	3	9	1	1	2	10
Syracuse.....	19	3	0	-----	0	8	2	7
New Jersey:								
Camden.....	7	5	5	-----	0	65	7	2
Newark.....	111	15	10	12	0	8	10	9
Trenton.....	2	3	0	8	0	2	5	6
Pennsylvania:								
Philadelphia.....	166	66	9	27	16	612	36	87
Pittsburgh.....	128	19	8	25	21	52	40	62
Reading.....	3	2	0	-----	0	166	29	4
<b>EAST NORTH CENTRAL</b>								
Ohio:								
Cincinnati.....	9	9	3	15	9	55	21	16
Cleveland.....	149	23	9	130	17	12	166	40
Columbus.....	14	3	2	5	4	2	3	7
Toledo.....	33	5	6	8	5	1	50	11
Indiana:								
Fort Wayne.....	2	3	2	-----	2	33	0	7
Indianapolis.....	41	6	3	-----	2	144	27	19
South Bend.....	1	1	0	-----	0	0	0	5
Terre Haute.....	0	1	0	-----	1	1	0	9
Illinois:								
Chicago.....	119	95	78	22	12	155	72	67
Springfield.....		0	-----	-----	-----	-----	-----	-----
Michigan:								
Detroit.....	127	45	21	56	16	9	36	44
Flint.....	8	2	0	130	4	0	2	7
Grand Rapids.....	6	1	0	10	3	0	0	1
Wisconsin:								
Kenosha.....	14	2	0	1	0	0	95	0
Madison.....	55	1	0	4	-----	1	57	-----
Milwaukee.....	105	14	2	7	8	49	419	19
Racine.....	13	1	1	2	0	6	5	0
Superior.....	6	0	0	-----	0	0	0	0
<b>WEST NORTH CENTRAL</b>								
Minnesota:								
Duluth.....	5	0	0	1	3	0	1	3
Minneapolis.....	81	5	3	-----	7	48	120	18
St. Paul.....	47	7	2	-----	4	8	1	11
Iowa:								
Davenport.....	1	1	0	-----	-----	2	0	-----
Des Moines.....	3	2	0	-----	-----	0	3	-----
Sioux City.....	17	0	0	-----	-----	5	22	-----
Waterloo.....	0	0	0	-----	-----	0	0	-----
Missouri:								
Kansas City.....	64	5	4	1	2	58	9	23
St. Joseph.....	1	2	1	-----	1	9	0	3
St. Louis.....	32	40	18	17	2	215	11	-----
North Dakota:								
Fargo.....	1	0	0	-----	0	0	10	0
Grand Forks.....	0	0	1	-----	-----	0	0	-----
South Dakota:								
Aberdeen.....	2	0	0	-----	-----	0	0	-----
Sioux Falls.....	0	0	0	-----	-----	0	0	-----
Nebraska:								
Omaha.....	29	4	7	-----	0	1	14	13
Kansas:								
Topeka.....	14	2	2	1	1	0	44	1
Wichita.....	5	1	0	-----	0	1	1	2
<b>SOUTH ATLANTIC</b>								
Delaware:								
Wilmington.....	2	3	2	-----	0	2	7	4
Maryland:								
Baltimore.....	163	24	13	26	3	761	52	42
Cumberland.....	0	0	1	6	0	0	0	14
Frederick.....	0	0	0	-----	0	1	0	0

1 Including 3 deaths, nonresidents.

City reports for week ended March 7, 1931—Continued

Division, State, and city	Chicken pox, cases reported	Diphtheria		Influenza		Measles, cases re- ported	Mumps, cases re- ported	Pneu- moni, deaths reported
		Cases, estimated expect- ancy	Cases reported	Cases reported	Deaths reported			
<b>SOUTH ATLANTIC—CON.</b>								
District of Columbia:								
Washington.....	49	12	17	4	3	154	0	25
Virginia:								
Lynchburg.....	23	1	0		0	6	5	3
Norfolk.....	8	1	2		0	6	4	1
Richmond.....	2	3	3	298	2	0	0	8
Roanoke.....	10	1	1		2	6	1	0
West Virginia:								
Charleston.....	9	0	0	1	0	0	6	2
Wheeling.....	9	1	0		2	0	0	8
North Carolina:								
Raleigh.....	10	1	1		0	12	0	1
Wilmington.....	16	0	0	1	0	2	0	3
Winston-Salem.....	12	1	1	3	0	12	0	3
South Carolina:								
Charleston.....	0	0	0	72	6	58	1	7
Columbia.....	0	0	0		0	0	3	7
Greenville.....	1	0	0		0	0	0	0
Georgia:								
Atlanta.....	6	3	3	385	10	59	1	12
Brunswick.....	0	0	0		0	0	6	1
Savannah.....	0	1	1	33	5	0	1	2
Florida:								
Miami.....	5	3	2	1	0	6	0	3
St. Petersburg.....		0			0			0
Tampa.....	4	2	4	4	4	60	0	2
<b>EAST SOUTH CENTRAL</b>								
Kentucky:								
Covington.....	0	0	0	1	1	6	0	2
Tennessee:								
Memphis.....	28	4	2		5	32	3	13
Nashville.....	2	1	0		11	9	0	13
Alabama:								
Birmingham.....	8	1	0	44	5	129	1	5
Mobile.....	1	0	3	9	0	0	0	3
Montgomery.....	15	1	0	3		2	0	
<b>WEST SOUTH CENTRAL</b>								
Arkansas:								
Fort Smith.....	1	0	0			4	0	
Little Rock.....	8	0	0		0	1	1	0
Louisiana:								
New Orleans.....	1	13	18	6	5	0	0	11
Shreveport.....	6	1	0		0	0	0	4
Oklahoma:								
Muskogee.....	3	0	0	7		0	1	
Oklahoma City.....	0	2	0		2	0	0	6
Tulsa.....	5	1	0			2	0	
Texas:								
Dallas.....	31	6	5	2	2	12	50	8
Fort Worth.....	28	3	5		0	1	1	0
Galveston.....	0	1	0		0	0	0	1
Houston.....	4	5	7		1	0	0	8
San Antonio.....	10	2	5		7	3	0	11
<b>MOUNTAIN</b>								
Montana:								
Billings.....	9	0	0		0	0	0	1
Great Falls.....	5	0	0		0	0	0	0
Helena.....	1	1	0		0	0	0	0
Missoula.....	0	0	0		0	0	0	0
Idaho:								
Boise.....	0	0	0		0	0	0	2
Colorado:								
Denver.....	50	8	7		3	27	30	10
Pueblo.....	4	0	0		1	121	0	0
New Mexico:								
Albuquerque.....	12	0	0	1	1	1	0	1
Utah:								
Salt Lake City.....	4	2	0		1	5	7	0
Nevada:								
Reno.....	2	0	0		0	0	0	1

## City reports for week ended March 7, 1931—Continued

Division, State, and city	Chicken pox, cases reported	Diphtheria		Influenza		Measles, cases reported	Mumps, cases reported	Pneumonia, deaths reported			
		Cases, estimated expectancy	Cases reported	Cases reported	Deaths reported						
<b>PACIFIC</b>											
Washington:											
Seattle.....	83	4	3			2	22				
Spokane.....	3	2	0			2	0				
Tacoma.....	13	0	1			0	0	3			
Oregon:											
Portland.....	38	7	1	17		2	11	11			
Salem.....	0	0	0			0	7	0			
California:											
Los Angeles.....	102	37	21	131		5	21	17			
Sacramento.....	20	1	5	34		1	0	8			
San Francisco.....	71	14	2	283		5	3	14			
Division, State, and city	Scarlet fever		Smallpox			Tuberculosis, deaths reported	Typhoid fever			Whooping cough, cases reported	Deaths, all causes
	Cases, estimated expectancy	Cases reported	Cases, estimated expectancy	Cases reported	Deaths reported		Cases, estimated expectancy	Cases reported	Deaths reported		
<b>NEW ENGLAND</b>											
Maine:											
Portland.....	4	12	0	0	0	0	1	0	0	17	30
New Hampshire:											
Concord.....	1	2	0	0	0	1	0	0	0	0	11
Manchester.....	1	11	0	0	0	0	0	0	0	0	13
Vermont:											
Barre.....	0	1	0	0	0	1	0	0	0	7	7
Massachusetts:											
Boston.....	84	97	0	0	0	13	1	2	0	40	229
Fall River.....	4	14	0	0	0	2	0	0	0	3	34
Springfield.....	9	3	0	0	0	1	0	0	0	1	43
Worcester.....	10	22	0	0	0	1	0	0	0	22	61
Rhode Island:											
Pawtucket.....	1	14	0	0	0	0	0	0	0	5	25
Providence.....	13	32	0	0	0	2	0	0	0	3	79
Connecticut:											
Bridgeport.....	12	9	0	0	0	2	0	0	0	3	28
Hartford.....	7	10	0	0	0	1	0	0	0	5	50
New Haven.....	10	3	0	0	0	1	0	0	0	9	39
<b>MIDDLE ATLANTIC</b>											
New York:											
Buffalo.....	30	28	0	1	0	8	0	1	0	15	167
New York.....	318	394	0	0	0	116	6	4	1	202	1,774
Rochester.....	9	103	0	0	0	2	1	1	0	11	79
Syracuse.....	14	9	0	0	0	1	0	0	0	17	49
New Jersey:											
Camden.....	6	7	0	0	0	0	0	0	0	1	33
Newark.....	48	58	0	0	0	7	0	0	0	39	116
Trenton.....	5	20	0	0	0	2	1	0	0	0	61
Pennsylvania:											
Philadelphia.....	95	138	0	0	0	41	1	0	0	60	598
Pittsburgh.....	31	45	0	0	0	6	0	0	0	28	222
Reading.....	6	1	0	0	0	1	0	0	0	0	37
<b>EAST NORTH CENTRAL</b>											
Ohio:											
Cincinnati.....	22	46	1	0	0	8	0	0	0	1	153
Cleveland.....	60	70	0	0	0	17	0	1	1	21	261
Columbus.....	11	18	1	0	0	4	0	0	0	0	91
Toledo.....	13	9	1	2	0	0	1	0	0	6	84
Indiana:											
Fort Wayne.....	4	3	0	0	0	0	1	0	0	1	29
Indianapolis.....	13	57	1	22	0	0	0	0	6	28	
South Bend.....	3	2	0	2	0	0	0	0	0	5	31
Terra Haute.....	3	3	0	0	0	1	0	0	0	1	33

City reports for week ended March 7, 1931—Continued

Division, State, and city	Scarlet fever		Smallpox			Tuberculosis, deaths reported	Typhoid fever			Whooping cough, cases reported	Deaths, all causes
	Cases, estimated expectancy	Cases reported	Cases, estimated expectancy	Cases reported	Deaths reported		Cases, estimated expectancy	Cases reported	Deaths reported		
<b>EAST NORTH CENTRAL—contd.</b>											
<b>Illinois:</b>											
Chicago	139	221	3	0	0	54	2	0	0	41	750
Springfield	3		1				1				
<b>Michigan:</b>											
Detroit	122	82	3	0	0	23	1	0	0	52	331
Flint	15	8	1	0	0	0	0	0	0	1	34
Grand Rapids	12	16	0	0	0	0	0	1	0	9	36
<b>Wisconsin:</b>											
Kenosha	3	1	0	0	0	0	0	0	0	0	9
Madison	5	1	0	0	0	0	2	0	0	5	
Milwaukee	32	26	1	0	0	7	1	0	0	13	123
Racine	4	11	0	0	0	0	0	0	0	3	11
Superior	3	0	0	0	0	1	0	0	0	0	13
<b>WEST NORTH CENTRAL</b>											
<b>Minnesota:</b>											
Duluth	9	0	0	0	0	2	0	2	0	0	33
Minneapolis	50	18	0	0	0	0	0	0	0	27	110
St. Paul	32	8	1	0	0	0	0	1	0	11	78
<b>Iowa:</b>											
Davenport	1	0	1	15			0	0		0	
Des Moines	11	3	1	2			0	0		2	27
Sioux City	1	17	0	0			0	0		0	
Waterloo	2	2	1	1			0	1		0	
<b>Missouri:</b>											
Kansas City	23	9	1	0	0	9	0	0	0	8	128
St. Joseph	3	3	0	0	0	1	0	0	0	2	25
St. Louis	38	106	2	2	0	19	1	1	0	14	292
<b>North Dakota:</b>											
Fargo	3	1	0	0	0	0	0	1	0	3	5
Grand Forks	1	0	0	0	0	0	0	1	0	2	
<b>South Dakota:</b>											
Aberdeen	0	0	0	0	0	0	0	0	0	0	
Sioux Falls	2	0	1	3			0	0		0	11
<b>Nebraska:</b>											
Omaha	4	3	2	7	0	0	0	0	0	13	60
<b>Kansas:</b>											
Topeka	3	0	1	1	0	2	0	0	0	0	11
Wichita	6	0	1	19	0	0	0	0	0	6	26
<b>SOUTH ATLANTIC</b>											
<b>Delaware:</b>											
Wilmington	5	4	0	0	0	1	0	0	1	1	38
<b>Maryland:</b>											
Baltimore	40	42	0	0	0	10	0	1	0	16	269
Cumberland	1	1	0	0	0	0	0	0	0	0	10
Frederick	0	1	0	0	0	0	0	0	0	0	3
<b>District of Col.:</b>											
Washington	27	26	1	0	0	8	1	0	0	9	161
<b>Virginia:</b>											
Lynchburg	1	2	0	0	0	1	0	0	0	0	10
Norfolk	2	3	0	0	0	2	0	0	0	3	
Richmond	4	8	0	0	0	6	0	0	0	0	35
Roanoke	1	3	0	0	0	0	0	0	0	2	15
<b>West Virginia:</b>											
Charleston	0	5	0	0	0	0	0	0	0	2	15
Wheeling	2	3	0	0	0	1	0	0	0	0	32
<b>North Carolina:</b>											
Raleigh	1	1	1	0	0	0	0	0	0	24	14
Wilmington	0	0	0	0	0	0	0	0	0	3	11
Winston-Salem	1	2	1	0	0	2	0	0	0	4	16
<b>South Carolina:</b>											
Charleston	0	0	0	0	0	2	0	0	0	0	40
Columbia	0	0	0	0	0	1	0	0	0	0	20
Greenville	0	1	1	0	0	0	0	0	0	0	
<b>Georgia:</b>											
Atlanta	5	77	2	0	0	0	0	3	1	1	92
Brunswick	0	0	0	0	0	0	0	0	0	0	4
Savannah	1	0	1	0	0	1	1	2	0	0	31
<b>Florida:</b>											
Miami	1	0	0	0	0	2	1	0	0	0	30
St. Petersburg	0	0	0	0	0	0	0	0	0	0	9
Tampa	1	4	0	0	0	0	2	0	0	1	30

## City reports for week ended March 7, 1931—Continued

Division, State, and city	Scarlet fever		Smallpox			Tuber- culosis, deaths re- ported	Typhoid fever			Whoop- ing cough, cases re- ported	Deaths, all causes
	Cases, esti- mated expect- ancy	Cases re- ported	Cases, esti- mated expect- ancy	Cases re- ported	Deaths re- ported		Cases, esti- mated expect- ancy	Cases re- ported	Deaths re- ported		
<b>EAST SOUTH CENTRAL</b>											
<b>Kentucky:</b>											
Covington.....	3	10	0	0	0	0	0	0	0	0	15
<b>Tennessee:</b>											
Memphis.....	8	43	1	4	0	4	1	3	1	2	91
Nashville.....	2	5	0	0	0	5	1	0	0	1	67
<b>Alabama:</b>											
Birmingham....	3	6	1	0	0	4	1	0	0	0	77
Mobile.....	0	3	1	0	0	2	0	0	0	0	24
Montgomery....	0	2	0	0			0	0		2	
<b>WEST SOUTH CENTRAL</b>											
<b>Arkansas:</b>											
Fort Smith.....	0	1	0	0			0	0		0	
Little Rock.....	1	1	0	3	0	0	0	0	0	0	
<b>Louisiana:</b>											
New Orleans....	8	15	1	3	0	12	2	0	0	0	124
Shreveport.....	1	0	1	4	0	1	0	0	0	0	29
<b>Oklahoma:</b>											
Muskogee.....	0	0	2	2			0	0		0	
Oklahoma City.....	3	2	3	13	0	2	0	1	1	0	46
Tulsa.....	2	1	1	5			0	0		0	
<b>Texas:</b>											
Dallas.....	5	1	4	1	0	0	0	0	0	13	50
Fort Worth.....	3	5	2	5	0	0	0	0	0	0	
Galveston.....	0	0	0	0	0	0	0	0	0	0	13
Houston.....	3	1	4	3	0	5	0	0	0	0	78
San Antonio....	1	2	1	0	0	5	0	0	0	0	78
<b>MOUNTAIN</b>											
<b>Montana:</b>											
Billings.....	1	1	0	0	0	0	0	0	0	1	7
Great Falls....	4	5	1	0	0	0	0	0	0	25	7
Helena.....	0	1	0	2	0	0	0	0	0	0	3
Missoula.....	1	0	0	0	0	0	0	0	0	0	5
<b>Idaho:</b>											
Boise.....	0	1	0	0	0	1	0	0	0	0	12
<b>Colorado:</b>											
Denver.....	14	19	0	0	0	8	0	0	0	25	87
Pueblo.....	1	0	0	0	0	0	0	0	0	15	12
<b>New Mexico:</b>											
Albuquerque....	1	1	0	0	0	4	0	0	0	0	13
<b>Utah:</b>											
Salt Lake City..	4	8	1	0	0	1	0	0	0	29	35
<b>Nevada:</b>											
Reno.....	0	0	0	0	0	0	0	0	0	0	4
<b>PACIFIC</b>											
<b>Washington:</b>											
Seattle.....	11	14	2	2			1	0		45	
Spokane.....	7	4	9	2			0	0		0	
Tacoma.....	2	2	3	1	0	3	0	0	0	1	42
<b>Oregon:</b>											
Portland.....	8	4	15	16	0	1	0	1	0	5	80
Salem.....	1	0	1	0	0	0	0	0	0	0	
<b>California:</b>											
Los Angeles....	43	38	2	1	0	26	2	0	0	16	253
Sacramento....	3	4	1	0	0	2	0	1	0	25	58
San Francisco..	28	0	1	0	0	13	0	0	1	40	185



City reports for week ended March 7, 1931—Continued

Division, State, and city	Meningo- coccus meningitis		Lethargic en- cephalitis		Pellagra		Poliomyelitis (infan- tile paralysis)		
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases, esti- mated expect- ancy	Cases	Deaths
<b>NEW ENGLAND</b>									
Massachusetts:									
Boston.....	1	1	1	1	0	0	1	0	0
Springfield.....	1	0	0	0	0	0	0	0	0
<b>MIDDLE ATLANTIC</b>									
New York:									
Buffalo.....	1	0	0	0	0	0	0	0	0
New York.....	12	6	2	1	0	0	1	1	0
Pennsylvania:									
Philadelphia.....	9	3	0	0	1	2	0	0	0
Pittsburgh.....	0	0	0	1	0	0	0	0	0
<b>EAST NORTH CENTRAL</b>									
Ohio:									
Cincinnati.....	1	2	0	0	0	0	0	0	0
Cleveland.....	1	0	0	0	0	0	0	0	0
Columbus.....	6	4	0	0	0	0	0	0	0
Indiana:									
Indianapolis.....	2	2	0	0	0	0	0	0	0
South Bend.....	1	0	0	0	0	0	0	0	0
Terre Haute.....	1	0	0	0	0	0	0	0	0
Illinois:									
Chicago.....	8	2	1	0	0	0	0	0	0
Michigan:									
Detroit.....	3	2	1	0	0	0	0	0	0
Flint.....	3	2	0	0	0	0	0	0	0
Grand Rapids.....	1	0	0	0	0	0	0	0	0
Wisconsin:									
Milwaukee.....	0	0	0	0	0	0	0	1	0
<b>WEST NORTH CENTRAL</b>									
Minnesota:									
Minneapolis.....	1	0	0	0	0	0	0	0	0
St. Paul.....	2	0	0	0	0	0	0	0	0
Iowa:									
Des Moines.....	0	0	0	0	0	0	0	1	0
Missouri:									
Kansas City.....	0	1	0	0	0	0	0	0	0
St. Louis.....	5	0	0	0	0	0	0	0	0
North Dakota:									
Fargo.....	0	0	1	0	0	0	0	0	0
<b>SOUTH ATLANTIC</b>									
District of Columbia:									
Washington.....	2	2	0	0	0	0	0	0	0
Virginia:									
Norfolk.....	1	0	0	0	0	0	0	0	0
North Carolina:									
Winston-Salem.....	0	0	0	0	1	0	0	0	0
South Carolina:									
Charleston <sup>1</sup> .....	0	0	1	0	3	0	0	0	0
Columbia.....	2	0	0	0	0	0	0	0	0
Georgia:									
Atlanta.....	1	1	0	0	0	0	0	0	0
Florida:									
Tampa.....	0	1	0	0	0	0	0	0	0
<b>EAST SOUTH CENTRAL</b>									
Tennessee:									
Memphis.....	5	2	0	0	0	0	0	0	0
Nashville.....	0	0	0	0	1	0	0	0	0
Alabama:									
Birmingham.....	3	1	0	0	2	1	0	0	0
Mobile.....	0	1	0	0	0	1	0	0	0
Montgomery.....	0	0	0	0	3	0	0	0	0

<sup>1</sup> Dengue: 2 cases at Charleston, S. C.

## City reports for week ended March 7, 1931—Continued

Division, State, and city	Meningococcus meningitis		Lethargic encephalitis		Pellagra		Poliomyelitis (infantile paralysis)		
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases, estimated expectancy	Cases	Deaths
<b>WEST SOUTH CENTRAL</b>									
Louisiana:									
New Orleans.....	2	0	0	0	0	0	0	0	0
Oklahoma:									
Muskogee.....	1	0	0	0	0	0	0	0	0
Oklahoma City.....	0	0	0	1	0	1	0	0	0
Texas:									
Dallas.....	0	0	0	0	2	0	0	0	0
<b>MOUNTAIN</b>									
Montana:									
Freat Falls.....	1	0	0	0	0	0	0	0	0
Colorado:									
Denver.....	0	1	0	0	0	0	0	0	0
<b>PACIFIC</b>									
California:									
Los Angeles.....	2	0	2	1	0	0	0	1	1
Sacramento.....	2	0	0	0	0	0	0	0	0
San Francisco.....	0	0	0	0	0	0	0	1	0

The following tables give the rates per 100,000 population for 98 cities for the 5-week period ended March 7, 1931, compared with those for a like period ended March 8, 1930. The population figures used in computing the rates are estimated mid-year populations for 1930 and 1931, respectively, derived from the 1930 census. The 98 cities reporting cases have an estimated aggregate population of more than 33,000,000. The 91 cities reporting deaths have more than 31,500,000 estimated population.

Summary of weekly reports from cities February 1 to March 7, 1931—Annual rates per 100,000 population, compared with rates for the corresponding period of 1930<sup>1</sup>

## DIPHTHERIA CASE RATES

	Week ended—									
	Feb. 7, 1931	Feb. 8, 1930	Feb. 14, 1931	Feb. 15, 1930	Feb. 21, 1931	Feb. 22, 1930	Feb. 28, 1931	Mar. 1, 1930	Mar. 7, 1931	Mar. 8, 1930
98 cities.....	78	92	67	95	68	91	70	104	73	88
New England.....	82	119	75	104	70	109	89	121	106	92
Middle Atlantic.....	53	92	53	78	64	83	56	103	61	85
East North Central.....	96	102	85	114	66	101	78	122	75	94
West North Central.....	89	83	55	107	59	95	55	120	71	118
South Atlantic.....	75	76	59	102	47	120	77	96	93	78
East South Central.....	52	72	52	66	58	96	58	54	29	36
West South Central.....	156	157	118	130	186	80	132	101	118	143
Mountain.....	78	70	78	62	35	70	87	35	61	88
Pacific.....	69	36	49	75	59	53	57	63	63	38

<sup>1</sup> The figures given in this table are rates per 100,000 population, annual basis, and not the number of cases reported. Populations used are estimates as of July 1, 1931 and 1930, respectively.

<sup>2</sup> Columbia, S. C., not included.

<sup>3</sup> Springfield, Ill., not included.

Summary of weekly reports from cities February 1 to March 7, 1931—Annual rates per 100,000 population, compared with rates for the corresponding period of 1930—Continued

MEASLES CASE RATES

	Week ended—									
	Feb. 7, 1931	Feb. 8, 1930	Feb. 14, 1931	Feb. 15, 1930	Feb. 21, 1931	Feb. 22, 1930	Feb. 28, 1931	Mar. 1, 1930	Mar. 7, 1931	Mar. 8, 1930
	98 cities.....	* 473	317	521	411	668	446	703	538	* 748
New England.....	502	322	534	472	541	418	635	506	909	693
Middle Atlantic.....	353	176	397	213	652	254	645	346	874	417
East North Central.....	151	171	183	251	255	267	300	345	* 286	442
West North Central.....	1,488	610	1,314	810	1,086	775	874	939	643	938
South Atlantic.....	* 1,294	268	1,817	334	2,202	441	2,800	148	2,238	535
East South Central.....	1,024	72	896	233	1,123	604	1,042	753	1,036	717
West South Central.....	3	648	17	693	24	745	24	704	68	505
Mountain.....	1,123	405	688	758	1,567	767	1,209	1,507	1,332	2,106
Pacific.....	112	1,028	168	1,243	243	1,271	223	1,636	347	1,581

SCARLET FEVER CASE RATES

98 cities.....	* 320	323	348	302	346	294	373	357	* 345	321
New England.....	534	530	683	392	589	409	606	402	527	431
Middle Atlantic.....	304	260	321	234	342	242	331	308	359	283
East North Central.....	331	427	375	434	353	421	364	510	* 346	448
West North Central.....	480	370	474	331	497	327	509	341	492	345
South Atlantic.....	* 304	222	320	252	304	236	363	258	354	206
East South Central.....	419	191	378	149	529	149	553	173	401	173
West South Central.....	88	129	105	108	139	94	125	108	71	139
Mountain.....	261	361	409	423	296	308	305	388	305	300
Pacific.....	145	289	123	269	94	202	145	352	121	241

SMALLPOX CASE RATES

98 cities.....	* 23	29	18	26	20	24	20	30	* 13	25
New England.....	0	2	0	7	0	0	0	0	0	2
Middle Atlantic.....	2	0	0	0	3	0	0	0	0	0
East North Central.....	12	34	10	33	13	20	11	40	* 15	24
West North Central.....	151	60	84	48	128	93	128	91	57	70
South Atlantic.....	* 0	4	0	6	2	2	0	2	0	2
East South Central.....	29	0	12	24	17	12	23	6	23	18
West South Central.....	81	94	132	98	51	52	64	111	47	63
Mountain.....	44	18	0	35	44	18	9	26	17	9
Pacific.....	24	126	29	89	22	101	39	87	12	105

TYPHOID FEVER CASE RATES

98 cities.....	* 4	4	3	6	4	5	7	8	* 4	8
New England.....	2	0	2	2	0	5	5	0	5	3
Middle Atlantic.....	1	3	2	6	3	6	6	4	3	4
East North Central.....	2	5	1	3	0	1	3	1	* 1	3
West North Central.....	2	2	2	10	4	2	11	6	11	8
South Atlantic.....	* 18	12	0	8	10	14	22	60	12	40
East South Central.....	6	18	29	18	0	6	6	30	17	12
West South Central.....	24	7	14	7	7	3	14	0	0	81
Mountain.....	0	0	0	0	9	9	0	0	0	0
Pacific.....	0	2	10	4	12	10	4	6	2	6

\* Columbia, S. O., not included.

\* Springfield, Ill., not included.

Summary of weekly reports from cities February 1 to March 7, 1931—Annual rates per 100,000 population, compared with rates for the corresponding period of 1930—Continued

## INFLUENZA DEATH RATES

	Week ended—									
	Feb. 7, 1931	Feb. 8, 1930	Feb. 14, 1931	Feb. 15, 1930	Feb. 21, 1931	Feb. 22, 1930	Feb. 28, 1931	Mar. 1, 1930	Mar. 7, 1931	Mar. 8, 1930
91 cities.....	60	14	59	20	60	19	50	19	44	16
New England.....	46	5	46	5	43	17	24	12	19	19
Middle Atlantic.....	68	10	49	14	42	15	40	16	32	13
East North Central.....	52	12	56	17	61	16	61	16	48	12
West North Central.....	21	21	56	12	68	12	74	15	59	3
South Atlantic.....	129	12	118	32	122	22	79	28	73	36
East South Central.....	63	32	63	58	139	71	76	52	133	58
West South Central.....	73	50	159	68	97	68	45	64	52	32
Mountain.....	52	44	17	35	61	26	17	18	44	35
Pacific.....	12	7	14	17	26	2	41	10	34	2

## PNEUMONIA DEATH RATES

91 cities.....	231	175	220	171	217	177	212	193	192	166
New England.....	286	160	291	193	276	242	236	232	185	220
Middle Atlantic.....	293	180	254	191	236	190	217	219	229	181
East North Central.....	176	138	182	128	187	151	193	179	148	141
West North Central.....	135	159	124	111	147	153	218	138	218	129
South Atlantic.....	325	216	373	214	340	222	312	236	265	222
East South Central.....	176	207	164	220	265	239	271	175	227	214
West South Central.....	214	270	176	256	228	174	221	185	149	160
Mountain.....	209	379	183	256	200	247	191	247	131	150
Pacific.....	72	130	72	107	70	67	91	62	101	75

‡ Columbia, S. C., not included.

‡ Springfield, Ill., not included.

## FOREIGN AND INSULAR

### BRAZIL

*Yellow fever.*—During the month of January, yellow fever was reported in Brazil as follows: January 1–25, 3 cases and 3 deaths at Cambucy; January 18–24, 1 case and 1 death at Padua, Rio State; January 25–30, 1 case at Friburgo, imported from Padua. Three fatal cases of a disease suspected to have been yellow fever were reported in Brazil, February 7, 1931. One case was reported in Barbalha, Ceara State, 1 in Cambucy, and 1 in Padua, Rio State.

### CANADA

*Provinces—Communicable diseases—Week ended March 7, 1931.*—The Department of Pensions and National Health of Canada reports cases of certain communicable diseases for the week ended March 7, 1931, as follows:

Province	Cerebro-spinal fever	Influenza	Small-pox	Typhoid fever
Prince Edward Island <sup>1</sup> .....				
Nova Scotia.....		26		
New Brunswick.....				2
Quebec.....	1			9
Ontario.....		85	8	5
Manitoba.....	2			
Saskatchewan.....			10	2
Alberta <sup>1</sup> .....				
British Columbia.....		16		
Total.....	3	127	13	18

<sup>1</sup> No case of any disease included in the table was reported during the week.

*Ontario Province—Communicable diseases—Four weeks ended February 28, 1931.*—During the four weeks ended February 28, 1931, and the corresponding period of 1930, certain communicable diseases were reported in the Province of Ontario, Canada, as follows:

Disease	4 weeks, 1930		4 weeks, 1931	
	Cases	Deaths	Cases	Deaths
Cerebrospinal meningitis.....	4	5	4	1
Chancroid.....	1			
Chicken pox.....	795	2	1,028	
Diphtheria.....	218	13	150	11
Erysipelas.....	3		1	
German measles.....	288		34	
Goitre.....	1			
Gonorrhoea.....	111		275	
Influenza.....	68	13	239	35
Lethargic encephalitis.....		2	1	1
Malaria.....				1
Measles.....	1,605	2	162	
Mumps.....	102		888	
Paratyphoid fever.....			3	
Pneumonia.....		211		204
Poliomyelitis.....			2	
Scarlet fever.....	905	3	747	4
Septic sore throat.....	2	1	1	1
Smallpox.....	77		125	
Syphilis.....	169		260	
Tuberculosis.....	101	52	126	31
Typhoid fever.....	27	1	17	1
Undulant fever.....	2		14	
Whooping cough.....	380		831	8

<sup>1</sup> The cases of smallpox were distributed as follows: Sault Ste. Marie, 9; Toronto, 4; Hagar, 2; Hanover, 2; Kingston Tp., 2; and one each in Burwash, Hamilton, Capreol, Parry Sound, Ottawa, and Sarnia.

*Quebec Province—Communicable diseases—Week ended March 7, 1931.*—The Bureau of Health of the Province of Quebec, Canada, reports cases of certain communicable diseases for the week ended March 7, 1931, as follows:

Disease	Cases	Disease	Cases
Cerebrospinal meningitis.....	1	Mumps.....	37
Chicken pox.....	85	Paratyphoid fever.....	1
Diphtheria.....	23	Scarlet fever.....	72
Erysipelas.....	7	Tuberculosis.....	48
German measles.....	5	Typhoid fever.....	9
Measles.....	107	Whooping cough.....	49

### GREECE

*Typhus fever.*—According to information recently received, 10 cases of typhus fever (*typhus exanthematicus*) occurred in the village of Cato Nevrocopi, in the District of Drama, Greece, during the latter part of January. Only one of the cases was of a serious nature. All necessary prophylactic measures have been taken, and no further cases have been reported.

## MEXICO

*Tampico—Communicable diseases—February, 1931.*—During the month of February, 1931, certain communicable diseases were reported in Tampico, Mexico, as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Chicken pox.....	4	-----	Smallpox.....	1	-----
Enteritis (various).....	-----	25	Tuberculosis.....	-----	24
Influenza.....	6	-----	Typhoid fever.....	5	2
Malaria.....	83	5	Whooping cough.....	13	-----
Measles.....	1	-----			

*Vera Cruz—Deaths from certain diseases—Five weeks ended January 31, 1931.*—During the five weeks ended January 31, 1931, deaths from certain diseases were reported in Vera Cruz, Mexico, as follows:

Disease	Deaths	Disease	Deaths
Anthrax.....	1	Pneumonia.....	6
Bronchitis.....	4	Septicemia.....	1
Cancer.....	2	Syphilis.....	3
Gastro-intestinal disorders.....	39	Tetanus.....	3
Locomotor ataxia.....	1	Tuberculosis.....	23
Malaria.....	3	Typhoid fever.....	2
Meningitis.....	1		

## PANAMA CANAL ZONE

*Communicable diseases—January, 1931.*—During the month of January, 1931, certain communicable diseases, including imported cases, were reported in the Panama Canal Zone and terminal cities as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Chicken pox.....	18	-----	Pneumonia.....	-----	32
Diphtheria.....	11	-----	Scarlet fever.....	8	-----
Dysentery (amebic).....	7	1	Smallpox.....	1	2
Dysentery (bacillary).....	-----	1	Tuberculosis.....	-----	32
Malaria.....	183	2	Typhoid fever.....	3	-----
Measles.....	64	-----	Whooping cough.....	20	1

<sup>1</sup> Imported.

## TRINIDAD

*Port of Spain—Vital statistics—January, 1930 and 1931.*—The following statistics for the month of January, 1930 and 1931, are taken from a report issued by the Public Health Department of Port of Spain, Trinidad:

	January			January	
	1930	1931		1930	1931
Number of births.....	157	175	Death rate per 1,000 population.....	23.9	16.4
Birth rate per 1,000 population.....	27.9	30.6	Deaths under 1 year.....	35	14
Number of deaths.....	135	94	Deaths under 1 year, 1,000 births.....	223.0	80.0

## UNION OF SOCIALIST SOVIET REPUBLICS

*Reports of plague—Quarantine measures by Persia and Turkey.*—A report from Teheran, Persia, dated February 4, 1931, states that during the preceding week plague had appeared in the village of Gouranduz, in Soviet territory near the Persian frontier town of Khudafarin. Twenty-eight deaths were said to have occurred, including a physician. The Persian Government ordered that the frontier be closed, passengers and merchandise to enter only via Julfa and Astara.

Information from Istanbul, Turkey, dated March 16, 1931, states that no sanitary measures have been taken by Turkey against Russian ports but that measures affecting land communication were understood to be in effect along the eastern Turkish-Soviet frontier.

## VIRGIN ISLANDS

*Communicable diseases—February, 1931.*—During the month of February, 1931, cases of certain communicable diseases were reported in the Virgin Islands, as follows:

St. Thomas and St. John:		Cases	St. Croix:		Cases
Pellagra.....	1		Chicken pox.....	6	
Syphilis.....	1		Tuberculosis.....	2	













Place	July, 1930	Aug. 1930	Sept., 1930	Oct., 1930	Nov., 1930	Dec., 1930	Place	July, 1930	Aug. 1930	Sept., 1930	Oct., 1930	Nov., 1930	Dec., 1930
British East Africa (see also table above):							Peru.....	8	21	10	42	84	8
Kenya.....	97	87	53	56	62	50	Senegal:	1	8	2	20	14	
Greece (see also table above).....	1	2	5	2	5	1	Baol.....	62	79	48	53		
Indo-China (see also table above).....							Dakar.....	48	20	23	35	4	
Madagascar (see also table above):							Antistrabe Province.....	140	108	3			
Ambositra Province.....				4	44		Louga.....	122	90	8			
Antistrabe Province.....	24	11	21	3	18	18	Thies.....	138	75	61	37	10	
Miarinarivo Province.....	24	11	21	3	18	18	Tivaouane.....	103	33	30	25	3	
Moramanga Province.....	1	2	7	18	12	7		64	34	12	24	27	2
Moramanga Province.....	1	2	7	18	12	7		30	20	4	15	23	1
Moramanga Province.....	1	2	7	18	12	7		119	110	20	53	31	2
Moramanga Province.....	1	2	7	18	12	7		70	54	14	31	25	1
Tananarive Province.....	28	39	79	125	170								
Tananarive Province.....	28	38	79	116	164								

1 Reports incomplete.

### SMALLPOX

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

Place	Week ended—														
	Aug. 24— Sept. 20, 1930		Sept. 21— Oct. 13, 1930		Oct. 14— Nov. 13, 1930		Decembar, 1930		January, 1931				February, 1931		Mar. 7, 1931
	20	27	3	10	17	24	31	7	14	21	28				
Algeria:															
Algiers.....							1						1		
Bone.....															
Constantine.....															
Oran.....															
Arabia, Aden.....															
Belgium.....															
Brasil:															
Porto Alegre (alastrim).....	1	26													
Porto Alegre.....															
Rio de Janeiro.....	522	95	17	386	23	1	57	3	21	25					
British East Africa (see also table below):															
Tanganyika.....	60	6	1	36	1		3		1	1					
British South Africa: Southern Rhodesia.....	1	153	95	18			18	2							













Place	Aug., 1930	Sept., 1930	Oct., 1930	Nov., 1930	Dec., 1930	Jan., 1931	Aug., 1930	Sept., 1930	Oct., 1930	Nov., 1930	Dec., 1930	Jan., 1931
Palestine.....	0	0	0	0	0	0	3	22	37	3	7	42
Poland.....	0	0	0	0	0	0	2	1	4	2	18	6
Portugal: Oporto.....	0	0	0	0	0	0	2	2	2	3	3	7
Rumania.....	0	0	0	0	0	0	4	4	41	34	20	34
Spain.....	0	0	0	0	0	0	14	2	2	1	2	2
Tunisia.....	0	0	0	0	0	0	2	1	4	1	1	1
Turkey (see table below). Union of South Africa. Cape Province.....	0	0	0	0	0	0	12	6	12	28	7	4
Municipality of East London.....	0	0	0	0	0	0	P	P	P	P	P	P
Natal.....	0	0	0	0	0	0	2	1	1	1	1	1
Orange Free State.....	0	0	0	0	0	0	P	P	P	P	P	P
Transvaal.....	0	0	0	0	0	0	P	P	P	P	P	P
Yugoslavia (see table below).	0	0	0	0	0	0	P	P	P	P	P	P

Place	Aug., 1930	Sept., 1930	Oct., 1930	Nov., 1930	Dec., 1930	Jan., 1931	Aug., 1930	Sept., 1930	Oct., 1930	Nov., 1930	Dec., 1930	Jan., 1931
China: Harbin (see also table above).....	C	5	3	3	1	1	7	24	1	5	6	26
Chosen: Seoul.....	C	2	1	7	16	28	1	1	2	1	3	3
Czechoslovakia.....	C	1	4	4	10	10	26	47	47	28	3	2
Greece: Athens.....	C	6	4	4	4	10	11	11	28	2	2	20
Latvia.....	C	1	2	2	2	2	2	2	1	1	1	2
Lithuania.....	C	7	7	7	7	7	7	7	1	1	1	1
Mexico (see also table above).....	D	1	1	1	1	1	D	D	D	D	D	D
Turkey.....	C	1	1	1	1	1	1	1	1	1	1	1
Yugoslavia.....	C	1	1	1	1	1	D	D	D	D	D	D

## YELLOW FEVER

Place	Aug., 1930	Sept., 1930	Oct., 1930	Nov., 1930	Dec., 1930	Jan., 1931	Aug., 1930	Sept., 1930	Oct., 1930	Nov., 1930	Dec., 1930	Jan., 1931
Brazil:												
Ceara State—Barbalha.....					1	1						
Para, July 29, 1930.....					1	1						
Rio de Janeiro State— Cambucy— Jan. 1-25, 1931.....					3	3						
Feb. 1-7, 1931.....					1	1						
Friburgo (imported), Jan. 25-30, 1931.....					1	1						
Brazil—Continued. Rio de Janeiro State—Continued. Padua— Jan. 18-24, 1931.....											1	1
Feb. 1-7, 1931.....											1	1
Gold Coast: July 10, 1930.....											1	1
Alborno, Aug. 4, 1930.....											1	1
Nigeria: Lagos, July 12, 1930 (probably laboratory infection).....											1	1

! The Director General of Public Health of Guatemala reports an unusual outbreak of typhus fever in a small village in Guatemala.