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# **EDITORIAL**

#### FURTHER STUDY OF BCG VACCINATION

At the 1946 conference on BCG vaccination, held in Washington in September of that year, certain recommendations were made which were reported in the March 7, 1947, issue of PUBLIC HEALTH REPORTS. Since that time, nation-wide interest in this immunizing procedure has grown to an unprecedented level of intensity. So great, indeed, had been the demand from every quarter for additional information concerning the course of BCG investigations that an evaluation and review of recent work in the field had become increasingly appropriate. To that end, a second conference convened in New York City on March 9, 1948, attended by the same group which had met in 1946 to formulate the original policy.

In considering the present status of BCG, the New York conference recognized that many fundamental problems are yet to be resolved concerning the vaccination technique and the vaccine itself. Accordingly, the committee of specialists recommended that the entire problem of BCG continue to receive further attention in the form of intensified research and critical study, and that its application in this country be restricted to certain groups and circumstances.

The decision to limit the use of BCG for the present would appear to be wholly sound and practical. In certain other diseases, such as smallpox, where the desirability of vaccination procedures has been so clearly established, it would be difficult, indeed, to conceive of control without the practice of immunization. In tuberculosis, however, where our fund of knowledge regarding immunization is as yet incomplete, vaccination must continue to be carried out under appropriate safeguards.

The results of careful study leave little doubt that BCG is harmless. As for the degree of immunity which the agent confers, however, there has been very little unanimity of opinion. Although it has become increasingly evident that properly administered BCG vaccination does increase individual resistance to tuberculous infection, there is still a singular lack of definitive information concerning the exact duration of the protection bestowed by the agent. The reason for this is simply that to date, there has been no reliable study of sufficient duration to permit precise evaluation of the vaccine's effectiveness over long periods of time.

Should further study demonstrate that BCG vaccination confers only short-term protection, this would not necessarily argue against its use. In such an eventuality, revaccination might serve to reestablish temporary protection, as is sometimes necessary in the case of other immunizing agents when the immunity conferred by such agents wanes with the passage of time. It can be reasonably expected that further research will provide solutions to these and other problems now confronting BCG investigators.

Regardless of the ultimate place of this immunizing agent in the nation's tuberculosis control program, however, it is extremely unlikely that BCG will ever obviate entirely the necessity for the conscientious prosecution of proved control measures. These must be exploited to the fullest in order to secure past gains and to meet extant needs. Indeed, there is a considerable body of opinion in this country which holds that modern methods of diagnosis and treatment make possible the effective control of the disease without resort to vaccination procedures, especially in areas of low prevalence which possess adequate diagnostic and medical-care facilities. In such locales, the widespread use of BCG could be expected to make relatively little contribution to the control of the disease at this time. In some respects, indeed, it might serve only to confuse existing epidemiological patterns, particularly with reference to the alteration of tuberculin sensitivity. From this point of view, one can appreciate the concern expressed in some quarters that the present balance of tuberculosis control may be disturbed or possibly dislocated by the unqualified acceptance of an insufficiently tried alternative to present control measures.

Therefore, until all the problems of BCG vaccination as a tuberculosis control technique are resolved, and until we can be certain of the implications of a change in emphasis at this time, we have no right to relax our efforts in the application of measures which long experience has shown to be eminently practical and profitable. To do so prematurely might conceivably prove wasteful, if not disastrous, for when incompletely proved techniques are hastily adopted, it frequently happens that "those who cannot remember the past are condemned to repeat it." True progress lies not in that direction.

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# STUDIES OF FUNGUS ANTIGENS. III.

#### Sensitization of Normal Animals With Skin Test Antigens<sup>1</sup>

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#### INTRODUCTION

It has been shown (1, 2) that repeated intradermal injections of 0.1 ml. of 1-10 and 1-100 dilutions of each of several lots of histoplasmin and blastomycin into normal guinea pigs does not sensitize these animals. It has also been shown that coccidioidin (3) and other skin test antigens (4, 5, 6), injected subcutaneously or intraperitoneally, may sensitize guinea pigs. The following experiment was undertaken, therefore, to determine the effects of repeated intradermal injections of more concentrated dilutions of histoplasmin, blastomycin, and other fungus antigens on normal guinea pigs.

#### MATERIALS AND METHODS

Each of 20 normal albino guinea pigs was tested simultaneously with a skin test dose (0.1 ml.) of undiluted histoplasmin, a 1-10, and a 1-100 dilution of histoplasmin, lots H-15 and H-6 (2). At the same time, 10 of these were tested with similar doses of a 1-100 dilution of a heat-killed yeast-phase antigen of *Histoplasma capsulatum* (2); the other 10 with a 1-10 dilution of this antigen. After 35 days, 19 of these animals were retested with the same amount of the same 3 dilutions of histoplasmin, lot H-15, and with a 1-100 dilution of the yeast-phase antigen. At intervals thereafter, the animals were retested with a 1-100 dilution of lot H-15 histoplasmin.

A second group of 10 normal albino guinea pigs were tested simultaneously with 0.1 ml. of undiluted, 1–10, and 1–100 dilutions of blastomycin, lots B–2 and B–7, and a 1–100 dilution of a heat-killed yeast-phase antigen of *Blastomyces dermatitidis* (2). Thirty-five days later the tests were repeated with the yeast-phase antigen and lot B–7. At intervals thereafter, the animals were retested with a 1–100 dilution of lot B–7 blastomycin.

A third group, composed of 38 normal albino guinea pigs, were tested with a skin test dose of each of several dilutions of an autoclaved filtrate antigen prepared from *Candida (Monilia) albicans (7)*. Fifteen of these were tested with a 1-100 dilution of this antigen, 11 with a 1-10 and a 1-100 dilution, and 12 with undiluted, a 1-10, and a 1-100 dilution. Fifteen days later these tests were repeated on the same animals in the same manner.

A fourth group, composed of 20 normal albino guinea pigs were skin-tested with 0.1 ml. of a 1-100 dilution of a heat-killed suspension of *Candida (Monilia) albicans* ("vaccine-type" antigen) and a 1-100 dilution of histoplasmin, lot H-15. Fifteen days later these tests

<sup>&</sup>lt;sup>1</sup> From the Office of Field Studies, Tuberculosis Control Division.

were repeated. After 182 days, 19 of these 20 were retested with 0.1 ml. of the autoclaved filtrate antigen of *C. albicans* and lot H-15 histoplasmin. Sixteen of this group were eventually autopsied and cultures prepared from the spleen of each (8).

All tests were read at 24 hours; a reaction with 5 millimeters or more of induration was considered positive.

#### RESULTS

The results of these repeated skin tests on normal guinea pigs are summarized in tables 1–10.

 

 TABLE 1.—Results of simultaneous tests on normal guinea pigs with 1-100 dilution of heat-killed yeast-phase antigen of Histoplasma capsulatum and with specified dilutions of histoplasmin, lots H-15 and H-6

	Heat- killed			Histop	olasmin		
Item -			Lot H-1	5		Lot H-6	
				Dilution			
	1-100	Undi- luted	1–10	1-100	Undi- luted	1–10	1-100
Number of animals tested Number of reactors Percentage of reactors	10 0 0	10 0 0	10 0 0	10 0 0	10 0 0	10 0 0	19 0 0

From table 1 it can be seen that none of the 10 animals which were first tested simultaneously with a skin test dose (0.1 ml.) of a 1-100 dilution of the heat-killed yeast-phase antigen of *Histoplasma* and the undiluted, 1-10, and 1-100 dilutions of histoplasmin, lots H-15 and H-6, reacted to any of these antigens in these dilutions. However, when retested 35 days later with the 1-100 dilution of the yeastphase antigen and each of the three dilutions of lot H-15 histoplasmin (table 2) eight reacted to the undiluted H-15 but none to the other dilutions of H-15 nor to the yeast-phase antigen. Furthermore, on

**TABLE 2.**—Results of retesting guinea pigs with 1–100 dilution of heat-killed yeastphase antigen of Histoplasma capsulatum and with specified dilutions of histoplasmin, lot H–15.

	Heat- killed yeast- phase antigen		Histop Lot	olasmin H-15			
Item	35 days after initial tests 79 d						
	Dilution						
	1-100	Undiluted	1–10	1-100	1-100		
Number of animals tested Number of reactors Percentage of reactors	10 0 0	10 8 80. 0	10 0 0	10 0 0	9 22 22.2		
Average diameter of reaction 1		8.5			5.5		

the seventy-ninth day (table 2), two of nine, having received one test with undiluted H-6 and two with undiluted H-15 (tables 1 and 2), reacted to a 1-100 dilution of H-15. One of these two still reacted to this dilution of H-15 after 182 days.

Of the 10 animals which were tested simultaneously with a 1-10 dilution of the yeast-phase antigen and with undiluted, 1-10, and

TABLE 3.—Results of simultaneous tests on normal guinea pigs with 1–10 dilution of heat-killed yeast-phase antigen of Histoplasma capsulatum and with specified dilutions of histoplasmin, lots H-15 and H-6

	Heat- killed		Histoplasmin							
۵ Item –			Lot H-1	5		Lot H-6				
		Dilution								
		Undi- luted	1–10	1-100	Undi- luted	1-10	1-100			
Number of animals tested Number of reactors Percentage of reactors Average diameter of reaction 1	10 9 90. 0 6. 7	10 0 0	10 0 0	10 0 0	10 0 0	10 0 0	10 0 0			

<sup>1</sup> Induration in millimeters.

1-100 dilutions of histoplasmin, lots H-15 and H-6 (table 3), 9 reacted on the first test to the 1-10 dilution of the yeast-phase antigen but not to the other antigens in the dilutions employed. When retested 35 days later with the same dilutions of H-15 and a 1-100 dilution of the yeast-phase antigen (table 4), 7 of 9 reacted to undiluted, 1 of 9 to the 1-10 dilution of H-15 and 4 of 9 to the 1-100 dilution of the yeast-phase antigen, but none to the 1-100 dilution of H-15. At 79 days, however, 6 of 9, having received 1 test with a 1-10 dilution of yeast-phase antigen, 2 with undiluted H-15 and 1

 

 TABLE 4.—Results of retesting guinea pigs with 1-100 dilution of heat-killed yeastphase antigen of Histoplasma capsulatum and with specified dilutions of histoplasmin, lot H-15

	Heat- killed Histoplasmin yeast- phase Lot H-15 antigen						
Item		79 days					
			Dilution				
	1-100	Undiluted	1-10	1-100	1-100		
Number of animals tested Number of reactors Percentage of reactors Average diameter of reaction 1	9 4 44. 4 5. 4	9 7 77. 8 8. 5	9 1 11. 1 5. 0	9 0 0	9 6 66. 7 6. 7		

Similar results were obtained with the 10 normal guinea pigs tested with undiluted blastomycin (tables 5 and 6), and with the undiluted

 

 TABLE 5.—Results of simultaneous tests on normal guinea pigs with 1-100 dilution of heat-killed yeast-phase antigen of Blastomyces dermatitidis and with specified dilutions of blastomycin, lots B-7 and B-2

Heat- killed			Blasto	mycin		
yeast- phase antigen		Lot B-7			Lot B-2	
			Dilution			
1-100	Undi- luted	1-10	1-100	Undi- luted	1-10	1-100
11 1 9.1 5.0	11 2 18.2 5.0	11 0 0	11 0 0	11 0 0	11 0 0	11 0 0
	Heat- killed yeast- phase antigen 1-100 11 1 9.1 5.0	Heat-killed yeast-phase antigen	Heat-killed yeast-phase antigen         Lot B-7           1-100         Undi-luted         1-10           11         11         11           1         2         0           9.1         18, 2         0           5.0         5.0	Heat-killed yeast-phase         Blasto           Johase         Lot B-7           1-100         Undi-luted         1-10           11         11         11           1         12         0         0           9.1         18.2         0         0           5.0         5.0	Heat-killed yeast-phase antigen         Blastomyein           Lot B-7         Dilution           1-100         Undi-luted         1-10         1-100         Undi-luted           11         11         11         11         11         11           1         2         0         0         0         0           9.1         18.2         0         0         0         0           5.0         5.0           0         0	Heat-killed yeast-phase         Blastomycin           Lot B-7         Lot B-2           Dilution         Dilution           1-100         Undi-luted         1-10         1-100         Undi-luted         1-10           11         11         11         11         11         11         11         11           19.1         18.2         0         0         0         0         0         0           5.0         5.0         5.0         0         0         0         0         0         0

<sup>1</sup> Induration in millimeters.

TABLE 6.—Results of retesting guinea pigs with 1-100 dilution of heat-killed yeastphase antigen of Blastomyces dermatitidis and with specified dilutions of blastomycin, lot B-7

		1					
	Heat- killed yeast- phase anti- gen						
Item	:	79 days					
	Dilution						
	1-100	Undiluted	1-10	1-100	1-100		
Number of animals tested Number of reactors Percentage of reactors	10 0 0	10 9 90. 0 7. 3	10 0 0	10 0 0	10 1 10.0 5.0		

<sup>1</sup> Induration in millimeters.

 

 TABLE 7.—Results of testing normal guinea pigs with 1-10 dilution of autoclaved filtrate of Candida (Monilia) albicans and of retesting 15 days later with 1-10 and 1-100 dilutions of the filtrate

	Autoclaved filtrate of C. albicans				
	D	ay of observatio	n		
ltem	1	5			
	Dilution				
	1-10	1-10	1-100		
Number of animals tested Number of reactors Percentage of reactors Average diameter of reactions <sup>1</sup>	11 0 0	11 5 45. 5 5. 3	11 3 27.3 5.7		

and 1-10 dilutions of the autoclaved filtrate antigen prepared from C. albicans (tables 7 and 8). Repeated testing with a 1-100 dilution of the autoclaved filtrate of C. albicans, however, did not result in any reactions to this dilution of this antigen on the second test 15 days after the first.

TABLE 8.—Results of testing normal guinea pigs with undiluted autoclaved filtrate of Candida (Monilia) albicans and of retesting 15 days later with undiluted and with 1-10 and 1-100 dilutions of the filtrate

	Autoclaved filtrate of C. albicans						
	Day of observation						
Item	• 1	15					
	Dilution						
	Undiluted	Undiluted	1–10	1-100			
Number of animals tested	12 0 0	12 6 50.0 7.8	12 2 16.7 5.0	12 1 8.3 5.0			

<sup>1</sup> Induration in millimeters.

TABLE 9.—Results of simultaneous tests on normal guinea pigs with 1-100 dilution of heat-killed antigen of Candida (Monilia) albicans and with 1-100 dilution of histoplasmin, lot H-15

	Heat-killed antigen <i>C. albicans</i>	Histoplasmin Lot H-15
Item	Dih	ation
	1-100	1-100
Number of animals tested	20 9 45.0	20 0 0
Average diameter of reaction <sup>1</sup>	5.7	

Induration in millimeters.

TABLE 10.—Results of retesting guinea pigs with heat-killed antigen and with autoclaved filtrate of Candida (Monilia) albicans and with histoplasmin, lot H-15

	Heat-killed antigen C. albicans	Autoclaved filtrate of C. albicans	Histoplasmin Lot H–15	
	D	ay of observati	ion	
Item	15 182			
	1-100	1-100	1-100	
Number of animals tested	20 20 100. 0 7. 9	19 16 84. 2 7. 1	19 12 63. 2 8. 5	

Of the 20 normal animals tested with the heat-killed suspension of C. *albicans*, 9 reacted to the first injection of a 1-100 dilution (table 9) and 20 of 20 to the same amount of the same antigen when retested 15 days later (table 10).

Cultures were prepared from the spleen of each of 11 guinea pigs in the first group, tested repeatedly with histoplasmin; 4 in the second group, tested with blastomycin; and 15 from the fourth group tested with the heat-killed suspension of *C. albicans*. All were negative for pathogenic fungi as reported elsewhere (8).

#### DISCUSSION

It has been shown previously (1, 2) that repeated testing with a 1-100 dilution of various lots of histoplasmin and blastomycin and heat-killed antigens prepared from the yeast-phase of *Histoplasma capsulatum* and *Blastomyces dermatitidis* does not irritate nor sensitize normal guinea pigs. However, from the evidence presented above (tables 1-6) it would seem that repeated skin tests with 0.1 ml. doses of undiluted histoplasmin or blastomycin, or two or more injections (intradermally) of the undiluted antigens simultaneously, or tests with a 1-10 dilution of the heat-killed yeast-phase antigen prepared from cultures of *Histoplasma* may sensitize normal guinea pigs to some degree so that they may subsequently react to tests with a 1-10 or occasionally a 1-100 dilution of the same antigen whereas they did not react to these dilutions previously.

The finding that multiple tests with undiluted histoplasmin or blastomycin may sensitize is, as indicated above, based in part on work previously reported (1, 2). In these papers it has been shown, for example, that repeated tests with 1-10 and 1-100 dilutions of these particular lots of histoplasmin and blastomycin do not sensitize. Therefore, it is assumed that when used simultaneously with the undiluted antigens, any subsequent reactions of these animals to these antigens are due to the previous use of the undiluted materials.

Similar results have been obtained with an autoclaved filtrate, which is probably carbohydrate in nature, prepared from *Candida* (Monilia) atbicans (tables 7 and 8).

The finding that these filtrate antigens, if used in sufficient concentration, may sensitize normal guinea pigs to some degree is supported by the observations of Hirsch and D'Andrea (3) and T'Ung and Wong (5). The former found that normal guinea pigs could be sensitized by repeated subcutaneous injections of coccidioidin so that they would subsequently react to an intradermal injection of coccidioidin or to the "specific substance," probably carbohydrate in nature, which was isolated from coccidioidin. T'Ung and Wong found that a polysaccharide isolated from *Monilia* (*Candida*) tropicalis, injected intraperitoneally, was capable of inducing a low degree of sensitivity in guinea pigs, although this substance was inferior to the whole yeast cells as a sensitizing agent.

In table 9 it can be seen that 9 of 20 normal guinea pigs reacted to a skin-test dose of a 1-100 dilution of a heat-killed suspension of Candida (Monilia) albicans on the first injection. Fifteen days later, 20 of 20 reacted to a second injection of the same amount (table 10). Several investigators have found that in animals, injection of whole, dead cells of Candida usually sensitizes (4, 6) although such sentitization is weaker than that produced by actual invasion of the tissues by living cells.

The subsequent reaction of the group of animals sensitized by intradermal injections of the heat-killed suspension of C. albicans (table 10) to a 1-100 dilution of lot H-15 histoplasmin must be regarded as evidence of a cross reaction, although it should be pointed out that this dilution of this lot of histoplasmin is approximately 10 times the critical titer of this antigen for guinea pigs (2). Studies on other animals sensitized with living cells of C. albicans have shown a much lower degree of cross reaction with this lot of histoplasmin (9).

The sensitization of normal animals by repeated injections or two or more simultaneous injections of undiluted histoplasmin or by the use of a 1-100 heat-killed suspension of C. albicans would seem to explain the reactions of normal animals to histoplasmin reported in the following paper (8).

#### SUMMARY

The effects of simultaneous and repeated intradermal injections of 0.1 ml. of various dilutions of histoplasmin, blastomycin, an autoclaved filtrate of Candida (Monilia) albicans, heat-killed suspensions of the yeast-phase of Histoplasma capsulatum and Blastomyces dermatitidis, and of a 1-100 dilution of a heat-killed suspension of C. albicans on normal guinea pigs have been studied.

It has been shown that these antigens, if used in sufficient concentrations, may sensitize normal guinea pigs.

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# ISOLATION OF PATHOGENIC FUNGI FROM EXPERIMEN. TALLY INOCULATED GUINEA PIGS <sup>1</sup>

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#### INTRODUCTION

Numerous investigators have reported variable results in attempts to infect laboratory animals with *Histoplasma capsulatum* (1-8), *Blastomyces dermatitidis* (9-16), and *Candida albicans* (17-21). The following study was undertaken, therefore, to determine (1) a sublethal dosage of each of these fungi which would sensitize the animals to skin test antigens prepared from the homologous fungi and (2) to learn if these fungi could be isolated from the inoculated animals after variable periods of time, with or without the production of an apparent generalized infection.

#### MATERIALS AND METHODS

The strains of *H. capsulatum (22)* and *B. dermatitidis (23)* employed in these studies were those previously reported. The strains of *Candida (Monilia) albicans* were isolated from specimens received at the United States Public Health Service laboratory at the University of Kansas Hospital.

Each of 80 normal albino guinea pigs was inoculated intraperitoneally with graded doses of a 1-100 saline suspension of the living yeast phase of *H. capsulatum*, 82 with graded doses of a similar suspension of the living yeast phase of *B. dermatitidis*, and 35 with graded doses of a 1-100 saline suspension of living cells of *Candida* (*Monilia*) *albicans*.

The suspension of the yeast phase of *Histoplasma* was prepared from 5-day-old cultures grown on sealed blood agar slants and incubated at 37° C. (24); that of *Blastomyces* from 7-day-old cultures of the yeast phase grown on Difco brain heart infusion agar at 37° C.; and that of *C. albicans* from 2-day-old cultures grown on Sabouraud's agar at 37° C.

The dosages employed are shown in table 1.

TABLE 1.—Number of guinea pigs inoculated intraperitoneally with specified dosages of 1-100 suspension of yeast-phase of Histoplasma capsulatum, of Blastomyces dermatitidis, and of Candida (Monilia) albicans

	Dosage (ml. 1-100 suspension per gram of body weight)									Ī.
Fungus employed	0. 00100- 0. 00199	0. 00200 0. 00299	0. 00300- 0. 00399	0. 00400- 0. 00499	0. 00500- 0. 00599	0. 00600- 0. 00699	0. 00700- 0. 00799	0. 00800- 0. 00899	0. 00900- 0. 00999	Tota
Histoplasma capsula- tum Blastomuces dermati-	7	13	20	16	15	9	0	0	0	8
tidis Candida albicans	5 7	9 12	19 12	26 4	8 0	4 0	5 0	5 0	1 0	82 35

<sup>1</sup> From the Office of Field Studies, Tuberculosis Control Division.

All animals were skin-tested prior to inoculation with a skin-test dose of a 1-100 dilution of an antigen prepared from the homologous organism [i. e., histoplasmin, blastomycin, or an antigen prepared from C. albicans (25)]. No animal reacted to any antigen in the dilution employed.

The animals were weighed at the time of inoculation and at intervals thereafter and were skin-tested with various antigens at intervals. Thirteen of those inoculated with *Histoplasma* died between 30 and 247 days after inoculation; the remainder were sacrificed at intervals varying from 2 to 10 months. Twenty-eight of those inoculated with *Blastomyces* died between 18 and 289 days after inoculation; the remainder were sacrificed at intervals of 1 to 11 months. Four of the group inoculated with *C. albicans* died between 11 and 63 days after inoculation; 24 of the remainder were sacrificed at intervals varying from 49 to 76 days after inoculation.

All animals were autopsied and any marked pathological change was noted. If abscesses or other lesions were present material from these lesions was used for culture. In all animals in which there were no marked pathological changes the spleen was removed, a portion of each fixed for sectioning, and the remainder used for cultures.

Cultures from the animals inoculated with *Histoplasma* were made on each of two plates of brain heart infusion blood agar and potato dextrose agar as previously reported (22); those from animals inoculated with *Blastomyces* or *C. albicans* on two plates of the same blood agar and two plates of Sabouraud's agar. Streptomycin and penicillin in concentrations of 40 and 20 units, respectively, per milliliter of medium were added to all media. One plate of each medium was then incubated at 37° C. and the other at room temperature (approximately 25° C.).

In addition to the animals which were inoculated with Histoplasma, Blastomyces, and C. albicans, 41 normal albino guinea pigs were studied as controls. These animals were divided into three groups. The first group, composed of 10 animals, were skin-tested with a skin-test dose of a 1-100 dilution of each of several antigens on the day they were received at the laboratory and sacrificed 3 days later. The second group, composed of 15 animals, were kept under observation for a total of 182 days and were kept in the normal animal room. The third group, composed of 16 animals, were kept in the same room with the inoculated animals described above and were under observation for 232 to 259 days. Three of this group died between the 244th and 258th day of observation. All of the animals in groups two and three were skin tested at intervals with various antigens. All were then sacrificed at the end of the periods indicated.

Each of these 41 normal animals was autopsied. At autopsy any

marked pathological changes were noted and the spleen of each removed. A portion of the spleen of each was fixed for sectioning and the remainder used for cultures.

Cultures of each were made on two plates of the brain heart infusion blood agar, one plate of potato dextrose agar and one plate of Sabouraud's agar. One plate of the blood agar was incubated at  $37^{\circ}$  C.; the other three plates at room temperature (approximately  $25^{\circ}$  C.).

All positive cultures or cultures suspected of being positive were confirmed by subculturing the suspected colonics on the appropriate medium at room temperature.

#### RESULTS

1. Animals inoculated with Histoplasma capsulatum.—With the dosages employed, in animals inoculated intraperitoneally with the living yeast phase of H. capsulatum there appeared to be no correlation between the size of the inoculating dose and the number of animals which developed an apparently generalized infection.

Of the 80 guinea pigs in this group, an apparently generalized infection developed in 3, or 3.8 percent, of the total inoculated (table 2).

**TABLE 2.**—Summary of findings on guinea pigs developing apparently generalized infection following intraperitoneal inoculation with 1–100 saline suspension of yeast-phase of Histoplasma capsulatum

		Skin reaction to				Net cha	weight ange		-						
Guinea pig No.	Dosage (ml. 1-100 suspen- sion per gram of body weight)     Ilistoplasmin, lot H-15     Polysaccharide fraction (his- toplasmin, lot H-17)       1-100 dilution     1.0 mg./ml.     Gms.     Gms.	II istor lot	olasmin, H-15	Polysa fractic topla lot I	ccharide on (his- usmin, H-17)			Time	Gross	Besults of culture					
		Per- cent- age	death (Days)	at autopsy											
								D	Days after inoculation						
		40	75	89	47										
230 260 267	0. 00345 0. 00294 0. 00291		_ 	_ 		-110 +15 -185	-25. 3 +2. 9 -35. 9	1 90 48 8 43	Moderate. Moderate. Moderate	Lung+; spleen+ Spleen+ Spleen unknown (contaminated)					

<sup>1</sup> Sacrificed.

<sup>2</sup> Only 5 mm. of induration. <sup>2</sup> Died as a result of a laboratory accident.

Two of these three animals underwent a progressive loss of weight, the third showed a slight increase in weight at the time of death. Of the two which showed a progressive weight loss, one died on the forty-third day apparently from a laboratory accident and the other was sacrificed 90 days after inoculation. None of the three reacted to any skin test at any time except one (table 2). All three showed moderate pathology at autopsy, particularly in the thoracic cavity. Cultures prepared from the lungs of guinea pig No. 230 were positive for *Histoplasma*: cultures of the lungs of the other two animals were overgrown with bacteria. Cultures prepared from the spleens of guinea pigs Nos. 230 and 260 were positive; cultures of the spleen of the third were overgrown with contaminants.

One of the 80 apparently was neither infected not sensitized by the inoculation. Repeated skin tests with a 1-100 dilution of histoplasmin, lot H-15 (23) were all negative. No gross pathology was noted at autopsy 91 days after inoculation, by which time the animal had gained approximately 20.0 percent in weight. Sections and cultures made from the spleen at autopsy were both negative for *Histoplasma*.

Of the remaining 76 animals inoculated with *Histoplasma*, 11 died (table 3). Two of these apparently died from laboratory accidents. These two reacted to a skin-test dose of a 1–1000 dilution of histoplasmin, lot H-15, 26 days after inoculation; both showed a marked increase in weight; neither showed any marked pathology at autopsy. However, cultures prepared from the spleens of both were positive.

The cause of death of the other 9 animals which died during the course of the experiment was not determined. All reacted to a skintest dose of a 1-1000 dilution of histoplasmin, lot H-15, 26 days after inoculation, and 2 to a 1-100 dilution of this same antigen 202 days after inoculation. Eight of the nine gained a considerable amount of weight while under observation; only two showed any marked pathology at autopsy. In these two, guinea pigs Nos. 193 and 200, there were slight to moderate changes in the thoracic cavity. Cultures of material from the lungs of both and of the spleen of No. 193 were overgrown with bacteria. Cultures of the spleen of guinea pig No. 200 yielded Histoplasma. Of the remaining seven which showed essentially no pathology at autopsy, Histoplasma was isolated from the spleens of four. These 4 animals were autopsied 79, 122, 30, and 140 days after inoculation. There is no clear evidence, therefore, that any of these 11 animals died from experimental histoplasmosis.

The remaining 65 guinea pigs remained apparently healthy. These were sacrificed 2 to 9 months after inoculation. All, at some time, reacted to a skin-test dose of at least a 1-100 dilution of histoplasmin, lot H-15, and 54 reacted, at some time, to a 1-1000 dilution of this antigen. All gained a considerable amount of weight, and none showed any marked pathology at autopsy. However, *Histoplasma* was isolated from the spleens of 39, or 60.0 percent of these animals. Among 31 animals kept under observation for a period of 6 months or longer, cultures prepared from 14, or 45.2 percent, were positive. It is interesting that those animals from which cultures were obtained were not necessarily those which had received the greater doses.

It was possible to isolate Histoplasma from the spleens of 4 of 10

se of Histoplasma capsulatum			Results of culture			Lung -: spleen Spleen +. Spleen +. Spleen +. Spleen +. Spleen Spleen Spleen Spleen Spleen Lung unknown (contaminated); Jung unknown (contaminated); Spleen Spleen taminated).
ssion of yeast-pha			Gross pathology at autopsy			Essentially none Essentially none Essentially none Essentially none Essentially none Essentially none Essentially none Essentially none Sight (lungs) Moderate (lungs)
) suspen			Time of death (days)			163 763 764 764 764 764 764 765 765 765 765 765 765 765 765 765 765
th 1–100		t cnange		Percent- age		$\begin{array}{c} + & + & + & + & + & + & + & + & + & + $
ation wi	datan tak	net weign		Gms.		+ 470 + 245 + 245 + 250 + 250 + 105 + 1105 + 1140 + 1140 + 1140
fter inocul	Н-15			oculation	228	+
ying <sup>1</sup> a	plasmin, lot H-1	Dilution	-100		oculation	202
a pigs d	to Histopl		1-100	s after inoc	186	+ +
n guine	n reaction			Day	171	+ + +
dings o	Ski		1-1000		36	+++++++++ ++
mary of fin		Dosage (ml.	1-100 suspen- sion per gram of body	weight)		0.00164 0.00257 0.00257 0.00258 0.00258 0.00556 0.00556 0.00556 0.00556
TABLE 3.—Sum			Guinea pig No.			158- 1640- 1670- 1670- 1670- 1670- 1640- 1930- 1940- 1

<sup>1</sup> Exclusive of guinea pigs number 260 and 267 included in table 1. <sup>2</sup> Died as a result of laboratory accidents.

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apparently normal, healthy animals which had been inoculated with large doses of this fungus intraperitoneally at least 9 months previously.

None of these 65 animals, at any time during the course of the experiment, nor at autopsy, showed any signs of infection with the fungus except for the development of a sensitivity to the homologous organism or its products at some time after inoculation.

Of the 77 animals which failed to develop any visible signs of experimental histoplasmosis, other than a skin sensitivity to histoplasmin, it was possible to isolate *Histoplasma*, after variable periods of time, from the spleens of 46, or 59.6 percent.

2. Animals inoculated with Blastomyces dermatitidis.—In animals inoculated intraperitoneally with the living yeast phase of Blastomyces dermatitidis, as with the animals similarly inoculated with Histoplasma, there appeared to be no correlation, with the narrow ranges of dosages employed, between the size of the inoculating dose and the number of animals which developed an apparent generalized infection

Of 82 guinea pigs in this group, 17 developed an apparent infection (table 4); 13 of these 17 died between the 18th and 127th day after inoculation; the remaining 4 were sacrificed between the 41st and 257th day. Of the 13 which died, 11 showed moderate to marked loss of weight, 5 consistently failed to react to a skin-test dose of a 1-100 dilution of blastomycin, lot B-2 (23); 10 showed extensive, and 3 moderately extensive, pathology at autopsy; cultures obtained from one or more organs of each were positive for *Blastomyces*. One of these, guinea pig No. 117, died as a direct result of a laboratory accident. This animal had failed to react to a skin test dose of a 1-100 dilution of blastomycin, lot B-2, and even though it had gained a considerable amount of weight, showed extensive pathology at autopsy.

Of the 4 in the above group which were sacrificed, 3 showed a slight to marked increase in weight; all 4 failed repeatedly to react to a skintest dose of a 1-100 dilution of blastomycin, lot B-2 or B-7 (23); and 2 showed moderate to extensive pathology at autopsy. A third, sacrificed 257 days after inoculation, by which time it had gained over 200 grams, or 47.9 percent, in weight, showed an abscess in the liver approximately 5 cm. in diameter at autopsy. Cultures obtained from one or more tissues of each of these 4 animals were positive for *Blastomyces*. The essential findings on each of these 17 guinea pigs are summarized in table 4.

Of the remaining 65 guinea pigs, 15 died (table 5). Two of these apparently died as a result of laboratory accidents. One of these reacted to a skin-test dose of a 1-1000 dilution of blastomycin, lot B-2, 47 days after inoculation, while the other did not. Both gained

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ident.	d as a result of laboratory acc	a Die			cicht at 56 days.	8 W			1 Sacrificed.	
Spleen +; "pancreas" +.	Moderate	141	+9.0	+40			1		0.00449	137
Subcut, abscess +.	Extensive.	127	-7.5	-45		+	៲ន		0. 00667	132.
Liver abscess +. Liver abscess +. Liver abscess +.	Liver abscesses	22 22 22	- 25.4 - 23.9 - 45.5	- 130 - 90 - 250	+++	64	38		0.00391 0.00531 0.00364	263 270 271
Spleen +; abdom. absc. +. Liver abscess +.	Extensive. Liver abscesses.	113 93	- 24.5	-135	+	1	+		0.00364	233.
					40	76	41			
Spleen +; "pancreas" +. Spleen +; liver absc. +. Spleen +; liver absc. +.	Moderate Extensive Liver abscess	1 190 40 1 257	-31.1 -26.8 +47.9	-220 -160 +210	1		111		0.00566 0.00570 0.00799	141 147 151
					187 252		8			
Spleen +: subcut. absc. +. Spleen +:	Extensive Extensive	- 65 62 63	6.6 6.6 1 1 1 1 1	110 112 120			11	+	0.00198 0.00198 0.00571	125 131 131
Liver +; spleen +; lung +. "Pancreas", +. "Pancreas", +; spleen +. "Pancreas", +; spleen +.	Extensive Extensive Extensive Extensive	62 89 80 80 80 80 80 80 80 80 80 80 80 80 80		-210 -5 +190			1 1 1		0.00471 0.00158 0.00440 0.00460	113 116 117
							47			
					по	er inoculati	Days aft			
AINTINO TO STINSAN	CIOSS patrones at autops	(days)	Percen- tage	Gms.	1-100	1-1000	1-100	1-1000	sion per gram of body weight)	Curines pig 100.
Doculte of aultured	Genes nothology of outpress	Time of				oilution	J		Dosage (ml. 1-100 suspen-	Outroo ate No
					ot B-7	Г	B-2	Lot		
			t change	Net weigh	mycin	on to blasto	skin reactio			
l inoculation with 1–100	ollowing intraperitoneal atitidis	fection f es derm	ulized in astomyc	ly genero ise of Bli	oing apparent n of yeast-pho	1s develor uspensio	vinea piç saline s	ıb uo sbı	ry of findi	TABLE 4.—Summa

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1 Sacrificed.

a large amount of weight before death. At autopsy, both showed some degree of pathology. Cultures from material taken at autopsy of both animals were negative for *Blastomyces*, though those from one of the animals were overgrown with bacteria.

The cause of death of the other 13 animals which died was undetermined. Twelve showed a marked increase in weight; and 10 at some time reacted to one or more repeated skin tests with a 1-1000 dilution of blastomycin, lot B-2 or B-7. At autopsy, six showed some degree of pathology. Of these, only one gave cultures positive for *Blastomyces*, while of the seven which showed essentially no pathology, *Blastomyces* was isolated from the spleen of two and the lungs of one. It would seem doubtful, therefore, that any of these animals died from experimental blastomycosis. The essential findings on each of these 15 animals are shown in table 5.

The remaining 50 guinea pigs remained apparently healthy. All, at some time, reacted to a skin-test dose of at least a 1-100 dilution of blastomycin, lot B-2 or B-7; 22 at some time to at least a 1-1000 dilution of lot B-2, and 37 to at least a 1-1000 dilution of lot B-7. All gained markedly in weight. None showed any marked pathology at autopsy, although there were small abscesses in the liver of two, in the pelvic region of two, "pancreas" of one, and abdominal wall of one. However, *Blastomyces* was isolated from 1 or more tissues removed at autopsy from 26, or 52.0 percent, of these animals. Among 33 animals kept under observation for a period of 6 months or longer cultures prepared from 15, or 45.5 percent, were positive.

It was possible to isolate *Blastomyces dermatitidis* from the spleens of four of 9 guinea pigs which had been inoculated intraperitoneally with this fungus at least 10 months previously.

Of the 65 which failed to show any visible signs of experimental blastomycosis, other than a skin sensitivity to blastomycin, it was possible to isolate *Blastomyces*, after variable periods of time, from 30, or 46.2 percent.

As with the animals inoculated with *Histoplasma*, the animals from which cultures were obtained were not necessarily those which received the greater doses.

3. Animals inoculated with Candida (Monilia) albicans.—Of 35 guinea pigs inoculated with C. albicans, none developed an apparently generalized infection. Four died between the 11th and 63d day after inoculation (table 6). The animal which died on the 11th day apparently died from an intestinal obstruction. The other three reacted to at least a 1–100 dilution of an autoclaved filtrate antigen prepared from the homologous fungus (25), two of them to a 1–1000 dilution, on the 41st day. Two of the three lost weight. However, there were no marked gross pathological findings at autopsy in any one of the four, and cultures from two were negative for C. albicans. No

TABLE 5.—Su	mmary of fi	inding	uo sb	guinea	pigs dyir	ıg <sup>1</sup> aj	ter ir	rocula	tion wi	h 1-100	suspens	ion of yeast-phase of	Blastomyces dermatitidis
			œ	škin reacti	on to blastc	mycin			Net weigl	nt change			
			Lot B	-2		Lot B-	r-						
Guinea nie no	Dosage (ml. 1-100 suspen- sion por			Γ	Dilution						Time of	Gross pathology at	Results of culture
country pre-mo-	gram of body weight)	1-1(	000	1-100	1-1000		1-100		Gms.	Percent- age	(days)	autopsy	
				Days af	tter inocula	tion							
		47	64		64	215	250	280					
191 100 1107 1127 1127 1127 1130 1130 1130	0,00447 0,00430 0,00430 0,00400 0,00400 0,00402 0,00402 0,00412 0,00412 0,00412 0,00412 0,00412 0,00412 0,00415	+++1+++++1	++1 +++ +		+++ +++ +	+ + ++ 1	++	+	+110 +1270 +1105 +110 +110	++116, 4 ++77, 1 ++77, 1 ++77, 1 ++77, 1 ++13, 0 ++110, 9 ++113, 9 ++113, 9 +27, 7	227 208 269 269 269 269 269 269 269 269	Ess ntially none Essentially none Essentially none Essentially none Moderate Orichitis Necrosis of liver Necrosis of liver Nicry absects Slight (lunge) Essentially none	Lung Spleen Spleen Testis Liver Liver Lurer abs Lung Lung Lung Lung Lung Lung Spleen Spleen Spleen Spleen
				Days (	after inocul	aticn							
				38	<b>%</b>								
149- 157- 162- 171	0.00860 0.00785 0.00802 0.00802 0.00769			+111	+			-	+150 +240	+32.3 +53.8	158 132 189	Abse. in diaphragm Essentially none Essentially none Essentially none	Spleen –. Spleen –. Spleen –. Lung +.
				Days a	fter inocula	tion							
					<b>8</b>	75	95	125					
291	0, 00400				+		+	+	+155	+31.0	130	Moderate	Spleen +.
		.											

<sup>2</sup> Died as a result of laboratory accidents.

<sup>1</sup> In addition to those summarized in table 4.

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Guinea pig num-	Dosage (ml. 1-100 suspen- sion per gram	Skin r to auto filtrat <i>albice</i> days inocu	eaction oclaved e of C. ins 41 after lation	Net v cha	veight inge	Time of death	Gross pathology at autopsy	Results of culture
ber	of body wgt.)	Dilu	ition	Gm3.	Per- cent- age	(days)		
		1-1000	1-100					
351	0.00351	+	+	+40	+7.0	63	Post mortem	No culture made.
357	0.00431	_	+	-90	1-15.5	54	Essentially none	Spleen
368	0.00364	+	+	-100	-18.2	45	Abdominal adhe-	Spleen-; lung-;
383	0. 00235			-30	-7.1	11	Intestinal obstruc- tion.	No culture made.

TABLE 6.—Summary of findings on guinea pigs dying after inoculation with 1–100 suspension of Candida (Monilia) albicans

1 Weight taken 5 days before death.

cultures were made from the other two. Therefore, although the cause of death of three of these animals was not determined, it would not seem that they died as a result of the inoculation of *C. albicans*.

Of the remaining 31 animals, 24 were sacrificed. All of these showed a definite and constant increase in weight, although the group sacrificed during the third month were markedly dehydrated in appearance at the time they were sacrificed. All but one reacted to a skin-test dose of at least a 1-100 dilution of the autoclaved filtrate antigen of *C. albicans* 41 days after inoculation. At autopsy, none of the 24 which were sacrificed showed any gross pathology except for abdominal adhesions in five. Cultures prepared from the spleens of each of these 24 were negative except for one sacrificed on the 49th day, from which *C. albicans* was isolated. It would seem, therefore, that none of these animals developed a widespread experimental infection, with the dosages employed for inoculation, although the majority (33 of 35, or 94.3 percent) did develop a skin sensitivity to the homologous fungus or its products.

4. Normal animals.—Forty-one normal guinea pigs, divided into 3 groups, were included in this study as controls.

The first group, composed of 10 animals, were tested with a skintest dose of a 1-100 dilution of histoplasmin, lot H-15, blastomycin, lot B-7, and the autoclaved filtrate antigen of *C. albicans* on the same day the animals were received into the laboratory. None reacted to any of these antigens in this dilution. Each of these animals was sacrificed 3 days later. At autopsy none showed any gross pathology; cultures from the spleen of each were negative for pathogenic fungi.

The second group, composed of 15 animals, were kept under observation for a period of 182 days in the normal animal room. At the time they were sacrificed (on the 182d day of observation) 4 reacted to a skin-test dose of a 1-100 dilution of histoplasmin, lot  $H-15.^2$  None reacted to the same dilution of blastomycin, lot B-7. At autopsy none showed any gross pathology; and cultures from the spleen of each were negative for pathogenic fungi.

The third group, composed of 16 animals, were kept in the same room with the animals inoculated with *Histoplasma*, *Blastomyces*, and *C. albicans*. Three of these animals died between the 244th and 258th day of observation. At autopsy two showed some gross pathology, but cultures from the spleens of each of the three were negative for pathogenic fungi.

Of the remaining 13, 8 were sacrificed on the 232d day of observation. At this time, three of these reacted to a skin-test dose of a 1-100 dilution of histoplasmin, lot H-15, and four to the same dilution of the *C. albicans* antigen.<sup>2</sup> None, however, reacted to a 1-100 dilution of blastomycin, lot B-7. The remaining 5 were sacrificed on the 259th day. At this time none of these reacted to a skin-test dose of a 1-100 dilution of histoplasmin, lot H-15, blastomycin, lot B-7, or the autoclaved filtrate antigen prepared from *C. albicans*. None of these 13 animals showed any marked gross pathology at autopsy. Cultures from the spleens of each were negative for pathogenic fungi.

#### DISCUSSION

From the data presented above it would seem that guinea pigs are relatively resistant to infection with H. capsulatum when this fungus is inoculated intraperitoneally, and that, in the dosage range used, there was little correlation between the dosage employed for inoculation and the number which developed a generalized extensive infection. Only 3 of 80, or 3.8 percent, of the animals included in this study appeared to develop such an infection from an intraperitoneal inocu lation of relatively large doses of the living yeast phase from 5-day-old cultures incubated at 37°C. This finding is in general agreement with most of the reports on infection of these animals with this Reid et al. (5), for example, reported a generalized infection in fungus. one guinea pig inoculated with growth from a culture of the yeast Hansmann and Schencken (2) reported that guinea pigs phase. inoculated intraperitoneally with material from a biopsy of skin and lymph nodes from a human case of histoplasmosis, from which Histoplasma was subsequently isolated in culture, failed to show any evidence of infection several months after inoculation. Similarly. Parsons and Zarafonetis (8) failed to induce infection in guinea pigs with material from a biopsy from a human case.

Of the remaining 77 animals in the series reported above (table 1). 76 developed some degree of skin sensitivity. This is evident from the fact that all of these 76 reacted, at some time after inoculation,

<sup>&</sup>lt;sup>2</sup> These reactions are explained in Studies of Fungus Antigens, III. See p. 595.

to a skin-test dose of at least a 1-100 dilution of histoplasmin, lot H-15, whereas none of them had reacted to this dilution of this antigen prior to inoculation.

It has also been demonstrated that *Histoplasma* may be recovered from the spleens of apparently healthy guinea pigs inoculated with this fungus as long as 10 months previously although the animals showed no signs of gross pathology at autopsy. This is in agreement with a recent paper by Emmons et al. (26) in which was reported the isolation of *Histoplasma* from 1 mouse and 10 rats, none of which showed any gross lesions at autopsy. From these animals *Histoplasma* was isolated most frequently from the spleen and liver. Emmons (26) further reported that guinea pigs commonly recover from the acute phase of infection with *Histoplasma* and survive indefinitely and that it was possible to isolate *Histoplasma* regularly from experimentally infected guinea pigs kept in the laboratory under observation for over 2 years, even though there were no gross abnormalities observed at autopsy.

It would also seem that guinea pigs are relatively resistant to infection with *B. dermatitidis*, when this fungus is inoculated intraperitoneally, and that there is little correlation between the dosage employed and the number which develop a generalized infection. Only 17 of 82, or 20.7 percent, apparently developed such an infection from the intraperitoneal inoculation of large doses of the living yeast phase from a 7-day-old culture incubated at 37° C. Similar results have been reported by various investigators. Benham (15) reported that dogs and monkeys are very susceptible to infection with this fungus but that less extensive lesions develop in guinea pigs. DeMonbreun (16) found that guinea pigs inoculated with this fungus develop localized abscesses which soon healed following subcutaneous or intradermal inoculations. Others (9-14) have obtained variable results.

Although it would seem that guinea pigs are relatively resistant to an intraperitoneal inoculation of *B. dermatitidis*, a comparison of this group and the group inoculated with *Histoplasma* indicates that they are more susceptible to inoculation with this fungus than to inoculation with *Histoplasma*. For example, of 70 guinea pigs which received doses of *Blastomyces* comparable in volume of packed cells, to the 80 inoculated with *Histoplasma*, 16 of the 70 developed a generalized infection whereas only 3 of 80 of those inoculated with *Histoplasma* appeared to develop such an infection.

Of the remaining 65 guinea pigs inoculated with *Blastomyces*, 61 reacted, at some time after inoculation, to a skin-test dose of at least a 1-100 dilution of blastomycin, lot B-2 or B-7. None had reacted to this dilution of blastomycin prior to inoculation. The reason for the failure of the remaining four animals to become sensitized was not determined. It has also been demonstrated above that *Blastomyces* may be recovered from the spleens of apparently healthy guinea pigs which had been inoculated with this fungus as long as eleven months previously, and which showed no gross lesions at autopsy.

Of 35 guinea pigs similarly inoculated with large doses of Candida (Monilia) albicans none apparently developed more than a transient infection. This is in accord with the results obtained by Ninni and Fittipaldi (21) who reported that one-fifth of an agar slant culture of pathogenic monilias inoculated intraperitoneally failed to kill guinea pigs, and of Benham (20) and Nye et al (19). Benham reported that guinea pigs are less susceptible to infection with C. (M.) albicans than are rabbits. Nye et al. reported that of 38 guinea pigs inoculated intraperitoneally with  $250 \times 10^6$  organisms from 4-day broth cultures of Parasaccharomyces A. (pathogenic for rabbits) only one developed an extensive infection. This animal died on the fourth day after inoculation with a purulent peritonitis. Others (17, 18) have reported variable results.

Although none of the animals inoculated with C. albicans developed an apparently generalized infection, 33 of 35 were sensitized so that at 41 days after inoculation they reacted to a skin-test dose of at least a 1-100 dilution of an autoclaved filtrate antigen prepared from this fungus (25). This group of animals were similar to those inoculated with both *Histoplasma* and *Blastomyces* in that in the majority of the animals there were no demonstrable lesions at autopsy. However, they differed in that C. albicans was recovered in culture from the spleen of only one of 26 animals autopsied, even though all of the 26 died or were sacrificed not later than 76 days after inoculation.

Finally, it has been shown that none of these pathogenic fungi could be isolated from the spleens of 41 normal animals, 31 of which were kept under observation for a minimum of 182 days in the laboratory before autopsy. Sixteen of these normal guinea pigs were kept in the same room with the animals inoculated with *Histoplasma*, *Blastomyces*, and *C. albicans*. This would seem to indicate that these infections are not readily transmitted from one individual to another, and is in agreement with the report of Emmons et al. (26) that histoplasmosis was not transmitted from a naturally acquired infection in a dog to other dogs kept for months in the same cage with it. This failure to isolate a pathogenic fungus from these normal guinea pigs lends support to the conclusion that the cultures isolated from the inoculated animals were isolated as a result of the inoculation.

It should be noted that although there appeared to be little correlation between the size of the dosage used and the number of animals which developed extensive infections with any of the three fungi studied, the dosages employed covered only a five-to nine-fold range.

It is possible that had larger doses been used for inoculation, some correlation might have become apparent. It would also seem that the percentage of experimentally inoculated animals from which H. capsulatum and B. dermatitidis can be isolated decreases with the length of time after inoculation.

#### SUMMARY

A study has been made on the susceptibility of guinea pigs to intraperitoneal inoculations with the yeast phase of H. capsulatum, B. dermatitidis, and Candida (Monilia) albicans. With the dosages and strains of these fungi employed, it has been shown that:

1. Only 3 of 80 guinea pigs inoculated in this manner with large doses of the yeast phase of Histoplasma and 17 of 82 similarly inoculated with Blastomyces developed a generalized infection. Of 35 similarly inoculated with C. albicans, none developed such an infection.

2. There was no correlation between the size of the inoculating dose and the number of animals which developed generalized infection.

3. Relatively small doses of these fungi are as effective as larger ones in producing skin sensitization of these animals.

4. Both H. capsulatum and B. dermatitidis could be readily isolated from the spleens of apparently healthy guinea pigs which had been inoculated with variable doses of these fungi 9 to 10 months previously, even though there were no gross lesions apparent at autopsy. C. albicans could not be recovered from guinea pigs inoculated with this fungus 2 to 3 months previously.

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UNITED NATIONS WORLD HEALTH ORGANIZATION INTERIM COMMISSION

NATIONS UNIES ORGANISATION MONDIALE DE LA SANTE COMMISSION INTÉRIMAIRE

# **EXPERT COMMITTEE ON TUBERCULOSIS**

**Report of the First Session** 

#### Office International d'Hygiène Publique, Paris.

July 30-August 2, 1947

At the third session of the Interim Commission of the World Health Organization held in Geneva in April 1947, it was resolved to set up an Expert Committee on Tuberculosis. The chairman of the Interim Commission and the executive secretary agreed to appoint the following members of this committee, after approaching their respective Governments:

Dr. P. D'Arcy Hart, Medical Research Council, London.

Dr. Herman E. Hilleboe, United States Public Health Service,<sup>1</sup> Washington, D. C.

Appointed Commissioner of Health, New York State, July 1, 1947.

Dr. Johannes Holm, State Serum Institute, Copenhagen.

An invitation to the Government of the U. S. S. R. to suggest the name of a Russian member of the committee was sent. The attendance of an expert was arranged, but his sudden illness prevented his coming to Paris.

The Expert Committee on Tuberculosis appointed by the Interim Commission met in Paris from July 30 to August 2, 1947.

Dr. Holm was elected chairman. The Secretary to the Expert Committee, Dr. J. B. McDougall, was in attendance.

The following report of the Committee was accepted by the Interim Commission at its fifth session for submission to the World Health Assembly:

#### A. Introduction

It is recognized that tuberculosis is a world problem of great magnitude. The committee is fully in accord with the decision of the Interim Commission that tuberculosis, malaria, and venereal disease are infectious diseases deserving the highest priorities for its activities.

There can be no isolationism in the field of health. The fight against infectious disease is not a national or a racial problem; it is a task for the whole of humanity. No nation is safe if another nation is vanquished by disease. The fortunate and relatively healthy nations, inspired by intelligent self-interest and humane considerations, will necessarily have to come to the aid of stricken nations, and through money, professional personnel and equipment, distribute existing resources to the needy and suffering areas of the world.

Tuberculosis control work of an international scope must go forward if present suffering and disability are to be alleviated and future generations protected. The all-inclusive objective of any sound tuberculosis program is the prevention and eventual eradication of tuberculosis from the peoples of the world. Poverty, shortages of food and housing, and the lack of opportunity for gainful occupation, complicate the task enormously, and make it necessary for us to share and distribute our resources where they will do the most good in the shortest possible time.

#### **B.** Fields of Activity

There are five well-defined fields of activity in which we must work and direct our efforts on a planned basis if tuberculosis is to be systematically eliminated: (1) Prevention, (2) case finding, (3) isolation and medical care, (4) rehabilitation and after-care, (5) social and economic protection of afflicted families.

No one of these activities can be effective alone. They all must operate together and in proper sequence. C. Techniques for Control

It is not enough merely to recognize and describe the objectives of a tuberculosis control program. It is also necessary to have clearly defined and firmly established techniques for the achievement of those objectives. The following recommendations include 11 principal techniques for tuberculosis control, which may be used singly, in groups, and finally all together, if the World Health Organization program is to be comprehensive and wholly effective:

1. The first technique is the determination of the extent of the problem of tuberculosis in each country, the present means and facilities of its disposal, the manner in which these facilities are being used to tackle the problem, and the additional facilities needed. Countries with little information available should be encouraged to record at least simple basic data. It is recommended that schedules (now being prepared by the Expert Committee) be filled in by the experts of the Secretariat, who, on request, actually go into the countries. These schedules should be kept up to date at regular intervals.

2. One of the most important techniques that works toward the realization of the objectives of tuberculosis control is the recruitment and training of professional personnel. In most countries there is at present an insufficient number of well-trained workers in this It is recommended that traveling fellowships be awarded to field. countries most in need, principally to train medical officers. There are four special fields in which trained medical officers are essential for every country-administration, epidemiology, laboratory work, and clinical work. It is estimated that one thousand such fellowships could be granted by the World Health Organization with good effect within the next few years. It would appear wise to recommend that only 50 of these be provided in the first year in order to get the program under way. To operate the scheme, the Secretariat should survey the teaching facilities throughout the world and designate acceptable teaching centers. At the same time, the Secretariat should ascertain the needs of countries for trained personnel, so that after such consultation, promising medical officers, especially those who show potentialities of leadership, can be selected for fellowships. Countries where the needs are greatest should be chosen first.

It is also recommended that consultation services of short duration be provided to countries, especially those with teaching centers, in order to make available the latest knowledge and viewpoints of outstanding specialists.

3. The provision of physical facilities, supplies and equipment for all phases of prevention, diagnosis and treatment is second in importance only to the provision for personnel. It is recommended that the World Health Organization should be prepared to give expert advice to the various countries requesting such information, on the number, type and location of facilities needed, and on the best means of financing the construction and maintenance of these facilities, drawing on the successful experience of other countries. Recommendations should be given only if they are to form a part of a long-range, comprehensive plan for the nation and its administrative subdivisions.

4. Heath education is recognized as an essential tool in tuberculosis control. The general public must know the seriousness of the disease and its cost in human misery and money before it will accept its responsibility to support the work financially. It is recommended that the World Health Organization should encourage national and international voluntary organizations to take the major responsibilities for informing the public and gaining their support.

To keep the medical profession informed on advances in tuberculosis, it is recommended that the World Health Organization prepare from time to time material on recent developments of special importance, and that the circulation of specialist literature be provided. The World Health Organization should encourage national and international professional organizations to develop the distribution of tuberculosis literature.

5. The best way to get a new program started, or to improve a poor one, in any country is by means of field services for the purpose of demonstrating practical activities in one or more of the special fields of administration, epidemiology, laboratory work and clinical work. Well-trained teams, even with limited supplies and equipment, can demonstrate what should be done to control tuberculosis and how to do it. It is recommended that the World Health Organization provide demonstration teams. The size of the team and the length of its stay would vary with needs, but in any event should be kept to a minimum. Certain supplies and equipment will be necessary for these teams. An essential condition for the demonstration will be that the country agrees beforehand to take over the project as soon as sufficient of its personnel has been trained to do so. When taken over, these field demonstrations should become national training centers, and in some cases should be designated also for international use of traveling fellows. For example, an international training center might be established in India for training workers from various parts of Asia, where the problems to be solved are similar in nature. Areas where it is proposed to set up international training centers should have first call on demonstrations, if such are necessary.

The persons charged with these demonstrations could be either regular staff members of the World Health Organization or professional personnel with temporary appointments. The person to take charge of the work, when it is taken over by the local group, could well be one of the persons who had received a traveling fellowship from the World Health Organization. 6. While it is recognized that present budgetary limitations do not permit grants of money for tuberculosis control to nations at this time, it is recommended that in future such grants should be made, in order to help nations unable to help themselves. Such grants should be made, however, only if great need is demonstrated, a complete plan submitted to show the joint use of national funds and those from the World Health Organization, and to show that the funds are used solely for tuberculosis control and that the World Health Organization's contributions are not used to replace local funds.

7. The best contribution that can be made by the World Health Organization in tuberculosis research would appear to be in developing and recommending uniform procedures. Special problems would require from time to time the services of small subcommittees of experts in highly specialized fields. Where possible, members of other expert committees of the World Health Organization should be used for this purpose. Whenever a problem comes up for the Expert Committee on Tuberculosis which involves the responsibility shared by another expert committee, one of the members of the second committee should be asked to take part in the deliberation. For example, when the Expert Committee on Tuberculosis considers the problem of tuberculin and tuberculin testing a member of the Expert Committee on Biological Standardization should be asked to participate, and vice versa. It is recommended that the Committee on International Classification of Morbidity and Mortality consult with the Expert Committee on Tuberculosis before final action is taken on classification of tuberculosis. There are several suggestions our Committee wishes to make on the first draft.

The principal problems which need action to establish uniform procedures are as follows:

- (1) Tuberculin and tuberculin testing.
- (2) Preparation and clinical use of BCG.
- (3) Classification of tuberculosis.
- (4) X-ray interpretation and mass radiography.
- (5) Laboratory diagnosis of tubercle bacilli.
- (6) Evaluation of new chemotherapeutic agents such as streptomycin.

Even during the period of the Interim Commission it is recommended that action be taken on (1), (2), and (6). Thus, it is urged that subcommittees be appointed on tuberculin and tuberculintesting, and on BCG, and that a conference be called early in 1948 on the use and value of streptomycin. This conference should bring together those who have been actively engaged in research on this drug.

8. It is recognized that several other international organizations have been carrying on activities and have contributed in many ways to tuberculosis control. It is recommended that the World Health Organization should take full advantage of these services and should establish working relationships with all groups genuinely interested in tuberculosis control. Such a cooperative effort would help to avoid duplication and would produce harmonious agreement in this collective enterprise. The Committee has been informed that the International Union Against Tuberculosis is about to establish a branch office in Geneva. It is urged that liaison be established at once between World Health Organization and the Union in order that their several activities go forward in unison. Cooperation with all private and official agencies, even those only partially engaged in tuberculosis control activities, should be extended at every opportunity. Furthermore, this Committee would welcome the opportunity to be consulted by other committees of the World Health Organization and United Nations whenever questions and problems involving tuberculosis arise.

9. Tuberculous cattle still form an important source of tuberculosis among human beings throughout the world. Infected milk is not the only source of spread, for it has recently been demonstrated that farm workers may contract bovine tuberculosis through direct contact with diseased cattle. It is recommended that the World Health Organization use its influence to encourage nations whose herds have high infection rates to take active steps to eradicate tuberculosis among cattle as quickly as possible.

10. It is recommended that the World Health Organization be prepared to give expert advice to national governments and health departments on sound laws and regulations pertaining to human and bovine tuberculosis. This committee proposes to study both the legal and epidemiological aspects of the problem of tuberculosis among migrants. This would form the basis of recommendations designed to prevent the spread of this disease from one country to another.

11. Modern public health practice demands that public health programs have review and evaluation at regular intervals, in order that any ineffective techniques may be discarded and that more modern ones be added as new knowledge is gained. This is particularly true of a new program. Accordingly, it is recommended that the World Health Organization make preparation for review and evaluation of its program at yearly intervals with the advice and counsel of the Expert Committee.

# D. Emergency Measures

Because of the epidemic proportions of tuberculosis in many

countries, certain emergency measures, which require relatively small expenditures, should be applied at once. It is recommended that small demonstration teams be sent into such countries, even for short periods, to carry on intensive programs of BCG vaccination similar to those at present in operation under the Danish Red Cross in several European countries which have appealed for aid.

The Committee wishes to emphasize that this measure is clearly of an emergency nature. It is hoped that the initiation and successful operation will encourage the local groups to develop and carry on a more comprehensive program.

# E. Tuberculosis Secretariat and Finance

In order to accomplish the above proposals, it is recommended that a permanent Tuberculosis Control Office be established within the World Health Organization.

Even though no funds are available yet for all these proposals, which the Committee hopes the World Health Organization will in due course accept, it is recommended that some funds be provided immediately by the Interim Commission for the emergency measure under heading D, namely, to start in certain countries, as soon as possible, programs for BCG vaccination and for identifying infectious cases.

It is further recommended that the Interim Commission provide immediate funds for the expenses of the subcommittee meetings (on tuberculin and tuberculin testing, and on BCG) and for the conference on streptomycin, referred to under heading C7.

# F. Dissemination of Information

If the World Health Organization Interim Commission approves of the proposals of this Committee, it is recommended that there should be wide dissemination of information concerning the services the World Health Organization can provide.

#### February 29-March 27, 1948

The accompanying table summarizes the incidence of nine important communicable diseases, based on weekly telegraphic reports from State health departments. The reports from each State for each week are published in PUBLIC HEALTH REPORTS under the section "Incidence of Disease." The table gives the number of cases of these diseases for the 4 weeks ended March 27, 1948, the number reported for the corresponding period in 1947, and the median number for the years 1943-47.

#### DISEASES ABOVE MEDIAN INCIDENCE

Influenza.—The number of cases of influenza dropped from 45,536 during the preceding 4 weeks to 25,459 during the 4 weeks ended March 27. Of the total cases, Texas reported 11,620, South Carolina 2,825, Virginia 2,213, Alabama 1,512, California, 1,447, Arkansas 985, and Arizona 834; 84 percent of the cases occurred in those 7 States. For the country as a whole the incidence was only about 20 percent of the 1947 incidence for the corresponding weeks, but it was 1.4 times the median for the preceding 5 years. The recent outbreak of this disease that has been confined to States in the Southern and Western sections followed the usual pattern of an influenza epidemic and the peak apparently was reached during the month of February. The 1947 epidemic did not begin until late in the season and the peak was not reached until in March, or during the 4 weeks corresponding to the period under consideration.

#### DISEASES BELOW MEDIAN INCIDENCE

Diphtheria.—The incidence of diphtheria continued to decline. For the 4 weeks ended March 27 there were 732 cases reported as compared with a median of 1,067 cases for the corresponding period in the preceding 5 years (1943–47). In the South Atlantic and Mountain sections the incidence was somewhat above normal, but in all other sections the numbers of cases were relatively low. For the country as a whole the current incidence was the lowest in the 20 years for which data are available in this form.

Measles.—For the current 4-week period there were 83,160 cases of measles reported. The number was more than 3 times that reported for the corresponding period in 1947, but it was slightly below the median for the preceding 5 years. The disease was most prevalent in the East North Central and West South Central sections; in the former section the number of cases (29,760) was 2.1 times the 1943–47 median and in the latter section the number of cases (8,364) was 1.5 times the normal seasonal median. A slight increase was reported from the Pacific section but in the other 6 sections the incidence was considerably below the expected seasonal incidence.

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Meningococcus meningitis.—The incidence of meningococcus meningitis (352 cases) was the lowest reported for this period since 1942 when 329 cases were reported for the corresponding 4 weeks. The New England, South Atlantic, and Pacific sections reported more cases than occurred during the same weeks in 1947, but the incidence in all sections was considerably below the median for the preceding 5 years. However, since the 1943–47 median fell within an epidemic period of this disease a better comparison is with the average incidence for nonepidemic years which is approximately 300 cases.

Poliomyelitis.—The number of cases (110) of poliomyelitis reported during the 4 weeks ended March 27 compared very favorably with the median for the preceding 5 years (112 cases). The median for this disease also falls within an epidemic period and, while the current incidence is about the same as the median, the number of cases is still higher than the average of 80 cases for nonepidemic years. While the numbers of cases were not large in the West North Central and Mountain sections (16 and 15, respectively) they were more than twice the medians for those sections. Minor increases were reported from 3 other sections and in the other 4 sections the incidence was lower than the median.

Scarlet fever.—The incidence of scarlet fever continued at a relatively low level, the current incidence (10,546 cases) being about 85 percent of the 1947 incidence for the corresponding period and 61 percent of the median for the preceding 5 years. While each section of the country has shared in the favorable situation for this disease that now exists, the greatest declines from the normal incidence during this particular 4-week period occurred in the New England, South Atlantic, and Mountain sections. Since 1944 this disease has been on the downward swing of a long-term cycle and for the current 4-week period the incidence was the lowest on record.

Smallpox.—Eight cases of smallpox were reported during the 4 weeks ended March 27, as compared with 19 in 1947 and a median for the preceding 5 years of 39 cases. Three cases occurred in Kansas and one each in Minnesota, North Dakota, North Carolina, Georgia, and Oklahoma. The number of cases was the lowest on record for these same weeks.

Typhoid and paratyphoid fever.—For these diseases the incidence (166 cases) during the 4 weeks ended March 27 was the lowest for a corresponding period in the 20 years for which these data are available. A few more cases than might be expected occurred in the West North Central and West South Central sections, but in other sections the incidence was about equal to or lower than the seasonal expectancy. The greatest declines were reported from the North Atlantic and East North Central sections.

Whooping cough.—The incidence of this disease was also relatively low, the 9,485 cases reported being less than 90 percent of the median for the preceding 5 years. Of the 9 geographic sections, 4 reported an increase over the normal seasonal median and in 5 sections the incidence was lower than the expectancy. The greatest increase in cases was reported from the West South Central sections and the greatest decline occurred in the Middle Atlantic section.

#### MORTALITY, ALL CAUSES

For the 4 weeks ended March 27 there were 39,148 deaths from all causes reported to the National Office of Vital Statistics by 93 large cities. The median number of deaths for the corresponding period in the years 1945–47 was 38,603. The number of deaths was higher than the preceding 3-year median in each week of the current 4 weeks except the first one and for the 4 weeks the number was 1.4 percent above the median.

Number of reported cases of 9 communicable diseases in the United States during the 4-week period February 29-March 27, 1948, the number for the corresponding period in 1947, and the median number of cases reported for the corresponding period, 1943-47

					-				
Division	Cur- rent period	1947	5-year median	Cur- rent period	1947	5-year median	Cur- rent period	1947	5-year median
	1	Diphther	ia	1	Influenza	1		Measles	
United States New England Bast North Central West North Central South Atlantic East South Central West South Central Mountain Pacific	732 24 77 99 76 152 67 88 92 57	1,068 85 131 145 111 138 121 164 55 118	1,067 40 131 142 111 138 108 204 52 118	25, 459 37 166 312 246 5, 574 2, 111 13, 462 1, 472 2, 079	125, 077 52 90 2, 620 17, 063 15, 939 3, 933 76, 571 7, 751 1, 058	17, 615 83 90 710 183 4, 540 1, 391 6, 921 1, 144 553	83, 160 3, 773 16, 981 29, 760 5, 648 4, 488 2, 098 8, 364 3, 397 8, 651	27,064 6,787 4,608 4,568 639 4,526 1,195 2,161 1,398 1,182	87, 789 6, 787 21, 783 13, 993 7, 371 5, 222 3, 863 5, 634 4, 969 8, 469
	Me	ningococ neningiti	cus s	Po	oliomyeli	tis	S	carlet fev	er
United States New England East North Central West North Central South Atlantic East South Central West South Central Mountain Pacifie	352 18 58 51 22 52 39 51 7 54	372 11 70 52 42 44 39 64 8 42	1, 018 45 239 199 70 158 93 101 13 111	110 1 14 12 16 13 9 11 15 19	156 6 12 18 16 14 12 22 7 49	112 6 12. 9 7 14 8 17 7 23	10, 546 924 2, 964 3, 480 834 671 289 274 326 784	12, 272 879 3, 112 4, 085 1, 082 818 553 313 498 932	16, 287 2, 361 4, 844 4, 413 1, 718 1, 522 553 465 848 1, 054
	8	mallpox		Ty para	phoid ar typhoid i	nd 'ever	Who	oping co	ough
United States New England Fast North Central West North Central South Atlantic East South Central West South Central Mountain Pacific	8 0 0 5 2 0 1 0 0	19 0 5 8 1 1 2 2 0	39 0 0 6 9 2 5 11 2 2	166 6 21 15 14 37 15 37 8 13	189 15 20 29 10 30 15 30 8 32	198 13 33 29 10 38 16 34 9 20	9, 485 780 1, 369 1, 661 464 1, 232 404 2, 172 645 758	10, 709 1, 002 1, 984 2, 451 345 1, 384 427 2, 006 237 873	10, 667 1, 168 1, 984 1, 569 377 1, 521 435 1, 196 399 873

<sup>1</sup>New York, North Carolina, and Pennsylvania excluded; New York City and Philadelphia included.

# **INCIDENCE 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

#### **REPORTS FROM STATES FOR WEEK ENDED APRIL 17, 1948**

#### Summary

A total of 32 cases of poliomyelitis (the same number as for the corresponding week last year) was reported for the current week, as compared with 37 last week and a 5-year (1943-47) median of 28. Only 2 States reported more than 2 cases—Texas 6 (last week 9), and Michigan 3 (last week 2). The total reported for the 4 weeks since the average date of seasonal low incidence is 120 cases, as compared with 124 for the same period in 1945, the highest number reported for a corresponding period of the past 5 years, 68 in 1944 the lowest, and a 5-year median for the period of 108 cases, reported in 1946.

For the current week, 25,616 cases of measles was reported, as compared with 25,842 last week (the highest incidence so far this year) and a 5-year median of 27,161. In 1946 the peak of incidence was reached in the week ended April 13 with a reported total of 40,746 cases. The total for the year to date is 250,733, as compared with 82,918 for the same period last year and 262,946 for the 5-year median.

Of the total of 2,044 reported cases of influenza (last week 2,702, corresponding week last year 23,536, 5-year median 1,917), 1,514 cases were reported in 4 States—Texas 879, South Carolina 283, Virginia 246, and Oklahoma 106.

Four cases of Rocky Mountain spotted fever were reported, 1 each in New Jersey, Wyoming, Colorado, and Oregon. New York reported 2 cases of anthrax, and New Jersey 1 case. One case of smallpox was reported, in Nebraska, and 1 case of psittacosis, in Michigan.

During the week 8,942 deaths from all causes were recorded in 92 large cities in the United States, as compared with 9,601 last week, 9,670 and 9,051 respectively, for the corresponding weeks of 1947 and 1946, and a 3-year (1945–47) median of 9,078. The total for the year to date is 160,698, as compared with 160,962 for the corresponding period last year. Infant deaths in the same cities totaled 655, as compared with 707 last week and a 3-year median of 631. The cumulative total is 11,006, as compared with 12,738 for the same period in 1947.

# Telegraphic morbidity reports from State health officers for the week ended Apr. 17. 1948, and comparison with corresponding week of 1947 and 5-year median

In these tables a zero indicates a definite report, while leaders imply that, although none was reported, cases may have occurred.

	Г	oiphthe	eria		Influer	128		Measl	es	M me	lening ningoc	itis, occus
Division and State	Wend	'eek led—	Me-	W en	<sup>7</sup> eek ded—	Me-	v en	Veek ded—	Me-	W end	'eek led—	Me-
	Apr. 17, 1948	Apr. 12, 1947	1943- 47	Apr. 17, 1948	Apr. 12, 1947	- 01an 1943- 47	Apr. 17, 1948	Apr. 12, 1947	- dian 1943- 47	A pr. 17, 1948	A pr. 12, 1947	1943- 47
NEW ENGLAND Maine New Hampshire Vermont Massachusetts Rhode Island Connecticut MIDDLE ATLANTIC					. 1	4 8 5 - 9	$\begin{array}{c}2\\0&1\\0\\0&1,37\\1\\3&14\end{array}$	6 250 7 28 3 360 9 200 6 86	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			0 0 1 0 5 1 3
New York New Jersey Pennsylvania	23	12 3 17	14 6 12	1 (2)		8 1 6 4 2	2 2, 25 7 1, 16 2 1, 58	2 533 5 451 7 283	2 2, 313 1, 831 8 898			17 10 13
Ohio Indiana Illinois Michigan <sup>3</sup> Wisconsin	5 10 5 1	10 4 4 4 4	13 3 15 8 3	1 2 1	3 1 1 1 1 29	2 1 7 1 6 10 1 3	4 1,099 7 663 6 1,804 1 1,479 6 1,891	8 582 8 120 5 92 9 69 1 326	2 916 224 2 1, 281 9 812 6 2, 277		13 0 16 7 2	13 5 16 7 4
Winnesota Iowa Missouri North Dakota South Dakota Nebraska Kansas	2 0 2 0 1 1	2 0 25 0 1 2 4	2 4 4 0 1 1 3	17	1, 57		2 462 359 3 550 2 16 45 2 244 5 88		96 181 73 8 38 166 623	0 1 3 0 0 0 2	4 2 3 1 0 1 0	4 2 5 0 0 1 3
SOUTH ATLANTIC Delaware. Mary land 3. District of Columbia. Virginia. West Virginia. North Carolina. South Carolina. Georgia. Florida.	0 7 0 1 2 6 2 4 5	0 14 0 4 6 9 5 2	0 6 0 4 6 5 1	5 246 11 283 19 35	11 4, 673 935 2, 650 485	( 1 274 12 292 43	42 145 169 145 324 160 77 39 960	23 44 288 221 210 155 127	12 168 83 488 116 221 251 216 127	0 1 0 4 0 2 2 0	1 5 2 3 3 5 0 0	1 10 2 8 3 8 1 4 2
EAST SOUTH CENTRAL Kentuck y Tennessee Alabama Mississippi 3	2 4 2 3	8 5 1 3	5 5 7 5	5 44 95 16	741 727 118	4 43 87	179 212 61 56	127 3 96 188 16	81 286 235	3 1 0 1	3 3 5 1	5 7 3 5 3
WEST SOUTH CENTRAL Arkansas Louisiana Oklahoma. Texas	0 3 4 12	3 2 3 18	2 2 3 29	73 5 106 879	1, 255 300 3, 347 3, 896	35 16 79 778	82 74 58 2, 927	113 26 11 374	193 84 51 1, 297	1 1 1 1	2 0 1 10	2 2 2 10
MOUNTAIN Montana Idaho Vyoming Colorado New Mexico Arizona Utah <sup>3</sup> Nevada	3 0 3 4 2 0 0	0 0 9 0 8 1 0	1 0 4 0 2 0 0	2 21 1 22 8 36 1	571 63 641 7 165 98	4 25 2 78 3	28 121 . 116 641 35 224 205	162 12 19 93 77 81 13	124 67 60 225 24 81 164 11	0 0 1 0 0 0 0	0 0 0 0 0 0 0 0	0 0 1 0 0 1 0 0
PACIFIC Washington Oregon California Total	0 0 7 116	2 1 20 230	5 7 20 244	4 34 53 2.044	480 85 79 23, 536	3 13 29 1, 917	761 4 87 3, 258 25, 616	28 27 178 7, 350	133 134 1, 536 27, 161	1 0 3 49	2 0 10 122	$     \begin{array}{r}       3 \\       1 \\       22 \\       194     \end{array} $
15 weeks	2, 976	4, 231	4, 231	126,054	266, 137	179, 321	250,733	82, 918	262, 946	1, 249	1,322	3, 617
Seasonal low week 5	(27th)	July	5-11	(30th) J	uly 26-	Aug. 1	(35th)	Aug. 30-	Sept. 5	(37th)	Sept.	3-19
Total since low	9.334	1. 797	2.888	169.612	299 112	299.112	4285.670	105 805	300 950	2 031	2 204	6 069

<sup>1</sup> New York City only.
 <sup>2</sup> Philadelphia only.
 <sup>3</sup> Period ended earlier than Saturday.
 <sup>4</sup> 69 additional cases reported in Arizona for week ended April 3—included in cumulative totals only.
 <sup>5</sup> Dates between which the approximate low week ends. The specific date will vary from year to year.

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Telegraphic morbidity reports from State health officers for the week ended Apr. 17, 1948, and comparison with corresponding week of 1947 and 5-year median—Con. tinued

	Po	liomye	litis	s	carlet fe	ver	s	mallpo	x	Typl typ	noid an phoid f	d para-
Division and State	W end	'eek led—	Me-	Wen	eek ded	Me-	W end	eek ed—	Me-	w end	eek ed-	Me-
	A pr. 17, 1948	A pr. 12, 1947	1943- 47	A pr. 17, 1948	Apr. 12, 1947	dian 1943 47	Apr. 17, 1948	Apr. 12, 1947	1943- 47	Apr. 17, 1948	A pr. 12, 1947	dian 1943- 47
NEW ENGLAND	]											
Maine New Hampshire			0	•	5 21	34	0	0	0	4	0	0
Vermont	ŏ	ŏŏ	ŏ		10	10	ŏ	ŏ	ŏ	ŏ	ŏ	
Massachusetts		. 0	0	182	115	366	0	0	0	5	6	i
Connecticut	ŏ	ŏ	ŏ	18	42	71	ŏ	ŏ	ŏ	l d	ŏ	Ö
MIDDLE ATLANTIC												
New York	2	7	4	• 269 67	343	535	0	7	0		0	0
Pennsylvania	Ô	ő	i	308	216	405	ŏ	ŏ	ŏ	3	4	4
EAST NORTH CENTRAL												
Ohio Indiana	1	0	0	311	358	358	0	0	1		2	1
Illinois	l ō	i i	l i	107	103	203	ŏ	ó	1	1	Ó	2
Michigan <sup>3</sup>	3	1	1	123	128	160	0	0	0	2	2	2
WEST NORTH CENTRAL	ľ		Ů		00	100	Ň	v	v		-	U
Minnesota	2	0	0	29	48	71	0	0	0	0	0	0
Iowa Missouri		0	0	26 • 33	40	57	0	0	0	0		0
North Dakota	ő	ŏ	ŏ	3	7	8	ŏ	ŏ	ŏ	l i	ŏ	ŏ
South Dakota		0	0	1	10	19	0	0 0	0	0	0	0
Kansas	ő	ŏ	ŏ	25	43	72	Ō	ŏ	ŏ	1	ŏ	ŏ
SOUTH ATLANTIC					_							
Delaware Maryland 3		0	0	3 1 34	7	149	0	0	0	0 3	0	0
District of Columbia	ŏ	ŏ	ŏ	8	8	24	ŏ	ŏ	ŏ	1	ŏ	ŏ
Virginia West Virginia	0	0	0	21	32	82 20	0	0	0	8	0	1
North Carolina	2	ŏ	ŏ	19	20	39	ŏ	ŏ	ŏ	1	ŏ	ŏ
South Carolina	0	0	0	2	2	3	0	0	0	0	0	0
Florida	1	2	1	6	13	10	ŏ	ŏ	ŏ	2	1	i
EAST SOUTH CENTRAL												
Kentucky Tennessee	0	3	0	10	26 42	38	0	0	0	1	2	2
Alabama	ŏ	Ô	ĭ	6	6	16	ŏ	ŏ	ŏ	ĩ	ĕ	Ō
Mississippi <sup>3</sup>	0	1	1	2	4	10	0	1	0	1	0	0
Arkansas	0	0	0	4	5	6	0	0	0	2	0	0
Louisiana	Ŏ	Ŏ	Ŏ	4	4	7	Ŏ	ŏ	Ŏ	2	4	4
Texas	6	2	3	29	31	16 63	0	0	1	5	1	7
MOUNTAIN		-									_	
Montana	0	0	0	22	3	15	0	0	0	0	0	0
Wyoming	Ó	0	Ő	2	2	28	0	Ő	ő	0	Ŏ	ŏ
Colorado	0	0	0	15	43	45	0	0	0	0	2	1
Arizona	0	0	0	46	11	11	0	Ő	0	0	0	2
Utah <sup>3</sup>	0	0	0	16	15	30	0	0	0	0	0	0
PACIFIC	U	v	0	U	U	0	0	0	U	"	U	U
Washington	2	1	1	53	28	44	o	0	0	0	0	0
Oregon	1	0	Q	12	47	41	0	0	0	0	1	1 2
Total				2 099	2 381	4 483						53
15 weeks	469	721	521	34, 960	40, 604	59, 767	37	77	160	00	641	802
Seasonal low week *	(11th)	Mar.	15-21	(32nd	i) Aug.	9-15	(35th	) Aug. ept. 5	30-	(11th)	Mar.	5-21
Total since low	120	109	108	57, 508	67, 290	98, 088	58	131	243	216	156	210

Period ended earlier than Saturday.
 Dates between which the approximate low week ends. The specific date will vary from year to year.
 Including cases reported as streptococcal sore throat.
 Including paratyphoid fever reported separately, as follows: Massachusetts 4 (salmonella infection), Virginia 1, Tennessee 1, California 1.

Telegraphic morbidity reports from State health officers for the week ended Apr. 17, 1948, and comparison with corresponding week of 1947 and 5-year median—Continued

	_			_		_					
	Wł	nooping	cough			Wee	k ende	d Apr. 1	7, 1948		
	Week	ended-	- Me-	1	Dysent	ery	En-	Rocky		Ţy-	Un-
Division and State	Am	Ant	dian			I Un.	- ceph-	Mt.	Tula	phus	du
	17,	12,	1943-	Ame	- Bacil	speci	infec-	ted	remis	en-	' lant
	1948	1947	4/	DIC	lary	fied	tious	fever		demic	, lever
NEW ENGLAND											
Maine	1	1 1	9 19		3	9	.		.		
New Hampshire		1				-		.	.		
Vermont	4	7 12	4 124			i	1				1 1
Rhode Island		i -	5 18								
Connecticut	2	5 3	6 36	6 I	l	-	. 1				2
MIDDLE ATLANTIC					1.						
New York			5 163	10		3					
Pennsylvania	6	2 16	3 161	1							\$ 2
EAST NORTH CENTRAL	1										1
Ohio	7	4 144	133	1							7
Indiana		5 48	3 35								2
Michigan <sup>3</sup>	8	5 148	8 93	14		/					
Wisconsin	110	0 127	104						1		12
WEST NORTH CENTRAL											1
Minnesota	20	5 2	10	2							4
10Wa Missouri	30	1 20	1 11								{
North Dakota		j	2	1							
South Dakota			1								
Kansas	4	5 18	28						1		10
SOUTH ATLANTIC		1				1					
Delaware		. 3	1								
Maryland 8	20	58	58			2					2
Virginia	36	84	84	1		48					
West Virginia	16	10	26								
North Carolina	99		94	;			;		1	2	
Georgia	18	30	30	i	1		1		3	1	3
Florida.	28	48	24	4							
EAST SOUTH CENTRAL											
Kentucky	7	9	34								
Alabama	42	25	29	1		1				i	1
Mississippi <sup>3</sup>		5		î	1						
WEST SOUTH CENTRAL										1	
Arkansas	23	17	11	16		2			2		2
Oklahoma	39	13	3 10	2					4		
Texas	502	583	351	14	402	33				2	8
MOUNTAIN				1						1	
Montana	6	1	2								
Wyoming	6	10	62								
Colorado	56	33	33					i			7
New Mexico	21	21	7			2					
Utah I	68 18	12	18			0					, r
Nevada.											
PACIFIC											
Washington	33	18	27	1		2		<u>-</u>	-		1
California	23	10	18	9 A				1	-		3
Total	9 140		- 520	100	461				19		107
10081	4, 149			100	107			<del></del>	i:		
Median. 1943-47	2, 528			<del>5</del> 2 36	261	74	8	2	14	30 36	100 29
5 weeks: 1948	32, 906			997	3, 977	2, 852	129	10	266	206	1, 369
1947	38, 015			697	4,612	3, 171	101	13	525	614	1, 564
**************************************	JU. 02/	· · · · · · · · · · · · · · · · · · ·	'	441'	2,404	1,02/1	119	<b>'</b> 0'	401	092	1,401

<sup>3</sup> Period ended earlier than Saturday.
 <sup>9</sup> 9 cases undulant fever reported in February and March in error; deducted from cumulative totals. Alaska: Chickenpox 3, measles 1, influenza 2, mumps 1, pneumonia 2, whooping cough 25. Territory of Hawaii: Rabies 0, measles 5, scarlet fever 3, typhus fever (endemic) 2, whooping cough 44. Anthraz: New York 2, New Jersey 1. Leprosy: Florida 2. Prittacosis: Michigan 1.
 \* 3-year median, 1945-47.

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#### **WEEKLY REPORTS FROM CITIES\***

City reports for week ended Apr. 10, 1948

This table lists the reports from 89 cities of more than 10,000 population distributed throughout the United States, and represents a cross section of the current urban incidence of the diseases included in the table.

	cases	s, in-	Influ	ienza	se	me- cus,	nia	litis	9 V B L	ses	and hoid	ough
Division, State, and City	Diphtheria	Encephaliti fectious, ce	Cases	Deaths	Measles case	Meningitis, ningococ cases	P n e u m o deaths	Poliomye cases	Scarlet fe cases	Smallpox ca	Typhoid paratypi fever cases	Whooping c cases
NEW ENGLAND												
Maine:												
New Hampshire:	Ů	0		0	2	0		0	3	0	0	
Concord Massachusetts:	0	0		0	3	0	2	0	1	0	0	
Boston.	1	0		0	493	0	9	0	55	0	0	9
Springfield	Ŏ	Ő		0 0	1	0	Ō	Ő	3	ŏ	0 0	3
Worcester Rhode Island:	0	0		0		0	14	0	11	0	0	2
Providence	0	0	2	1	1	0	3	0	4	0	0	
Bridgeport	0	0		0		0	0	0	2	0	0	
New Haven	ŏ	ŏ		ŏ	2	ŏ	3	ŏ	$\frac{2}{2}$	ŏ	ŏ	3
MIDDLE ATLANTIC												
New York: Buffalo	0	0		0	13	1	1	0	7	0		5
New York	8	Ö	4	ĩ	1, 544	5	79	Ő	56	Ŏ	Ŏ	21
Syracuse	ŏ	ŏ		ő	3 3	0	3	ŏ	5	ŏ	0	6
New Jersey: Camden	1	0		0	14	0	0	0	1	0	0	
Newark	0	0	1	1	167	0	0	0	5	0	0	
Pennsylvania:	â				700							
Pittsburgh	ő	ŏ	1	1	103	1	9	1	26	ő	Ö	19
Reading	0	0		0	9	0	3	0	14	0	0	3
Ohio												
Cincinnati	1	0	;-	1	87	2	6	0	11	0	0	3
Columbus	ŏ	ŏ	1	ō	57	ō	2	ŏ	6	ŏ	ŏ	13
Indiana: Fort Wavne	0	0		0	23	0	2	0	2	0	0	
Indianapolis	1	0		Ő	179	0	2	Ó	7	0	Ő	12
Terre Haute	ŏ	ŏ		ŏ		ŏ	2	ŏ	ő	ŏ	ŏ	1
Chicago	1	0		0	977	3	24	0	48	0	0	11
Springfield Michigan:	0	0		0	12	0	3	0	1	0	0	••••• <del>•</del>
Detroit	2	0		0	298	1	8	0	49	8	0	19
Grand Rapids	. Ŏ	Ŏ		ŏ	57	ŏ	$\hat{2}$	ŏ	i	ŏ	ŏ	2
Kenosha	0	0		0	78	0	0	0	0	0	0	
Milwaukee Racine	0	0		0	48 111	0	3	0	18 3	0	0	2 9
Superior	2	Ō		Ō	188	Ō	Ō	Ó	Ō	Ó	Ō	1
WEST NORTH CENTRAL						-						
Duluth	0	0		0	329	0	0	0	4	o	<u>o</u> ].	;
Minneapolis St. Paul	0	0		0	37 67	1	24	0	9	0	0	. 1
Missouri: Kansas City	0	0	7	0	38	1	9	0	1	0	1	10
St. Joseph	ŏ	ŏ.	····;-	ŏ	320	Ô	0	ŏ	1	ŏ	Õ.	12

\* In some instances the figures include nonresident cases.

City	reports	for	week	ended	l Apr.	. 10,	, 1948—0	Continued
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and the second												
	CISCS	s, in- ases	Influ	ienza	. sa	me-	nia	litis	ever	ses	-and hoid-	ough
Division, State, and city	phtheria	icephaliti ectious, c	Seg	aths	easles cas	eningitis, 1 ingococ ases	n e u m o deaths	oliomye cases	arlet-f	allpox ca	yphoid oaratyp ever case	hooping o
	Ā	E C	ల్	Å	ž	X"°	<u>6</u>	P	s	Sn	H	X
west NORTH CENTRAL- continued												
Nebraska: Omaha	0	0		0	95	0	4	0	1	0	0	
Kansas: Topeka	0	0		0	15	0	1	0	0	0	0	2
Wichita	0	0		0	6	0	4	0	2	0	0	2
SOUTH ATLANTIC												
Wilmington	0	0		0	30	0	1	0	2	0	0	
Maryland: Baltimore	2	0	1	1	56	1	13	0	9	0	0	7
Cumberland	01	0		0		0	0 0	0 0	0 0	0	10	
District of Columbia: Washington	0	0		0	123	2	5	0	5	0	0	5
Virginia:	0	0		0		0	0	0	0	0	0	3
Richmond	1	Ŏ		ŏ	1	ŏ	6	Ŏ	3 0	Ŏ	Ŏ	3
West Virginia:	0	0		0		0		0	1	0	0	
Wheeling	0	0		ŏ	11	0 0	0	Ŭ	1	Ŏ	0	1
North Carolina: Raleigh	0	0		0	1	0	0	0	0	0	0	
Wilmington Winston-Salem	0	0 0		0		01	02	$\begin{array}{c} 0\\ 2\end{array}$		0 0	0	53
South Carolina: Charleston	0	0	4	0	1	0	0	0	2	0	0	9
Georgia:	1	0	2	1	2	0	2	0	2	0	0	1
Brunswick	Ô	Ŏ		Ô		Ŏ	02	Ŏ	Ō	Ŏ	Õ	
Florida:	0			0	e	1	2	0	2	Ň	Ň	1
EAST SOUTH CENTRAL	v	v		U	0	1	-	v	Ĩ	v	Ŭ	1
Tennessee:												
Nashville	0	0		0	166	0	8	0	6	ŏ	ŏ	3
Alabama: Birmingham	0	0	1	0	1	0	2	0	3	0	0	2
Mobile	0	0		0	<b>-</b>	0	1	0	0	0	0	
WEST SOUTH CENTRAL												
Little Rock	0	0	5	0	2	0	2	0	0	0	0	1
New Orleans	2	0	1	1		2	5	0	1	0	1	
Oklahoma:	0	0		0		0	1	0		Ů	0	
Texas:	0	0		1	7	0	5	0	1	0	U	2
Dallas Galveston	0	1		0	131 7	0		0	0	0	0	1
Houston	0	0	3	02	2 29	0	8	0	0	0	1	1
MOUNTAIN	-	Ĩ	Ĩ	-			-	_		-		
Montana:												
Great Falls	Ŏ	Ő		0	3	- Ö	2	ŏ	4	ŏ	ŏ	
Missoula	0	0		0		0	0	0	1	ŏ	0	<u>.</u>
Idaho: Boise	0	0		0		0	3	0	0	0	0	<b>.</b>
Colorado: Denver	1	0	1	0	309	0	5	0	2	0	0	17
Pueblo Utah:	0	0		0	16	0	1	0	6	0	0	5
Salt Lake City	0	0		1	19	0	3	0	3	0	0	1

						,-				-		
Division, State, and city	Diphtheria cases	Encephalitis, in- fectious, cases	Influ Seese O	Deaths	Measles cases	Meningitis, me ningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
PACIFIC												
Washington: Seattle Spokane Tacoma California: Los Angoles	0 0 0 1	000000000000000000000000000000000000000	  16	0 0 0 1	38 3 21 191	0 0 0	3 2 0 0	0 0 0 2	6 2 0 20	0 0 0	0 0 0	4
Sacramento San Francisco	0 0	0	7	0 0	23 356	0	0 5	0	2 9	0	0	47
Total	36	1	64	15	7, 589	25	353	6	58 <b>6</b>	0	6	293
Corresponding week, 1947 <sup>1</sup> Average 1943-47 <sup>1</sup>	63 69		796 208	69 3 32	1, 393 37, 201		480 3 405		692 1,576	0	12 12	52 <b>3</b> 635

City reports for week ended Apr. 10, 1948-Continued

1 Exclusive of Oklahoma City.

<sup>2</sup> 3-year average 1945-47. <sup>3</sup> 5-year median 1943-47.

Rates (annual basis) per 100,000 population, by geographic groups, for the 89 cities in the preceding table (latest available estimated population, \$4,593,800)

	CBSB	case in- case		Influenza		me- case	leath	CBSB	CBS6	rates	para- ever	qâno
	Diphtheria	Encephalitis, fectious, rates	Case rates	Death rates	Measles case	Meningitis, ningococcus, rates	Pneumonia d rates	Poliom yelitis rates	Scarlet fever rates	Smallpox case	Tyhpoid and j typhoid fe case rates	Whooping o
New England	2.6 6.0 4.3 10.1 8.2 0.0 7.6 7.9 1.6	0.0 0.0 0.0 0.0 0.0 0.0 2.5 0.0 0.0	5.3 3.7 0.6 16.1 11.4 29.5 22.9 7.9 36.4	2.6 1.4 1.2 0.0 3.3 5.9 10.2 7.9 1.6	1, 331 1, 142 1, 299 1, 826 391 1, 021 452 2, 756 1, 000	0.0 3.7 4.3 4.0 8.2 0.0 5.1 0.0 1.6	89. 3 54. 6 38. 9 74. 4 55. 6 70. 8 73. 7 119. 1 15. 8	0.0 0.5 0.0 3.3 0.0 2.5 0.0 3.2	221 77 116 70 49 100 23 127 62	0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0	0.0 0.0 4.0 1.6 0.0 5.1 0.0 1.6	$\begin{array}{r} 45\\ 30\\ 46\\ 70\\ 64\\ 35\\ 13\\ 183\\ 46\end{array}$
Total	5.4	0.2	9.7	2.3	1, 147	3.8	53. 4	0. 9	89	0. 0	0. 9	44

Dysentery, amebic.—Cases: Memphis 1, New Orleans 1, Los Angeles 4, San Francisco 1. Dysentery, bacillary.—Cases: Worcester 3, St. Louis 1, Los Angeles 2. Dysentery, unspecified.—Cases: San Antonio 1. Tularemia.—Cases: New Orleans 1, San Antonio 1. Typhus fever, endemic.—Cases: New York 2, Tampa 1.

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#### **TERRITORIES AND POSSESSIONS**

#### **Panama Canal Zone**

Notifiable diseases-February 1948.-During the month of February 1948, certain notifiable diseases were reported in the Panama Canal Zone and terminal cities as follows:

	Residence 1											
Disease	Panama City		Colon		Canal Zone		Outside the Zone and terminal cities		Total			
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths		
Chickenpox Diphtheria Dysentery: Amebic	7 11				2 1		1 1		10 13 1			
Bacillary Malaria <sup>2</sup> Measles Meiningitis, meningococcus	1 3		2		8 6 1		148 13	1	8 157 16 1	1		
Pneumonia Poliomyelitis Relapsing fever Tuberculosis Typhoid fever	 1 1	9 		2 9	17 4 2	2	2	4	<sup>3</sup> 17 6 1 2 4	17 		

If place of infection is known, cases are so listed instead of by residence.
 16 recurrent cases.
 Reported in the Canal Zone only.

# DEATHS DURING WEEK ENDED APR. 10, 1948

[From the Weekly Mortality Index, issued by the National Office of Vital Statistics]

	Week ended Apr. 10, 1948	Correspond- ing week, 1947
Data for 93 large cities of the United States: Total deaths. Median for 3 prior years. Total deaths, first 15 weeks of year. Deaths under 1 year of age. Median for 3 prior years. Deaths under 1 year of age, first 15 weeks of year. Deaths under 1 year of age, first 15 weeks of year. Deaths industrial insurance companies: Policies in force. Number of death claims. Death claims per 1,000 policies in force, annual rate. Death claims per 1,000 policies, first 15 weeks of year, annual rate.	9, 690 9, 154 152, 347 714 599 10, 422 71, 084, 296 15, 613 11. 5 10. 3	10, 154 151, 812 723 12, 075 67, 308, 805 12, 738 9, 9 9, 9

# FOREIGN REPORTS

#### CANADA

Provinces—Communicable diseases—During the weeks ended March 20 and 27, 1948, cases of certain communicable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Bruns- wick	Que- bec	Onta- rio	Mani- toba	Sas- katch- ewan	Al- berta	British Colum- bia	Total
Chickenpox Diptheria		42		196 10	345	48	12	43 5	85	771
Dysentery, bacillary German measles Influenza		 41		2 73	21 20 1 276	1 1 2	2 7	7	1 6 19 146	3 110 81 2 328
Meningitis, meningococ- cus		23	1	1 283	1, 270 2 343	1 47	66	47	22	2, 020 5 831
Poliomyelitis Scarlet fever Tuberculosis (all forms)		3	2 4	47 87	82 37	4 30	9	1 5 3	 36 36	1 176 209
Typhoid and paraty- phoid fever Undulant fever				15 1	2		1 1	1 1	·····i	17 6
Venereal diseases: Gonorrhea Syphilis Other forms	. <b>4</b> . 1	17 13	7 7	75 85	69 34	33 8	18 9	33 8	73 22 1	329 187 1
Whooping cough				25	26	2	1	55	5	114

Week ended March 20, 1948.-

# Week ended March 27, 1948.-

Disease	Prince Edward Island	Nova Scotia	New Bruns- wick	Que- bec	On- tario	Mani- toba	Sas- katch- ewan	Al- berta	British Colum- bia	Total
Chickenpox Diphtheria Dysentery bacillary		34 1	3 1	171 8 1	264	60	20 1	13 1	89	654 12 1
German measles				9	18			2	12	41
Mensles		14		797	1.231	4	6	13	61	2, 112
Meningitis, meningococ-					_,	1				1
Mumps		23	1	205	288	25	65	32	10	649
Scarlet fever		1	2	- 34	67	1	4	4	6	119
Tuberculosis (all forms).		4	6	52	31	13	5	60	53	224
Typhoid and paraty- phoid fever Undulant fever				9		1			1 2	11 2
Venereal diseases: Gonorrhea Synhilis	•••••	8	9 10	98 76	84 28	30 8	18 11	45 2	40 12	332 153
Whooping cough				26	15	š		33	5	82

#### MADAGASCAR

Madagascar and Comoro Islands—Notifiable diseases—January and February 1948.—Notifiable contagious diseases were reported in Madagascar and Comoro Islands during January and February 1948 as follows:

		Jan	uary		February					
	Aliens		Na	tives	Al	iens	Natives			
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths		
Beri-beri	0	0	. 20	0	1	0	9	1		
Bilharziasis	1	0	86	Ó	0	Ō	114	Ō		
Cerebrospinal meningitis	0	0	9	1	0	0	12	7		
Diphtheria	2	0	8	2	3	Ó	2	1		
Dysentery amebic	23	0	400	11	20	0	598	14		
Dysentery, bacillary	0	0	21	0	2	0	11	0		
Ervsipelas	1	0	10	1	0	Ó	18	1 1		
Influenza.	4	Ó	2,330	28	5	Ō	2.247	25		
Leprosy	0	Ō	52	Õ	Ő	Ó	25	Ō		
Malaria	471	7	41.644	374	564	4	41, 906	369		
Measles.	2	Ó	57	2	1	Ō	39	0		
Munips	2	Ō	254	ō	õ	ŏ	182	ŏ		
Plague	ō	Ŏ	61	4ľ	ŏ	ŏ	46	29		
Pneumonia, broncho		ž	295	57	5	4	308	38		
Pneumonia, pneumococcie	5	ī	419	79	2	i i	293	58		
Poliomvelitis	Õ	ō	ň	Ö	ō	Ô	2	i õ		
Puerperal infection	ŏ	ŏ	4	i i	ŏ	ŏ	ลี	Ň		
Relapsing fever	ň	ŏ	ó	h î	ĭ	ŏ	Ň	Ň		
Scarlet fever	ĭ	ŏ	ŏ	ň	î	Ň	ň	Ň		
Trachoma	Ô	ň	ĭ	ň	î	Ň	Ň	Ň		
Tuberculosis pulmonary	3	ň	120	36	11		113	90		
Typhoid and paratyphoid fever	1	h h	123	19	3	1	30	6		
Whooping cough	6	Ŏ	82	12	2	Ô	88	Ö		

#### REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

NOTE.—Except in cases of unusual incidence, only those places are included which had not previously reported any of the above-mentioned diseases, except yellow fever, during recent months. All reports of yellow fever are published currently.

A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday in each month.

#### Cholera

India-Calcutta.-For the week ended April 3, 1948, 282 cases of cholera were reported in Calcutta, India.

Indochina (French)—Cochinchina—Rachgia.—During the period March 1–20, 1948, 58 cases of cholera with 23 deaths were reported in Rachgia, Cochinchina French Indo-China.

#### Plague

Belgian Congo-Stanleyville Province.--During the week ended April 3, 1948, 1 fatal case of plague was reported in the area northeast of Blukwa in Stanleyville Province, Belgian Congo.

British East Africa-Tanganyika-Central Province.-During the months of February and March 1948, 189 cases of plague with 85 deaths were reported in Singida District, Central Province, Tanganyika, British East Africa.

China—Kiangsi Province—Nanchang.—Information dated April 15, 1948, states that the usual spring epidemic of plague has re-appeared in Nanchang, Kiangsi Province, China. The epidemic is reported under control, but travelers have been advised to be innoculated.

India—Lucknow.—For the week ended March 27, 1948, 24 cases of plague with 8 deaths were reported in Lucknow, India.

*Portugal—Azores.*—For the period February 1–14, 1948, 3 cases of plague with 2 deaths were reported in the Ponta Delgada area, Azores, Portugal (4 cases with 1 death were reported in January 1948).

#### Smallpox

China-Shanghai.-For the week ended April 3, 1948, 94 cases of smallpox were reported in Shanghai, China.

France—Seine Department.—During the period February 16-March 31, 1948, 3 cases of smallpox were reported in Seine Department, France.

India-Calcutta.-For the week ended April 3, 1948, 212 cases of smallpox were reported in Calcutta, India.

Portugal—Lisbon.—For the period March 1-27, 1948, 25 cases of smallpox with 2 deaths were reported in Lisbon, Portugal.