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Complex Fluorides: Caries Reduction and Fluorine Retention in the Bones and Teeth of White Rats

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This study was made to obtain data on the physiological availability and effects of fluorine as it occurs in several complex chemical combinations. The criteria for evaluation of these fluorides (as administered by injection and in drinking water of growing rats) were (1) deposition of fluorine in bones and teeth, (2) development of incisor striations and, (3) ability to inhibit experimental rat caries. These and similar experiments not only help to elucidate the metabolism of fluorine but may also have a practical application to fluoridation of drinking water, which has become an effective procedure for the partial control of human dental caries. Although sodium fluoride (NaF) is now the most common fluoride in use for community water fluoridation, other compounds, particularly sodium fluosilicate (Na_2SiF_6), if found comparable to NaF in physiological effects, may have an advantage in being produced at less expense than NaF.[1]

In a previous publication (*1*) the junior author reviewed earlier reports of the effects of a number of different fluorides (NaF, Na_2SiF_6, Na_3AlF_6, $BaSiF_6$, NH_4F, KF, K_2SiF_6, and CaF_2) and reported that NaF and Na_2SiF_6, when ingested in drinking water by growing rats in amounts which furnished 5, 10, 15, 25, and 50 ppm of fluorine, resulted in equivalent retentions of fluorine in the bones and teeth, mandibles, and femurs, and produced similar incisor striations. In general, this study (*1*) indicated that fluorine in NaF and Na_2SiF_6 is equally available.

Deposition of fluorine in dental and skeletal tissues of hamsters receiving Na_3AlF_6, Na_2PO_3F, KPF_6, NaF, and "Flural"[2] (*2*) was also recently reported. Less fluorine was retained in the lower incisors of hamsters receiving "Flural", KPF_6, and Na_3AlF_6, than in hamsters

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[1] Since commercial grade NaF is 95 percent pure, and at current market quotations (*21*) sells for 11¢ per lb., and commercial Na_2SiF_6 is 98 percent pure and sells for 5¢ per lb., the cost per lb. of available fluorine is now approximately three times more for NaF than for Na_2SiF_6.

[2] Flural is a commercial preparation of the Ozark-Mahoning Company, Tulsa, Okla., containing alum and a fluoride. One commercial grade has a composition approximating the formula $AlFSO_4.2H_2O$ (*6*).

receiving NaF, but fluorine retained in the tibias was proportional to the fluorine ingested, regardless of the type of fluoride fed (*2*).

Data on the biological availability of covalent-bonded fluorine are very meager. Kempf et al. (*3*, *4*) reported that α-fluoronaphthalene produced mottled enamel, whereas p, p-difluorodiphenyl, p-fluorobenzoic acid and fluorobenzene had no such effect. No tissue analyses for fluorine were reported. Boyer et al. (*5*) did not find any increase of fluorine in the bones of rats fed 0.004 percent 3-fluorotyrosine in the diet; in fact, less fluorine was found than in control rats receiving no fluoride. Euler and Eichler (*7*), however, reported that 2 mg./kg. of 3-fluorotyrosine given by stomach tube produced mottling in rat incisors and histological changes in the bones and teeth. No tissue analyses for fluorine were reported. Armstrong et al. (*8*) recently have reported "bleaching of the teeth" and the presence of inorganic fluoride in the urine of rats receiving 4-fluorophenylalanine by mouth. Hagan et al. (*9*) have also presented evidence that sodium monofluoroacetate may be metabolized by the rat, since only 22 percent of the sodium monofluoroacetate fed could be recovered in the carcass and excreta as the parent compound.

One significant criterion of the physiological availability of different fluorine compounds is their effect on experimental animal caries. Comparable evidence is somewhat meager in this regard, since the majority of caries inhibition studies relate to the effects of sodium fluoride. Keyes and Shourie (*10*) reported that 50 ppm fluorine as sodium fluoride "was very effective in reducing caries activity in the molar teeth of hamsters, sodium fluosilicate was somewhat less effective, and calcium fluoride was essentially ineffective." More recently, the acute toxicity and ability to inhibit caries in hamsters were used as criteria for a comparison of NaF and Na_2PO_3F (*11*). Comparable caries reduction was attributed to Na_2PO_3F and NaF when administered in the drinking fluid at a level of 40 ppm F. However, on the basis of fluorine content, the complex fluoride Na_2PO_3F appeared to be 2.5 to 3.0 times less toxic than NaF (*11*). In further studies, this group of workers reported that Na_3AlF_6, "Flural", Na_2PO_3F, and NaF had "nearly maximal" inhibitory effects on hamster caries, but that KPF_6 did not reduce caries significantly (*2*).

It is generally true that the majority of the fluorine compounds studied up to this time, when ingested at levels just sufficient to produce characteristic striation in rats' incisor teeth, have similar effects. At higher intakes, differences in physiological effects generally have been attributed to different solubilities which seemingly affect absorption from the digestive tract. Aside from the factors of solubility and concentration, however, fluorine in some chemical compounds, even though adequately soluble and absorbed from the digestive tract may not be metabolized. Such fluorides would not be expected

to show characteristic effects of the fluoride ion per se, and would not deposit fluorine in body tissues. Thus, Boyer et al. (*5*), as noted above, reported that no fluoride could be found in rats fed 3-fluorotyrosine in the diet. Two inorganic fluorides, Al_2F_6 (*3*, *4*) and ZnF_2 (*3*), have also been reported not to produce incisor striations when fed in the diet at a concentration of 0.10 percent F. From our experiments reported below, it now appears that two other fluorides, KPF_6 and CF_3COONa, although highly soluble, do not produce characteristic fluorine effects and cause no deposition of fluorine in body tissues.

Experimental

One hundred and fifty female white rats of the Holtzman strain, 21–27 days of age, representing 30 litters of 5 rats each, were equally distributed into 5 groups. An additional 180 males of the Holtzman strain, 21–27 days of age, representing 30 litters of 6 rats each, were distributed equally into 6 groups. All rats received, *ad libitum*, a cariogenic diet of the following composition:

	Percent
Whole milk powder	30. 0
Yellow corn grits	42. 0
Cane sugar, granulated	25. 0
Whole dried liver substance (Wilson)	2. 0
Salt mixture	1. 0

Salt mixture	*Gram*
Sodium chloride	400
Potassium chloride	400
Magnesium carbonate	100
Iron and ammonium citrate	20
Manganous sulfate	28
Calcium hydrogen phosphate	50
Cupric acetate	2

The plan of the experiment was as follows:

Group	*Number rats*	*Sex*	*Fluid*	*Route of administration*
Control	30	F	Distilled water	Peroral.
Drink B	30	F	50 ppm F as Na_2SiF_6	Peroral.
Inject B	30	F	500 ppm F as Na_2SiF_6	I. P.
Drink C	30	F	50 ppm F as Na_2PO_3F	Peroral.
Inject C	30	F	500 ppm F as Na_2PO_3F	I. P.
Control	30	M	Distilled water	Peroral.
Drink D	30	M	50 ppm F as KPF_6	Peroral.
Inject D	30	M	500 ppm F as KPF_6	I. P.
Drink E	30	M	50 ppm F as NaF	Peroral.
Inject E	30	M	500 ppm F as NaF	I. P.
Drink FF	30	M	50 ppm F as CF_3COONa	Peroral.

All groups received approximately the same quantity of fluorine, except the rats receiving Na_2SiF_6 injected intraperitoneally. Injected rats received 3.5 mg. fluorine weekly, distributed over five daily injections. Because of its high acidity (pH 3.3), the inject Na_2SiF_6 solution was poorly tolerated; for this reason these rats received less fluoride, since the study was terminated when all the rats had been on the cariogenic diet the same length of time. The diet contained

1.3 ppm F, which was considered negligible in calculating the total fluorine consumption.

At the end of 91 days, the animals were killed and the teeth diagnosed for dental caries according to Cox et al. (*12*). The femurs, mandibles, molars, and incisor teeth were dried, extracted with alcohol and ether and ground to pass a 60-mesh sieve. The incisors and molars were separated into dentin and enamel by the Manly-Hodge technique (*13*). All tissues were then ashed at 550° C. for 3 hours and analyzed for total fluoride (*14*).

Analysis of Fluorine Compounds

The preparation of the fluoride solutions required a careful assay for purity and for free fluorine in KPF_6, Na_2PO_3F, and CF_3COONa, which were commercial grade samples. NaF and Na_2SiF_6, being analytical grade reagents, were accepted according to specifications. Na_2PO_3F was found to contain 13.5 percent total fluorine (*14*) (13.2 percent theory), and 1.85 percent free fluorine (*15*), indicating that 13.7 percent of the total fluorine was present as free fluorine. This commercial product specified a purity of 90–97 percent with NaF, $(NaPO_3)_x$, and Na_2CO_3 as impurities.[3] By repeated shaking of solutions of this commercial Na_2PO_3F with MgO, free fluorine was reduced to 7.0 percent of the total fluorine. This purified Na_2PO_3F solution was used to prepare the rats' drinking and injection solutions.

KPF_6 contained no free fluorine (*16*) and averaged 94.6 percent purity by the Willard and Winter fluorine analysis (*14*) and 98.6 percent purity by the PbClF precipitation procedure (*17*). Similarly, no free fluorine was found in CF_3COONa. However, analysis of CF_3COONa for total fluorine by the usual Willard and Winter perchloric acid distillation was unsatisfactory, no fluorine being detected in the distillate by $Th(NO_3)_4$ titration. Ashing of CF_3COONa for 3 hours at 550° C. in the presence of CaO gave only 65.9 percent recovery of theoretical fluorine. Further analysis of CF_3COONa by fusion with Na_2CO_3 followed by precipitation as PbClF (*17*) gave 92.0 percent of theoretical fluorine. The most satisfactory analysis was obtained by fusing 95.4 mg. CF_3COONa, 15 gm. Na_2O_2, and 0.4 gm. sucrose in the Parr bomb, dissolving the fused mixture in hot water, neutralizing with HCl, and diluting to 2 liters with distilled water. This solution when titrated for fluorine with $Th(NO_3)_4$ gave 98.0 percent of theoretical recovery, which agrees well with the reported assay of 98–99 percent.[4]

Results of Experiments

Without exception all the fluorine compounds, when injected, caused

[3] Ozark-Mahoning Co., FP Compounds. Tulsa, Okla., 1949.

[4] Hooker Electrochemical Co., Niagara Falls, N. Y. Preliminary Technical Data Sheet No. 377.

no reduction in dental caries (see table). Though this negative result cannot be explained by the absence of fluorine in the molar dentin and enamel of these rats, it is nonetheless possible that fluorine as acquired by these teeth from parenterally administered fluoride did not reach the oral enamel surface in sufficient time perhaps, or in sufficient quantity, to exert a cariostatic effect. It will be noted that the quantity of fluorine in molar enamel of injected rats is consistently lower than the fluorine in the molar enamel of rats receiving fluorides orally. This negative effect of injected fluoride agrees with previous results with rats (*18*) and, to some extent, with previous results with hamsters (*10*). Although hamster caries appeared to be inhibited by injected fluoride, it was suggested that fluorine may have reached the oral cavity via coprophagy.

Also, no caries inhibition occurred with orally administered KPF_6, which agrees with a previous hamster study (*2*), nor from oral CF_3COONa. The absence of any increased fluorine in the teeth of these rats and the lack of enamel striations are consistent with this observation. Reduction of caries was similar in the three groups of rats given NaF, Na_2SiF_6, and Na_2PO_3F in their drinking water. The teeth of these rats responded also by a greatly increased fluorine content in the enamel and dentin. The caries reducing effect of NaF has been repeatedly demonstrated (*19*), and the caries inhibiting effect of Na_2SiF_6 was anticipated by evidence of the availability of its fluorine (*1*). As previously mentioned, other studies (*11*) have also shown the ability of Na_2PO_3F to reduce caries in hamsters. Reduction in the percent of rats having caries, i. e., the reduced incidence of caries, was 21.3, 19.4, and 15.7 percent, respectively, for NaF, Na_2SiF_6, and Na_2PO_3F. Severity of caries as indicated by the caries score was reduced 39.2 percent by NaF, 45.0 percent by Na_2SiF_6, and 45.0 percent by Na_2PO_3F. These three fluorides, therefore, were essentially similar in their cariostatic effects.

As shown in the table, two groups of rats, one male, the other female, served as controls. Since differences in caries between these two groups were not statistically significant, they were combined to give a composite control group which was used as the standard of reference. This result thus contributes to the evidence that sex is probably not a factor in the production of rat caries.

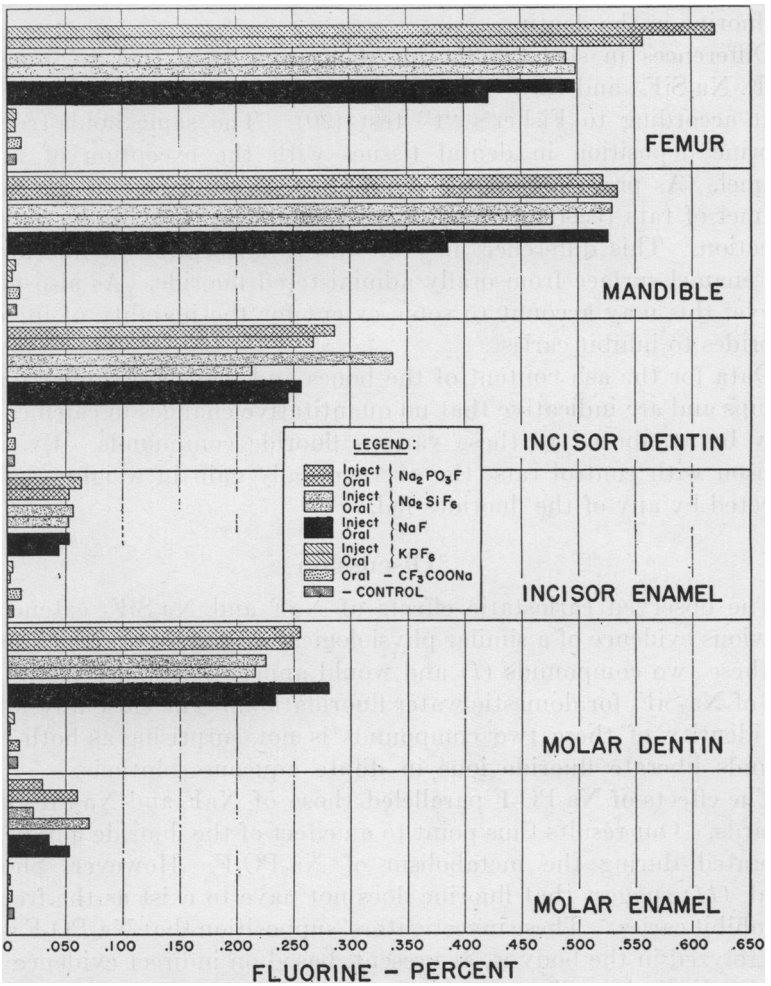
The complex fluorides KPF_6 and CF_3COONa were strikingly different from the other fluorides in the physiological availability of their fluorine. No fluorine was deposited in the bones and teeth of rats ingesting these compounds. The data are graphically presented on the chart.

Owing to difficulties in the fluorine analysis of CF_3COONa, some uncertainty arose as to the failure to find fluorine in bones and teeth of rats receiving this compound. The remote possibility existed that

Item	Control	Control	Control	NaF oral	NaF inj.	Na_2SiF_6 oral	Na_2SiF_6 inj.	Na_2PO_3F oral	Na_2PO_3F inj.	KPF_6 oral	KPF_6 inj.	CF_3COONa oral
	Male	*Female*	*Both*	*Male*	*Male*	*Female*	*Female*	*Female*	*Female*	*Male*	*Male*	*Male*
Total fluorine (mg.)	0.0	0.0	0.0	62.6	60.5	59.5	46.7	61.2	57.2	64.2	60.6	63.0
Days on experiment	92	92	92	91	91	91	91	91	92	91	91	91
Final weight (gm.)	260	187	222	275	247	195	178	187	189	280	255	275
Initial weight (gm.)	35	35	35	33	35	36	38	36	37	35	35	34
Average daily gain (gm.)	2.4	1.7	2.0	2.7	2.3	1.7	1.5	1.7	1.7	2.7	2.4	2.6
Caries diagnosis												
Number of rats	27	30	57	29	23	27	29	27	27	27	26	27
Number of litters	27	30	57	29	23	27	29	27	27	27	26	27
Rats with caries (number)	27	28	55	22	23	21	28	22	25	26	26	26
Rats with caries (percent)	100.0	93.3	96.5	75.9	100.0	77.8	96.6	81.5	92.6	96.3	100.0	96.3
Carious teeth per carious rat (number)	4.1	3.5	3.9	3.6	4.7	2.8	3.9	3.0	4.0	4.4	4.3	4.2
Carious teeth per carious rat (percent)	34.2	29.2	32.5	30.0	39.2	23.3	32.5	25.0	33.3	36.7	35.8	35.0
Carious areas per carious rat (number)	6.5	5.3	5.9	3.7	7.3	3.2	6.5	3.4	5.7	7.2	8.0	6.4
Caries score per carious rat	13.2	10.8	12.0	7.3	15.0	6.6	14.6	6.6	13.4	15.4	17.7	13.8
Fluorine analysis of teeth and bones (ash basis)												
Molar enamel (percent)	0.005	----------	[1](0.005)	0.053	0.036	0.071	0.022	0.059	0.029	0.001	----------	0.003
Molar dentin (percent)	.004	0.011	(.008)	.233	.280	.216	.224	.249	.255	.001	0.006	.009
Incisor enamel (percent)	.003	.005	(.004)	.044	.053	.053	.057	.053	.064	.001	.004	.012
Incisor dentin (percent)	.004	.008	(.007)	.244	.256	.213	.336	.266	.284	.001	.004	.007
Mandible (percent)	.009	.006	(.007)	.383	.524	.476	.528	.533	.520	.003	.006	.010
Mandible total (mg.)	.01	.02	(.02)	1.2	1.1	1.3	1.1	1.3	1.1	.01	.01	.03
Femur (percent)	.004	.009	(.007)	.419	.496	.497	.488	.555	.619	.006	.007	.012
Femur total (mg.)	.04	.01	(.03)	2.2	2.2	2.4	2.0	2.3	2.3	.03	.03	.06
Percent ash content of teeth and bones												
Molar enamel	94.8	94.7	[1](94.7)	94.2	94.4	94.6	94.4	94.4	94.3	94.2	94.4	94.2
Molar dentin	75.8	74.9	(75.3)	76.9	77.1	77.6	76.8	77.0	77.4	76.4	77.1	75.7
Incisor enamel	95.6	95.2	(95.4)	94.8	94.5	94.8	95.2	94.5	95.2	94.8	94.9	94.6
Incisor dentin	75.3	75.6	(75.5)	73.4	75.0	76.0	75.6	75.1	74.9	74.6	75.1	75.3
Mandible	69.9	70.5	(70.2)	71.5	71.0	72.1	72.3	72.2	70.9	70.2	69.8	70.8
Femur	69.7	64.9	(67.3)	68.1	66.5	68.4	70.5	70.8	66.2	66.1	66.9	68.6
Enamel striations	[2]	[2]	[2]	[3]	[3]	[3]	[3]	[3]	[3]	[2]	[2]	[2]

[1] Arithmetic mean of male and female control rats. [2] None. [3] Marked.

fluorine could be deposited as trifluoroacetate or some metabolic intermediate, which would not be detected by the Willard and Winter procedure (*14*). Thus, when standard solutions of CF_3COONa were added to fresh bone samples, which were then ashed and distilled in the usual procedure (*14*), no fluorine was found in the distillate. However, CF_3COONa added to ashed bone resulted in 62.4 percent of fluorine recovery, indicating some interference due to the organic matrix of skeletal tissues. The recovery of fluorine added as CF_3COONa to bone could be improved by a preliminary distillation of the fresh bone plus CF_3COONa, using H_2SO_4 at 160° to 165° C., followed by a second distillation using $HClO_4$ (*15*); 81.1 percent of the CF_3COONa was recovered by this procedure. Bone samples alone



Fluorine in ash of bones and teeth of rats receiving fluorine as NaF, Na_2SiF_6, Na_2PO_3F, KPF_6, and CF_3COONa.

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analyzed by this technique gave no fluorine over and above that obtained by the usual $HClO_4$ distillation.

It seems reasonable to assume, therefore, that no fluorine, free or combined, was deposited in these animals' skeletal or dental tissues. Availability of fluorine in NaF, Na_2SiF_6, and Na_2PO_3F, however, was similar and pronounced, as indicated by the high fluorine content of the skeletal and dental tissues of rats exposed to these fluorides. The similarity in availability of fluorine in NaF and Na_2SiF_6 was previously shown by McClure (*1*) and the availability of fluorine in Na_2PO_3F as fed to hamsters was also previously reported (*11*). It is of interest to note the similarity of the fluorine deposits in molar dentin and incisor dentin. Although the incisor is actively growing as compared with the fully developed molar, both have retained similar quantities of fluorine in the dentin.

Differences in skeletal fluorine deposition from oral vs. injected NaF, Na_2SiF_6, and Na_2PO_3F were found not to be statistically significant according to Fisher's "t" test (*20*). The same holds true for fluorine deposition in dental tissues with the exception of molar enamel. As previously noted, more fluorine is present in the molar enamel of rats receiving NaF, Na_2SiF, and Na_2PO_3F orally than by injection. This difference may be due to adsorption of fluorine on the enamel surface from orally administered fluoride. As also noted above, this may account to some extent for the inability of injected fluorides to inhibit caries.

Data for the ash content of the bones and teeth are similar for all groups and are indicative that no quantitative changes in calcification may be attributed to these various fluoride compounds. By comparison with control rats, the average daily gain in weight was not affected by any of the fluorides fed.

Discussion

The observed cariostatic effects of NaF and Na_2SiF_6 extend our previous evidence of a similar physiological availability of the fluorine in these two compounds (*1*) and would appear to further justify the use of Na_2SiF_6 for domestic water fluoridation. The close physiological identity of these two compounds is not surprising as both compounds liberate fluoride ions in dilute aqueous solutions.

The effects of Na_2PO_3F paralleled those of NaF and Na_2SiF_6 in all regards. Our results thus point to an effect of the fluoride ion, per se, liberated during the metabolism of Na_2PO_3F. However, Shourie et al. (*11*) suggest that fluorine does not have to exist as the free ion to inhibit caries. These investigators' supposition that Na_2PO_3F is not hydrolyzed in the body is, at present, based on indirect evidence that Na_2PO_3F, both orally and parenterally administered in single doses, is 2.5 to 3 times less toxic that NaF on the basis of fluorine content.

Further studies seem to be in order to clarify the *in vivo* hydrolysis of Na_2PO_3F. The data of our experiments support the belief that Na_2PO_3F is metabolized by the rat in a manner similar to NaF and Na_2SiF_6, since all these compounds had similar effects on dental caries, enamel striations, and storage of skeletal and dental tissue fluorine. This belief is also supported by the statement that Na_2PO_3F slowly hydrolyzes in acid solution to give fluoride ions.[5]

Viewed as a basic problem in the metabolism of fluorine, the results obtained with KPF_6 and CF_3COONa are perhaps the most interesting outcome of this study. Fluorine in these combinations seems to be totally unavailable to the rat when administered either orally or parenterally.

There seems to be a relation of "saturation" of fluorine in complex fluorides (perfluoro compounds) to the physiological stability of fluorine. Thus, sodium monofluoroacetate appears to be metabolized to furnish inorganic fluoride (*9*), whereas sodium perfluoroacetate (CF_3COONa) does not yield inorganic fluoride. Similarly, sodium monofluorophosphate is metabolized, whereas potassium perfluorophosphate (KPF_6) does not appear to be hydrolyzed by the rat. It would seem, therefore, that the metabolism of simple and complex fluorides does not follow a similar pattern, and more evidence is needed to elucidate these differences.

Summary

A comparative study of the physiological effects of NaF, Na_2SiF_6, KPF_6, Na_2PO_3F, and CF_3COONa was made using the young growing rat as the experimental animal. Fluorine was ingested in the drinking water at a level of 50 ppm and, with the exception of CF_3COONa, all the compounds were also injected intraperitoneally. NaF, Na_2SiF_6, and Na_2PO_3F in the drinking water reduced dental caries, deposited fluorine in the bones and teeth, and caused marked incisor striations to essentially the same extent. None of the fluorides had any cariostatic effect when administered by intraperitoneal injection. However, injected NaF, Na_2SiF_6, and Na_2PO_3F produced enamel striations and deposited fluorine in the bones and teeth. KPF_6 and CF_3COONa were physiologically inert insofar as could be indicated by caries inhibition, enamel striations, and deposition of fluorine in bones and teeth.

The data suggest that NaF, Na_2SiF_6, and Na_2PO_3F may be equally effective as water fluoridating agents for caries prevention.

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[4] Ozark-Mahoning Co., FP Compounds. Tulsa, Okla.

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Histoplasmosis Survey of Dogs in Louisville, Kentucky

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The east central portion of the United States has been regarded as an area in which infection with *Histoplasma capsulatum*, a diphasic fungus, is endemic (*1*). This area extends from Kansas City eastward and from southern Iowa and Ohio south through Tennessee (*2*). The belief that this is an endemic area of histoplasmosis is based on two sets of data. First, a disproportionately large number of the more than 100 cases of human histoplasmosis that have been reported in the medical literature have come from this area (*3*). Second, histoplasmin skin sensitivity surveys have shown that a high percentage of individuals native to this area give a positive reaction (*2*, *4*, *5*).

In regard to the first set of data, human histoplasmosis has been reported from other areas of the United States, Central and South America, Europe, South Africa, the Philippines, and Asia. It is possible that the east central area of the United States has had more cases reported because of greater awareness by the clinicians and laboratories in looking for this infection, particularly because this area has a high incidence of pulmonary calcification in human beings who also give negative tuberculin reactions. The disease has, however, been looked for in other parts of the world, Brazil, Panama, Italy, and South Africa, by competent clinicians and mycologists, and a similarly large number of cases has not yet been found.

There has been considerable controversy in regard to the second set of data, which is based on the histoplasmin intradermal test. The controversy has centered largely about the specificity of histoplasmin since cross reactions with other systemic fungus infections have been reported (*6*, *7*). Howell (*8*) has confirmed earlier observations of Emmons, et al. (*6*) that in experimental animals skin reactivity varies with the lot of histoplasmin used, the dilution of the antigen, and the physiological status of the animal. Howell recommended the standardization of histoplasmin as to both antigenicity and dilution in order to be more certain of its degree of specificity and its comparative use with other antigens in order to make a reliable diagnostic interpretation.

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Emmons (*9*) has approached the problem of geographic distribution of human histoplasmosis in a different manner. His approach to this problem is based on the observation that animals are susceptible to histoplasmosis, and the isolation of *H. capsulatum* from wild-caught dogs, cats, rats, and other animals definitely establishes the presence of the fungus in the area. *Histoplasma*, therefore, constitutes a potential hazard to man in such an area. Ruhe and Cazier (*10*) have reviewed the literature on the incidence of histoplasmosis among animals, and Emmons (*9*) has summarized surveys of animals from various areas in the Unites States in order to determine the presence of this disease. Thus far, some 35 dogs from various parts of the world, though chiefly from the United States, have been found naturally infected. Emmons has also found the house mouse, brown rats, roof rats, domestic cats, spotted skunks, and an opossum naturally infected with *H. capsulatum* in his surveys.

During the past 10 years about 10 cases of acute histoplasmosis have been diagnosed in persons coming to the Louisville medical clinics. These cases were mostly in infants and children from central Kentucky and southern Indiana, as well as Louisville. In view of the fact that there have been only a little more than 100 cases reported in the medical literature, these 10 cases seem to be an unusually high number for such a small area. It seemed to us that this apparently high incidence of human infection might be complemented by a high incidence of animal infection. For this reason, a survey was made for evidence of the infection in dogs of the Louisville area.

Material and Methods

Preparation of Dog Cultures

All animals used in the survey were obtained from the Louisville dog pound from March 1950 through January 1951. These dogs were all routine admissions with no selection being made as to age, sex, or breed. Some selection was made in regard to size and rabid condition. All dogs weighing approximately 100 pounds or more were excluded to facilitate transportation. Also, dogs suspected of rabies could not be obtained for study. All dogs were killed with carbon monoxide gas and were autopsied within 2 hours after death. Before autopsy, the ventral and left lateral surfaces of the dogs were thoroughly wetted with 70 percent ethyl alcohol. Sterile instruments were used for each dog. Under as aseptic conditions as possible, the left humerus and a small portion of the spleen (approximately 2 inches long and 1 inch wide) were removed. The humerus was used as a source of bone marrow. The liver and lungs were examined grossly for lesions, but no specimens were taken unless gross pathology was evident.

Cultures were made from both the spleen and bone marrow. A

small portion of the spleen (approximately one-fourth-inch square) was streaked over the surface of a modified Sabouraud's agar slant and left near the top of the slant. The humerus was then opened with bone scissors or with a carpenter's hammer. Two to three loopsful of the exposed bone marrow were inoculated into the following culture media: a modified Sabouraud's agar slant and a modified Sabouraud's agar slant containing 20 units of penicillin G and 40 units of dihydrostreptomycin hydrochloride per milliliter of medium. All cultures were incubated at room temperature and examined at the end of 2 and 4 weeks before being discarded as negative.

A bone marrow smear and a splenic impression were made from each dog. These preparations were stained with Leishman's stain and the entire slide was examined for *H. capsulatum*.

Infected Mouse Experiment

To determine the effect of carbon monoxide gas on *H. capsulatum*, seven white mice of unknown strain were inoculated intraperitoneally with 0.5 ml. of a saline suspension of *H. capsulatum* (our Sallee strain, ground mycelial phase). One month from the date of inoculation these mice were killed in the same carbon monoxide gas chamber used for killing the dogs and were exposed to the gas for the same length of time as were the dogs. The mice were then taken directly to the autopsy room and autopsied under the conditions outlined in the dog experiment. Small portions of spleen and liver (approximately one-fourth-inch square) were streaked over the surface of a modified Sabouraud's agar slant and usually left near the top of the slant. These cultures were incubated at room temperature and examined at the end of 4 weeks.

The cultures made with portions of the infected mouse spleens and livers were carefully examined microscopically and the large tuberculate chlamydospores characteristic of *H. capsulatum* were found in every culture.

The results of this control experiment indicate that carbon monoxide gas does not kill *H. capsulatum* in infected tissue.

Results

The direct microscopic examination of stained bone marrow smears and splenic impressions from 303 dogs collected in the Louisville area during the period from March 1950 to January 1951, failed to reveal the fungus, *H. capsulatum*, in any instance. All cultures of bone marrow and portions of spleen from these dogs were also negative for *H. capsulatum* after incubation at room temperature for 1 month.

Discussion

The negative results obtained in this survey may be explained in

two ways. First, the isolation technique of the investigators may have been faulty and inadequate in recovering the fungus in the tissues of the dogs at autopsy. Second, the spleens and bone marrow of the dogs may not have been infected with the fungus at the time of examination. There is some indication that rural animals are more likely to be infected with *Histoplasma* than urban animals, on the basis of Emmons' report (*9*). It may be for this reason that these Louisville dogs were negative. It must be noted, however, that although these dogs were obtained from the Louisville dog pound, there was no way of determining whether the dogs had spent their full lives in Louisville.

The culture technique used in this survey is the same as that employed by Emmons and Ashburn (*11*) in their survey of histoplasmosis in wild rats. A modified Sabouraud's medium was used by them. This medium has been shown to be quite satisfactory in recovering *H. capsulatum* from infected tissues in some of our unpublished experiments (*18*).

As this fungus primarily infects the reticulo-endothelial tissues, the spleen and bone marrow samples of infected animals readily reveal the yeast-like, parasitic phase of the organism. The researches of Howell (*12*), Emmons and Ashburn (*11*), Ruhe and Cazier (*10*), and Menges, Furcolow and Ruhe (*13*), as well as our own unpublished work (*18*), indicate that the spleen and bone marrow harbor the parasite in a very high percentage of infected animals. In view of these facts, it seems unlikely that our failure to find any infected animals was the result of an inadequate technique.

The question of animal reservoirs for *H. capsulatum* has been raised by a number of investigators. Ruhe and Cazier (*10*) believe that domestic animals, like the dog, may serve as reservoirs and play a significant role in the epidemiology of this infection. A number of reported human cases had contact with dogs. Thus, Para (*14*) cites a case of a Brazilian child who had contact with a *Histoplasma*-infected dog. Kuzma and Schuster (*15*) have reported a fatal case of histoplasmosis in a dog breeder. Olson, Bell, and Emmons (*16*) reported human and canine cases in Loudoun County, Virginia, although there was no proved contact between the infected human beings and dogs. In spite of these few cases in which there may have been some association between the human and canine cases, the vast majority of human cases have given no evidence of contact with infected dogs. It seems likely that dogs are merely coincidental hosts for this parasite and play no significant role in the epidemiology of human infections. This fact seems to be borne out partially by our findings, since no canine infections were found, although human infections were reported in this area. It is interesting to note, however, that McClellan (*17*) has recovered *H. capsulatum* from five dogs from the Lexington, Ky.,

area in a period of about 2 years. These sick dogs were referred to him by veterinarians and dog owners and, therefore, represented a selected group.

Summary

A search for *H. capsulatum* was made on 303 dogs collected in the Louisville, Ky., area between March 1950 and January 1951. No selection of dogs was made with the exception that all dogs suspected of being infected with the rabies virus and those weighing 100 or more pounds were excluded.

The direct microscopic examination of stained bone marrow smears and splenic impressions failed to reveal the fungus in the 303 dogs. Cultures of bone marrow and portions of spleen from these dogs failed to yield organisms resembling *H. capsulatum* when incubated on a modified Sabouraud's medium at room temperature for 1 month.

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Relative Pathogenicity of Certain *Salmonella* Strains for Man and Mice

By Norman B. McCullough, Ph.D., M.D.*

During a study of the pathogenicity for man of certain *Salmonella* strains, the minimal infective dosage for man of a number of species and strains was determined. An opportunity was thus afforded to determine the relative pathogenicity of these species and strains for man and mice.

Materials And Methods

The materials and methods employed in the study on experimental human salmonellosis have been previously described and the results presented in detail (*1–4*). The *Salmonella* strains employed were obtained from spray-dried whole egg and were isolated by the Bureau of Agricultural and Industrial Chemistry, U. S. Department of Agriculture. The ID_{50} of these strains for mice was determined according to the procedure of Reed and Muench (*5*). The organisms were grown for 24 hours on trypticase-soy agar (B–B–L). The growth was suspended in saline and the resulting suspensions were standardized turbidimetrically. Decimal dilutions were prepared in saline and the calculated dosages were injected intra-abdominally into mice. At the same time, decimal dilutions of each inoculum were cultured in duplicate on trypticase-soy-agar medium for determination of bacterial count. Adult white mice weighing approximately 20 grams each were employed. The mice were obtained from a colony maintained at the laboratory for several years without clinical or bacteriological evidence of *Salmonella* infection. Fifty mice were used for each strain with groups of 10 receiving the same dosage. At the end of 2 weeks, surviving mice were sacrificed and the liver, spleen, and heart's blood were cultured on SS agar (Difco). Some of the mice died prior to the expiration of the 2-week period. In culturing these carcasses, portions of liver and spleen were also cultured in tetrathionate broth (Difco) containing brilliant green 1/100,000 and subsequently subcultured on SS agar medium. The resulting isolates were identified by the usual procedures and specifically typed according to the Kauffmann-White schema.

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Results

The table presents the strains according to the dosages which produced illness in man and the ID_{50} for mice. It is clearly apparent that the ID_{50} for mice of these strains is in no way correlated with the dosage producing disease in man. Most of the strains did not kill mice even in dosages as large as 100 million; hence the LD_{50} was not determined. Exceptions to this were *Salmonella newport* and *Salmonella derby*. With *S. newport*, of eight infected mice in a group of ten, there were three deaths at a dosage of 11.7 million. Seven of nine infected mice receiving 121 million organisms died. With *S. derby*, of ten mice infected at a dosage of 141 million organisms, there were three deaths. None of the other strains produced death in any mice at dosages up to 100 million or slightly greater.

Discussion

Several strains of *Salmonella pullorum* were studied in the human experiments, but no data for these strains are included in this report. Although *S. pullorum* was recovered from some mice at all levels employed, even with a dosage of 10,000 organisms, recovery was so irregular that a satisfactory ID_{50} for these strains could not be obtained. Furthermore, the human volunteers employed in the studies had all received typhoid immunization, some of them on repeated occasions. As the dosage of *S. pullorum* required to produce illness in these subjects was markedly greater than for any of the other species, one may question whether, in view of the somatic antigenic similarity of *S. pullorum* and *Salmonella typhosa*, significant

Showing relative pathogenicity of certain Salmonella *strains for man and mice*

Organism	Clinical illness in man		ID_{50} for mice in millions of organisms
	Dosage in millions of organisms	Fraction of group becoming ill	
S. meleagridis, Strain I	24	1/5	119
	50	4/6	
S. meleagridis, Strain II	10	1/6	9
	20	2/6	
	41	5/6	
S. meleagridis, Strain III	7.7	1/6	103
	10	2/6	
S. anatum, Strain I	.59	2/6	17
	.86	3/6	
S. anatum, Strain II	44.5	1/6	7.8
	67.2	4/6	
S. anatum, Strain III	1.2	2/6	7.6
	4.7	4/6	
S. newport	.15	1/6	.92
	.38	2/6	
	1.3	3/6	
S. bareilly	.12	1/6	59
	.69	2/6	
	1.7	4/6	
S. derby	15	3/6	.39

immunity may have been conferred against *S. pullorum* by such immunization. The infective dosages of *S. pullorum* for man thus determined may not be comparable to those obtained with the other species.

The relatively large dosages of most of these strains which were required to infect mice are of interest. This may be a reflection of the previous history of the cultures which were obtained from spray-dried egg and hence presumably were fowl-adapted strains.

The routes used to produce infection in man and mice were necessarily different, but both were those which would normally be employed. Likewise, the infections cannot be regarded as comparable.

It is interesting to speculate whether the lack of relationship of the pathogenicity for man and mice shown here is peculiar to the strains in question, or whether strains from other sources, particularly mouse-adapted strains, might behave differently.

Summary

The pathogenicity for man of three strains each of *Salmonella meleagridis* and *Salmonella anatum* and one strain each of *S. newport*, *Salmonella bareilly*, and *S. derby* were determined by administering these organisms to human volunteers. The ID_{50} for mice, using the intra-abdominal route, was determined for each strain. There was no apparent relationship between the pathogenicity of these strains for human volunteers and the ID_{50} for mice.

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Plague in the Territory of Hawaii

II. Plague Surveillance, Hamakua District, Island of Hawaii

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The current status of plague infection in the Island of Hawaii has recently been published (*1*), and the routine plague surveillance program is discussed in this report. The program was established to determine when plague infection is present in rodents and their ectoparasites and where it is found.

In the Hamakua coast region plague surveillance activities are currently conducted in an area approximately 3 to 5 miles wide extending from the village of Ookala, located 32 miles northwest of the port of Hilo, to Waipio Valley 20 miles beyond Ookala. The upper or mountain-side limit of this narrow plague infected coastal region roughly follows the 2,000-foot elevation contour. The area below this level slopes sharply towards a rugged, almost vertical, pali or cliff which drops off abruptly to the sea. There are many gorges or gulches which tortuously make their way down toward the ocean. Many of these gulches, which are deep and precipitous, have been produced by, and are subject to, flash streams. They are heavily covered with vegetation, are difficult of access, and afford ample food and harborage for rodents.

Sugar cane is cultivated extensively throughout the region. Approximately 20,000 acres are planted in cane. These fields border on plantation communities and villages and extend to the edges of the gulches. The dense growths of the mature sugar cane furnish ideal harborage for rodents and a preferred type of food is available continuously until the field is harvested. At harvest time, usually 18 to 22 months from planting, rodents migrate to adjacent canefields or to the gulches.

According to the preliminary figures of the 1950 census, the number of persons residing in the Hamakua District is 5,973. The population living in the region are Filipinos, Japanese, Chinese, Hawaiians, part Hawaiians, and Caucasians. The majority live in small villages or plantation communities located below an elevation of 1,500 feet. The villages are essentially rural and, in most instances, they are contiguous to rodent infested canefields, gulches, or woodlands.

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Four species of rats are found in the Hamakua region. These are *Rattus hawaiiensis* Stone, *Rattus rattus rattus* (Linn.), *Rattus rattus alexandrinus*[1] (Geoffroy), and *Rattus norvegicus* (Erxleben). One mouse species is present, *Mus musculus* Linn. Plague infection has been determined in each of the above named species. As far as is known, no other rodent species is present which plays an active role in the transmission of plague in this region. The mongoose, *Herpestes javinicus auropunctatus* (Hodgson), is present in fairly large numbers. Although one trapped specimen was proved to be naturally infected with *Pasteurella pestis* by Passed Assistant Surgeon George W. McCoy, United States Public Health and Marine Hospital Service, in February 1912, no additional evidence is available that this animal actively figures in the transmission of plague infection in Hawaii.

Seven species of fleas are known to occur in the Territory of Hawaii all of which are present in the Hamakua region. These are *Xenopsylla cheopis* (Rothschild), *Ctenocephalides felis* (Bouché), *Nosopsyllus fasciatus* (Bosch), *Echidnophaga gallinacea* (Westw.), *Leptopsylla segnis* (Schönherr), *Pulex irritans* Linn, and *Xenopsylla hawaiiensis* Jordan. Augustson(*2*)has recently shown that this species is apparently identical with a species from Australia, *Xenopsylla vexabilis*, previously described by Jordan, and has reduced *X. hawaiiensis* to a synonym. The role played by fleas in plague transmission in Hawaii was discussed by Eskey (*3*), who concluded, primarily on epidemiological grounds, that *X. cheopis* and *X. hawaiiensis* Jordan were the principal insect vectors of plague in Hawaii.

Methods

The over-all goal of the plague surveillance and suppressive programs of the Bureau of Rodent Control of the Territorial Department of Health is to provide the people of this region and of the Territory with the maximum protection that is practicable against plague infection (*1*). Therefore, in the interests of the persons residing in the Hamakua region, surveillance and control efforts are currently directed toward those areas in, and immediately adjacent to, villages and plantation communities. The rodents which are examined for evidence of plague infection are obtained by trapping, gassing, and clubbing, or, they are found dead.

Approximately 5,000 snap traps are operated on a daily basis. About a third of this number is set within the communities. The remainder is utilized to make up fixed trap lines which extend about the

[1] Some authors distinguish between the Gray Bellied Roof Rat, *Rattus rattus alexandrinus* (Geoffroy) and the White or Lemon-Yellow Bellied Tree Rat, *Rattus rattus frugivorus* Rafinesque. These forms are considered to be subspecies of the Black Rat, *Rattus rattus* (Linn.). In Hawaii, these three forms have similar habits and are not infrequently found inhabiting the same nest. For practical reasons and because of the intergrading of belly-coloration, all gray and varicolored forms are classified as *R. r. alexandrinus* (Geoffroy) to distinguish them from the readily separated Black Rat, *Rattus rattus rattus* (Linn.).

periphery of the villages and camps. At the present time, rat snap traps are used almost exclusively. Each trap has a number painted on it and is treated with a wood preservative to protect it. The springs are lubricated with grease at frequent intervals to insure instantaneous snapping of the striker bow. These treatments do not appear to have any deterrent effect on the rodent catch.

Servicing of the trap lines begins at 6 a. m. so that trapped rodents may be retrieved as quickly as possible before they can be eaten or mangled by the mongoose which is diurnal in habit. Traps are baited with pieces of coconut meat approximately 1 inch square. An area of about 1 foot square is cleared adjacent to each trap station. After the trap is set, it is placed in the center of the cleared area and then tied securely with cord to a tree, bush, or some other stationary object. The traps which make up the lines that encircle the villages and camps are spaced 35 to 50 feet apart. Poison bait stations are located in between at equal intervals. The trapper in checking his line makes certain that the traps are in good working condition, resets the traps which have been sprung, and replaces missing or stale bait. The trapper carries with him a supply of cardboard tags which have been stamped with the number and letter of his trapping district. These tags also bear a rodent number which is one of a monthly series assigned to each man. When a rodent is caught, the trap number, the species, and sex are recorded on the tag which is then tied to the animal's leg. Pertinent details are entered in the trapper's field notebook and later transcribed to a daily rodent retrieval form. In this manner, it is possible to know exactly where every rodent is retrieved.

Considerable caution is exercised in the handling of dead rodents. The men do not touch the animals but free them by picking up the trap by the base and releasing the striker, allowing the rodent to fall into the particular type of receptacle that they are utilizing that day. On the days the rodents from a trapper's district are to be combed for fleas, the retrieved rodents are placed in a small paper bag in the field. One-quarter teaspoon of calcium cyanide is added to the bag, which is shaken and then tied tightly at the neck with string. This operation is conducted for two reasons: (1) To kill the fleas and to prevent them from escaping in transit, and (2) to protect workers in the laboratory. If the rodents from a trapper's district are not being used for flea combing on any given day, they are placed in gallon cans containing kerosene.

From time to time dead rodents are found in the plague infected region. Most of these are discovered by the men engaged in plague surveillance and suppressive activities. A few dead rodents are found by plantation workers or other members of the community and are reported to the local health office. The people of the region

have been thoroughly indoctrinated with the importance of not touching dead rodents. As a consequence, in nearly every instance a staff member, exercising adequate precautions, recovers the rodent.

The retrieval of rodents by gassing and clubbing, the management of poison stations located between traps, and other plague control measures will be discussed in a third article in this series.

The daily rodent retrieval is brought to the local plague laboratory, and all rats in good condition are dissected and examined macroscopically by experienced observers for evidence of plague infection. Special care is taken to note the condition of the liver, spleen, lungs, lymph glands, and subcutaneous blood vessels. When gross changes are observed, smears of suspected tissues or organs are stained with Wayson's stain and examined microscopically for the presence of bipolar staining plague-like organisms. The presence of plague-like organisms in the microscopical field together with the gross changes observed at autopsy are considered to be only a provisional diagnosis of plague infection. This procedure lends a basis for further suspicion and provides a quick check on possible active rodent plague infection. The failure to observe these organisms in the microscopic field is not held to be conclusive evidence of the absence of plague.

Following the microscopical examination of smears, suspect material is streaked on MacConkey's agar which is incubated at 20°–28° C. for 48 hours. Suspicious colonies are fished for further bacteriological investigation. At the same time, portions of the liver, spleen, heart, lymph glands, and lungs are triturated in normal saline and inoculated into a guinea pig. When the guinea pig becomes ill and dies within a 10-day period and typical plague-like lesions are noted at autopsy, or if bipolar staining organisms are seen in stained smears, a presumptive diagnosis of plague is made. If the guinea pig does not die within the 10-day period, it is sacrificed and then examined.

To confirm a presumptive diagnosis of plague, *P. pestis* is cultured and identified by biochemical tests. Currently, no reports of final diagnosis of positive plague infection are issued unless the provisional and presumptive diagnoses have been confirmed bacteriologically by the Bureau of Laboratories of the Territorial Department of Health. Complete reports on all rodent or rodent-flea plague infections are immediately forwarded to Federal health authorities and to local military commands.

Even though no gross evidences of plague infection are noted, rats and mice found dead or dying are treated as suspicious for plague and tissues from these animals are examined according to the above procedures. Decomposed or mummified rodents are not regularly utilized for inoculations because of the inherent difficulty of obtaining a satisfactory inoculum.

At regular intervals tissue is removed from groups of 15 to 20 rats

retrieved from the same trap line within a work zone and, after pooling and triturating in normal saline, is used to make a mass rat tissue inoculation into a guinea pig.

At the present time, approximately 20 mass mice tissue inoculations are undertaken each month. These inoculations are similar to those described for mass rat tissues. Mice are not regularly autopsied because of the time consumed in examining large numbers of small animals. Although plague infection has been detected in 24 out of 620 mice found dead and in 3 out of 688 mass mice tissue pools since 1940, it is generally considered that they play a relatively unimportant role in the spread of plague (*4*).

Systematic combing of rodents for fleas is carried on as a further check on the presence and distribution of plague infection in the region. The fleas, so obtained, are pooled by rodent species and by individual trap line, comminuted in normal saline, and inoculated subcutaneously into guinea pigs. These are known as "mass flea inoculations." The known endemic plague region is divided into six sections and although all sections are trapped daily, only the rodents retrieved in three sections are combed for fleas each day. This work is rotated to provide regular and progressive coverage of the entire region. In addition, the rodents retrieved in the zones on both sides of the North Hilo District boundary (*1*) are combed daily for fleas to determine if the plague region has been correctly delimited.

Discussion

The percentage of rats autopsied was consistently high for each calendar year during the period 1940 to 1950, as shown in table 1.

Table 1. *Number of rats retrieved and autopsied*

Calendar year	Number retrieved	Number autopsied	Percent autopsied	Retrieval method of autopsied rats		
				Trapped	Killed	Found dead
1940	32,306	30,038	93.0	25,914	2,229	1,895
1941	42,517	37,966	89.3	34,727	1,855	1,384
1942	55,597	50,365	90.6	45,603	3,922	839
1943	55,320	51,252	92.6	47,946	2,895	411
1944	38,727	35,168	90.8	31,518	3,482	168
1945	38,702	34,246	88.5	32,731	1,467	48
1946	19,556	19,115	97.7	18,599	486	30
1947	23,708	23,116	97.5	22,052	1,025	39
1948	18,908	18,676	98.8	17,556	1,097	23
1949	17,201	16,956	98.6	15,505	1,407	44
1950	13,496	13,431	99.5	12,656	758	17
Total	356,038	330,329	92.8	304,807	20,623	4,898

Of all the rats retrieved 92.8 percent were in a satisfactory condition and were autopsied for gross evidences of plague infection The remainder (7.2 percent) were partially eaten by mongooses, decom-

posed, or mummified and could not be autopsied satisfactorily. These figures represent a maximum practical effort to detect plague in the Hamakua region by this initial screening method.

The total trapped rats autopsied is numerically large compared to the number killed or found dead. The number varies from year to year, a fact attributable to fluctuations in rat populations, to the number of personnel available for the program, and to the degree of effort devoted to trapping activities. Variations in the number of rats killed are traceable to the emphasis placed on the gassing of burrows and rockpiles during any given period. The number of rats found dead each year also varies considerably, due in part to the same factors mentioned above for trapped and killed rats. During the period 1940 to 1944, when the incidence of plague infection in rats was high, intensive poison activities were conducted and special organized searches for dead rodents over wide areas were made. Such was not the case during the period 1945 to 1950.

When one examines plague infection in relation to the method by which the infected rats were retrieved (table 2), it immediately becomes apparent that the greatest number of infections were detected in individual rats found dead. By comparison, only a small portion of individual rats which were killed or trapped was found to be plague-infected. This may be due to the fact that sick or dying rats are usually not very active and cannot be flushed easily from burrows or taken by traps.

The autopsying of trapped rats has not resulted in the detection of a large amount of plague infection in Hamakua. Only 20 plague infections were detected in 304,807 trapped rats which were autopsied. The difficulties of detecting the plague organism by this method have previously been noted (*5*, *6*, *7*). However, it should be borne in mind that in addition to obtaining rodents for autopsy in the labo-

Table 2. *Plague infection detected in individual autopsied rats*

Calendar year	Total positive	Retrieval method					
		Trapped		Killed		Found dead	
		Number autopsied	Number positive	Number autopsied	Number positive	Number autopsied	Number positive
1940	53	25,914	2	2,229	3	1,895	48
1941	74	34,727	0	1,855	5	1,384	69
1942	122	45,603	7	3,922	7	840	108
1943	68	47,946	4	2,895	4	411	60
1944	42	31,518	4	3,482	0	168	38
1945	17	32,731	1	1,467	1	48	15
1946	6	18,599	1	486	0	30	5
1947	5	22,052	1	1,025	0	39	4
1948	2	17,556	0	1,097	0	23	2
1949	12	15,505	0	1,407	3	44	9
1950	0	12,656	0	758	0	17	0
Total	401	304,807	20	20,623	23	4,899	358

ratory, there are other important factors associated with the operation of trap lines. These are:

1. The men who check the trap lines pay special attention to the finding of dead rodents. Since the greatest number of plague infections have been detected in rodents found dead, every such rodent retrieved is regarded as particularly suspicious for plague and by this means, a continuous appraisal is made of the status of plague infection in and around villages and plantation camps. When a dead rodent is found and the laboratory makes a provisional diagnosis of plague, expeditious initiation of intensive plague suppressive measures becomes possible.

2. Trapped rodents are not only subjected to individual autopsy, but tissues are taken from them to make mass tissue inoculations. These rodents are also combed for fleas which are used to make mass flea inoculations. In this manner both rodent tissues and fleas are obtained from large numbers of animals over a wide area associated with human habitation and are available continuously for guinea pig inoculations.

3. Of 974,240 rodents retrieved (356,038 rats and 618,202 mice) during the period 1940 to 1950, more than 90 percent were obtained by traps. The trapping of nearly a million rodents in a 10-year period must have had some effect on the total rat population.

From table 3 it will be noted that during the years 1940 to 1950, 11 positive plague infections were detected among 2,153 mass rat tissue inoculations. Although there has been a decided increase in efforts to determine plague by mass tissue inoculation since 1946, there has been no corresponding increase in the number of infections detected. The lack of increase in plague detection by this method is difficult to evaluate for the years 1946 to 1950 as this was a quiescent period with the exception of one minor plague outbreak. An important

Table 3. *Plague infection detected by mass tissue inoculation*

Calendar year	Number rats autopsied	Number of rats contributing	Percent total autopsied	Mass tissue inoculations	
				Number of mass tissue inoculations	Number positive
1940	30,038			143	3
1941	37,966			36	0
1942	50,365	0	0.0	0	0
1943	51,252			4	0
1944	35,168	1,377	3.9	28	2
1945	34,246	1,877	5.5	46	1
1946	19,115	6,811	35.6	219	2
1947	23,116	8,339	36.1	271	2
1948	18,676	4,289	23.0	144	0
1949	16,956	8,407	49.6	459	0
1950	13,431	8,626	64.2	803	1
Total	330,329			2,153	11

Table 4. *Plague infection detected by mass flea inoculation*

Calendar year	Number fleas contributing	Mass flea inoculations	
		Number flea inoculations	Number positive
1941 [1]	2,606	58	5
1942	2,821	30	3
1943	759	14	0
1944	2,096	36	2
1945	2,459	62	2
1946	434	32	0
1947	1,725	137	1
1948	624	76	0
1949	2,267	183	6
1950	1,668	202	2
Total	17,459	830	21

[1] Mass flea inoculations not accomplished routinely prior to January 1941.

factor to consider from the standpoint of plague surveillance, however, is that in 1946 the procedure was established whereby tissue was taken from a much larger proportion of the total rats autopsied. This tissue was utilized in a greater number of mass tissue inoculations in a constant attempt to detect inapparent plague in rats retrieved in, and adjacent to, habitable areas located throughout the entire plague infected Hamakua region.

Plague was demonstrated in rat fleas 21 times in 830 mass flea inoculations as shown in table 4. Flea inoculations were first attempted routinely in the Hamakua region in January 1941. From this date until the latter part of 1946, the majority of the fleas utilized for such inoculations were obtained from rats cage-trapped in the peripheral areas of the region or from limited selected areas where plague foci were known to exist. In January 1947 this activity was reorganized and rats caught in snap traps throughout the entire region were combed for fleas and lice so that the scope and magnitude of the program to detect plague in rodent fleas was augmented (*8*). This intensified program did not result in the determination of an increased amount of plague.[2] Inasmuch as mass flea inoculation is generally considered to be a sensitive method of detecting plague infection (*9*), the lack of an increase in the number of infections detected in rat fleas may possibly be attributed to a low incidence of plague during this period.

In 1949 plague infection was detected six times by mass flea inoculation between February and August. These positive flea pools gave early warning of a possible reactivation of the infection throughout the region. During the following 3 months, plague was demonstrated in nine dead rats and one dead mouse, and in three killed

[2] From June 1947 to December 1950 a total of 140 mass lice pools were made involving 2,223 lice. All lice pools have proved negative for plague.

rats. In November a single human case was reported, the first in 4 years.

Summary

1. The immediate aim of the plague surveillance program conducted in the endemic plague region in Hamakua, Hawaii, is the determination of when plague infection is present in rodents and their ectoparasites and where it occurs.

2. Descriptions of the field and laboratory procedures employed in this plague detection program are given.

3. During the period 1940 to 1950, plague infections were detected in 460 rodents and their ectoparasites. Of this number, 358 were detected in rats found dead, 23 in killed rats, 20 in trapped rats, and 24 in mice found dead. In addition, 11 infections were determined by mass rat tissue inoculation, 3 by mass mice inoculation, and 21 by mass flea inoculation.

4. Emphasis is placed on the importance of finding dead rodents in and adjacent to communities, as the greatest number of plague infections were detected in rats found dead.

5. Since 1946 the effort to detect plague in rodents and rodent ectoparasites by means of mass tissue and mass flea inoculations has been greatly increased in and adjacent to habitable areas.

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Industrial Sickness Absenteeism Among Males and Females During 1950

With Index of the Previous Publications of the Series

By W. M. Gafafer, D.Sc.*

This report presents data on sickness absenteeism among male and female employees during the year 1950 and earlier years. The data are obtained from a group of reporting organizations comprising mutual sick benefit associations, group health insurance plans, and company relief departments and are limited to sickness and nonindustrial injuries causing absence from work for 8 consecutive calendar days or longer. Quarterly reports for 1950, based on the male experience of the reporting organizations have appeared (*1*, *2*). The last published report on both males and females was for the year 1949 (*1*).

Year, 1950. Table 1 presents frequency rates by cause for male and female workers during 1950 and comparable data for 1949 and the 10-year period 1941–50. During the year 1950, all sickness and nonindustrial injuries disabling for 8 consecutive calendar days or longer resulted in frequency rates of 116.8 per 1,000 males and 258.4 per 1,000 females.

Among males, the 1950 rate (116.8) is less than 1 percent below the 10-year average (117.7). For certain causes of disability, however, greater changes in frequency may be noted. The 1950 rates for the following causes are more than 25 percent above their 10-year averages: cancer, 83 percent above; diseases of the heart, 32 percent; diseases of genitourinary system, 31 percent; hernia, 29 percent; and other diseases of nervous system, 28 percent. Diseases occurring more than 25 percent below the 10-year averages are: influenza and grippe, 36 percent below; diseases of pharynx and tonsils, 33 percent; and tuberculosis of the respiratory system, 29 percent.

Among females, the 1950 rate (258.4) is 13 percent above the 10-year average (229.3). Attention is directed to the increase in the rate for cancer, and the decrease in tuberculosis of the respiratory system.

Postwar Down-trend. A downward trend of male sickness absenteeism began in the postwar period; the absenteeism rate for 1950, however, is somewhat above the rate for 1949 and

*From Division of Occupational Health, Public Health Service.

Table 1. *Annual number of absences per 1,000 persons on account of sickness and non industrial injuries disabling for 8 consecutive calendar days or longer, by cause: experience of male and female employees in various industries, 1950, 1949, and 1941–50, inclusive* [1]

Cause [2]	Annual number of absences per 1,000 persons beginning in specified period					
	Males			Females		
	1950	1941–50 [3]	1949	1950	1941–50 [3]	1949
Sickness and nonindustrial injuries	116.8	117.7	95.5	258.4	229.3	254.5
Percent of female rate	45	51	38			
Percent of male rate				221	195	266
Nonindustrial injuries (169–195)	13.7	12.1	10.9	19.3	16.2	18.5
Sickness	103.1	105.6	84.6	239.1	213.1	236.0
Respiratory diseases	34.1	43.2	27.0	106.1	93.8	98.2
Tuberculosis of respiratory system (13)	.5	.7	.7	.2	.5	.9
Influenza, grippe (33)	10.9	17.0	8.0	30.7	31.9	24.6
Bronchitis, acute and chronic (106)	5.9	6.9	4.4	11.6	10.7	12.1
Pneumonia, all forms (107–109)	5.4	5.1	4.0	5.4	3.5	5.5
Diseases of pharynx and tonsils (115b, 115c)	3.2	4.8	3.4	13.1	15.7	15.9
Other respiratory diseases (104, 105, 110–114)	8.2	8.7	6.5	45.1	31.5	39.2
Digestive diseases	20.1	17.9	16.8	28.5	30.3	27.9
Diseases of stomach except cancer (117, 118)	6.2	5.7	5.3	3.7	3.4	3.6
Diarrhea and enteritis (120)	2.6	2.2	2.1	7.3	5.8	6.9
Appendicitis (121)	4.1	4.2	3.5	7.2	12.3	7.8
Hernia (122a)	3.1	2.4	2.7	1.0	.6	.5
Other digestive diseases (115a, 115d, 116, 122b–129)	4.1	3.4	3.2	9.3	8.2	9.1
Nonrespiratory-nondigestive diseases	45.3	40.9	38.5	100.4	84.2	105.3
Infectious and parasitic diseases (1–12, 14–24, 26–29, 31, 32, 34–44) [4]	3.0	2.6	2.2	9.8	6.0	9.2
Cancer, all sites (45–55)	1.1	.6	.8	1.1	.6	.8
Rheumatism, acute and chronic (58, 59)	3.6	4.5	3.8	4.5	4.3	5.2
Neurasthenia and the like (part of 84d)	1.5	1.8	1.6	12.2	11.3	11.1
Neuralgia, neuritis, sciatica (87b)	2.1	2.6	2.0	3.3	2.9	3.8
Other diseases of nervous system (80–85, 87, except part of 84d, and 87b)	2.3	1.8	1.8	3.7	1.9	3.0
Diseases of heart (90–95)	5.4	4.1	4.4	2.3	2.3	3.0
Diseases of arteries and high blood pressure (96–99, 102)	2.3	2.0	2.0	1.6	1.3	1.4
Other diseases of circulatory system (100, 101, 103)	4.8	3.9	3.8	6.7	5.7	8.0
Nephritis, acute and chronic (130–132)	.4	.4	.4	.3	.4	.6
Other diseases of genitourinary system (133–139)	4.2	3.2	3.3	23.5	19.0	26.5
Diseases of skin (151–153)	3.6	3.4	3.1	5.3	5.4	5.6
Diseases of organs of movement except diseases of joints (156b)	3.5	3.4	2.8	7.4	5.5	7.5
All other diseases (56, 57, 60–79, 88, 89, 154, 155, 156a, 157, 162)	7.5	6.6	6.5	18.7	17.6	19.6
Ill-defined and unknown causes (200)	3.6	3.6	2.3	4.1	4.8	4.6
Average number of persons	173,881	2,384,914	210,494	14,113	215,267	15,116

[1] Industrial injuries and venereal diseases are not included.
[2] Numbers in parentheses are disease title numbers from International List of Causes of Death, 1939.
[3] Average of the 10 annual rates.
[4] Exclusive of influenza and grippe, respiratory tuberculosis, and venereal diseases.

may be the beginning of an upswing. This increase in frequency was participated in by each of the broad cause groups: respiratory diseases, nonrespiratory-nondigestive diseases, digestive diseases, and nonindustrial injuries. The female rate in the postwar period, on the other hand, has described generally a level trend with only a slight increase in the rate for 1950. The increase in sickness frequency during 1950 is in agreement with past experiences when higher sickness rates occurred in periods of increased industrial activity.

Index of the Reports, 1920–50. To expedite the locating of a particular number of the PUBLIC HEALTH REPORTS covering industrial sickness for a definite period of time, the following chronological index is presented:

Time period covered	Public Health Reports, date of issue
First 6 months, 1920	Dec. 3, 1920
First 9 months, 1920	Mar. 4, 1921
Year 1920	July 1, 1921
January 1920-June 1921	Jan. 6, 1922
Year 1921	Dec. 29, 1922
Years 1920–23	Oct. 31, 1924
Years 1922–24	Jan. 22, 1926
Years 1921–27	Feb. 22, 1929
Years 1921–28	Jan. 17, 1930
First quarter, 1929	Sept. 13, 1929
Second and third quarters, 1929	Feb. 14, 1930
Fourth quarter, 1929	May 23, 1930
First and second quarters, 1930	Oct. 24, 1930
Third and fourth quarters, 1930	Apr. 3, 1931
First quarter, 1931	July 31, 1931
Second quarter, 1931	Oct. 16, 1931
Third quarter, 1931	Jan. 15, 1932
Fourth quarter, 1931	Apr. 29, 1932
Years 1921–31	Apr. 29, 1932
First quarter, 1932	July 15, 1932
Second quarter, 1932	Nov. 25, 1932
Third quarter, 1932	Dec. 16, 1932
Fourth quarter, 1932	Mar. 31, 1933
Years 1927–32	July 28, 1933
First quarter, 1933	July 7, 1933
Second quarter, 1933	Sept. 29, 1933
Third quarter, 1933	Jan. 12, 1934
Fourth quarter, 1933	Mar. 30, 1934
Years 1928–33	May 25, 1934
First quarter, 1934	June 29, 1934
Second quarter, 1934	Oct. 19, 1934
Third quarter, 1934	Jan. 25, 1935
Fourth quarter, 1934	Apr. 26, 1935
Years 1929–34	Nov. 1, 1935
First quarter, 1935	Aug. 23, 1935
Second quarter, 1935	Nov. 15, 1935
Third quarter, 1935	Jan. 31, 1936
Fourth quarter, 1935	May 22, 1936
Years 1930–35	Jan. 1, 1937
First quarter, 1936	July 24, 1936
Second quarter, 1936	Dec. 4, 1936
Third quarter, 1936	Jan. 29, 1937
Fourth quarter, 1936	Apr. 30, 1937
Years 1931–36	Sept. 17, 1937
First quarter, 1937	Aug. 27, 1937
Second quarter, 1937	Oct. 29, 1937
Third quarter, 1937	Jan. 14, 1938
Fourth quarter, 1937	Apr. 8, 1938
Years 1932–37	Sept. 2, 1938
First quarter, 1938	Sept. 2, 1938
Second quarter, 1938	Oct. 28, 1938
Third and fourth quarters, 1938	Apr. 28, 1939
Years 1921–38, by triennia	May 31, 1940
First quarter, 1939	Aug. 25, 1939
Second quarter, 1939	Oct. 20, 1939
Third quarter, 1939	Jan. 5, 1940
Fourth quarter, 1939	Apr. 12, 1940
Year 1939	Aug. 2, 1940
First quarter, 1940	Aug. 2, 1940
Second quarter, 1940	Nov. 15, 1940
Third quarter, 1940	Dec. 27, 1940
Fourth quarter, 1940 (with index)	Apr. 11, 1941
Year 1940	Sept. 12, 1941
First quarter, 1941	Sept. 12, 1941
Second quarter, 1941	Oct. 17, 1941
Third quarter, 1941	Dec. 19, 1941
Fourth quarter, 1941	Apr. 17, 1942
Year 1941	Sept. 4, 1942
First quarter, 1942	Sept. 4, 1942
Second quarter, 1942	Oct. 23, 1942
Third quarter, 1942	Feb. 5, 1943
Fourth quarter, 1942	Apr. 23, 1943
Years 1933–42	Aug. 13, 1943
First quarter, 1943	Aug. 20, 1943
Second quarter, 1943	Dec. 24, 1943
Third quarter, 1943	Mar. 17, 1944
Fourth quarter, 1943	May 12, 1944
Year 1943	Sept. 29, 1944
First and second quarters, 1944	Sept. 29, 1944
Third quarter, 1944	Feb. 9, 1945
Fourth quarter, 1944	June 1, 1945
Year 1944	Sept. 7, 1945
First quarter, 1945	Sept. 7, 1945
Second quarter, 1945	Oct. 5, 1945
Third and fourth quarters, 1945	July 26, 1946
Year 1945	Nov. 8, 1946
First quarter, 1946	Nov. 15, 1946
Second and third quarters, 1946	Feb. 21, 1947
Fourth quarter, 1946	July 25, 1947
Years 1937–46	Oct. 24, 1947
First and second quarters, 1947	Dec. 19, 1947
Third and fourth quarters, 1947	May 21, 1948
Year 1947	Nov. 12, 1948
First and second quarters, 1948	Nov. 12, 1948
Third and fourth quarters, 1948	May 20, 1949
Year 1948	Oct. 28, 1949
First and second quarters, 1949	Oct. 28, 1949
Third and fourth quarters, 1949	June 23, 1950
Year 1949	Nov. 24, 1950
First and second quarters, 1950	Nov. 24, 1950
Third and fourth quarters, 1950	June 15, 1951
Year 1950	Present report

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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 November 3, 1951

In the United States meningococcal meningitis has been occurring in epidemic waves at intervals of 6 to 12 years during the past five decades. Since 1925 there have been three major epidemic periods centering in the years 1929, 1935, and 1943. Following 1943 there was a steady decrease in the numbers of cases and deaths, but in 1950 there was a slightly greater number of cases than for the preceding year. The number reported (3,495) for the first 44 weeks of 1951 is in excess of that (3,207) for the same period of 1950. This suggests that another period of increased incidence of meningococcal meningitis may be in the offing.

Between 1925 and 1930 there were two cases reported for every death registered. The advent of sulfonamide therapy after 1935 had little effect on the ratio. During the epidemic wave of 1943 and 1944, the ratio of cases to deaths increased to 6:1, but since that time the number of cases reported for each death has decreased to about 4:1. The institution of new and better therapeutic agents and possibly an improvement in completeness of reporting probably have been the most important factors in the changes in ratio of cases to deaths.

Since the seasonal low point of the disease early in September, the proportion of cases which have been reported in the various geographical regions has corresponded generally with the distribution of population—i. e., there has been no concentration of cases in any one part of the country except for the East South Central States. Tennessee has reported a large proportion of the cases.

Of the 34 cases of malaria in civilians, 24 were reported by Wisconsin. A civilian case, reported previously by Missouri for the week ended September 22, upon investigation was found to be a vivax type of infection. The patient had no previous history of malaria and had not been outside Missouri during her lifetime. She had not been more than 15 miles from her home in St. Louis during the past 2 years. Information on 121 cases of malaria reported in Texas for the first 6 months of 1951 indicates that 32 were confirmed by examination of blood smears.

Gastroenteritis

Dr. M. B. Goodman, New York State Health Department, has reported an outbreak of gastroenteritis among employees of an industrial plant located on Long Island. Some had an illness in which gastrointestinal symptoms predominated, and others had acute upper respiratory infection. Cases were evenly distributed throughout the various shops. Most of the cases had their onset within a period of 3 days. No explosive characteristics were noted, and person-to-person contact is regarded as the mode of spread.

Dr. Goodman reported an outbreak of Sonne dysentery which occurred in a State hospital. Sixty patients out of a susceptible population of 140 developed symptoms of diarrhea over a period of 3 weeks. A Sonne type of organism was cultured from the stools of 17. All patients were given a course of sulfadiazine. There were no fatalities. No common source of infection was found.

Comparative Data For Cases of Specified Reportable Diseases: United States

[Numbers after diseases are International List numbers, 1948 revision]

Disease	Total for week ended—		5-year median 1946–50	Seasonal low week	Cumulative total since seasonal low week		5-year median 1945–46 through 1949–50	Cumulative total for calendar year—		5-year median 1946–50
	Nov. 3, 1951	Nov. 4, 1950			1950–51	1949–50		1951	1950	
Anthrax (062)	1	------	------	(1)	(1)	(1)	(1)	50	40	43
Diphtheria (055)	138	171	322	27th	1,349	1,877	3,372	3,357	5,005	7,983
Encephalitis, acute infectious (082)	16	25	15	(1)	(1)	(1)	(1)	[2] 903	841	560
Influenza (480–483)	431	868	868	30th	4,445	6,912	6,912	120,500	145,676	133,876
Measles (085)	2,085	1,315	1,261	35th	[3] 11,384	7,120	7,018	[3] 480,295	295,291	562,393
Meningitis, meningococcal (057.0)	76	41	48	37th	434	408	401	3,495	3,207	2,977
Pneumonia (490–493)	706	1,169	(4)	(1)	(1)	(1)	(1)	51,753	69,921	(4)
Poliomyelitis, acute (080)	803	1,089	879	11th	[5] 24,353	27,777	24,022	[5] 25,565	28,908	24,372
Rocky Mountain spotted fever (104)	2	------	[2]	(1)	(1)	(1)	(1)	320	445	538
Scarlet fever (050) [6]	860	892	1,270	32d	5,719	6,207	8,120	59,105	46,377	64,234
Smallpox (084)	1	2	------	35th	2	3	4	13	29	51
Tularemia (059)	8	11	11	(1)	(1)	(1)	(1)	559	778	820
Typhoid and paratyphoid fever (040, 041) [7]	64	71	71	11th	2,276	2,542	2,930	2,711	3,051	3,415
Whooping cough (056)	1,216	1,673	1,673	39th	4,999	7,582	7,582	58,774	104,777	83,800

[1] Not computed.
[2] Addition: North Carolina, week ended October 20, 1 case.
[3] Addition: Iowa, week ended October 20, 4 cases.
[4] Data not available.
[5] Addition—Iowa, 7 cases, not allocated. Deduction—North Carolina, week ended October 20, 1 case.
[6] Including cases reported as streptococcal sore throat.
[7] Including cases reported as salmonellosis.

Reported Cases of Selected Communicable Diseases: United States, Week Ended Nov. 3, 1951

[Numbers under diseases are International List numbers, 1948 revision]

Area	Diphtheria (055)	Encephalitis, infectious (082)	Influenza (480–483)	Measles (085)	Meningitis, meningococcal (057.0)	Pneumonia (490–493)	Poliomyelitis (080)
United States	**138**	**16**	**431**	**2,085**	**76**	**706**	**803**
New England	**5**		**2**	**248**	**3**	**31**	**7**
Maine	2		2	55	2	16	
New Hampshire				21			
Vermont				29			
Massachusetts	3			103			2
Rhode Island				16	1		1
Connecticut				24		15	4
Middle Atlantic	**5**	**8**	**5**	**686**	**15**	**91**	**79**
New York	4	8	(1)	405	4		53
New Jersey			5	123	4	48	13
Pennsylvania	1			158	7	43	13
East North Central	**7**	**1**	**24**	**531**	**20**	**64**	**168**
Ohio	4			110	2		38
Indiana	3		20	12		5	4
Illinois		1	2	124	5	43	32
Michigan			2	219	4	16	49
Wisconsin				66	9		45
West North Central	**10**	**2**	**6**	**50**	**5**	**78**	**121**
Minnesota	6			9	2	11	23
Iowa	1			3	1		8
Missouri	3	1			2	1	46
North Dakota		1	5	16		59	6
South Dakota				4			1
Nebraska				16			9
Kansas			1	2		7	28
South Atlantic	**53**	**1**	**21**	**199**	**11**	**123**	**44**
Delaware				1	4		1
Maryland			1	87	3	29	1
District of Columbia				15		10	1
Virginia	9			21		41	4
West Virginia	5			32	1		14
North Carolina	18			2	1		4
South Carolina	6		2	2		1	1
Georgia	14		18	28	2	42	17
Florida	1	1		11			1
East South Central	**31**			**28**	**7**	**27**	**61**
Kentucky	3			5	1		
Tennessee	7			6	2		22
Alabama	15			6	1	18	16
Mississippi	6			11	3	9	23
West South Central	**19**		**151**	**29**	**9**	**184**	**71**
Arkansas	4		107	4	2	28	8
Louisiana	1		3			13	8
Oklahoma	4		41	1	1	13	9
Texas	10			24	6	130	46
Mountain	**3**		**127**	**159**		**60**	**83**
Montana	1		14	31			5
Idaho				4			14
Wyoming						3	12
Colorado			3	8		11	19
New Mexico	1			55		32	13
Arizona	1		110	35		14	7
Utah				26			12
Nevada							1
Pacific	**5**	**4**	**95**	**155**	**6**	**48**	**169**
Washington	1		66	28			18
Oregon	1		11	31	2	17	26
California	3	4	18	96	4	31	125
Alaska							
Hawaii			29	433		1	

(1) New York City only.

Reported Cases of Selected Communicable Diseases: United States, Week Ended Nov. 3, 1951—Continued

[Numbers under diseases are International List numbers, 1948 revision]

Area	Rocky Mountain spotted fever (104)	Scarlet fever [1] (050)	Smallpox (084)	Tularemia (059)	Typhoid and paratyphoid fever [2] (040, 041)	Whooping cough (056)	Rabies in animals
United States	**2**	**860**	**1**	**8**	**64**	**1,216**	**122**
New England		**55**			**11**	**211**	
Maine		4			1	6	
New Hampshire		1				11	
Vermont		1				94	
Massachusetts		38			10	95	
Rhode Island		1				1	
Connecticut		10				4	
Middle Atlantic		**125**			**3**	**196**	**24**
New York		71				82	19
New Jersey		21				58	
Pennsylvania		33			3	56	5
East North Central		**234**	**1**		**8**	**269**	**7**
Ohio		74	1		3	64	2
Indiana		14				12	
Illinois		35				45	3
Michigan		86			3	101	2
Wisconsin		25			2	47	
West North Central		**54**		**2**	**6**	**48**	**16**
Minnesota		17				1	13
Iowa		12			1	6	
Missouri		12		2	5	12	1
North Dakota						4	
South Dakota							
Nebraska		4				10	2
Kansas		9				15	
South Atlantic	**1**	**135**			**11**	**104**	**15**
Delaware		1				1	
Maryland		17			1	6	
District of Columbia		9				6	
Virginia		21			5	23	2
West Virginia		8				18	1
North Carolina	1	58			1	25	
South Carolina		3				2	4
Georgia		14			4	8	8
Florida		4				15	
East South Central		**73**		**1**	**2**	**47**	**33**
Kentucky		19				18	14
Tennessee		47				21	9
Alabama		5			1	6	6
Mississippi		2		1	1	2	4
West South Central		**17**		**3**	**9**	**146**	**25**
Arkansas		3		2	1	12	1
Louisiana		1			3	1	
Oklahoma		5			1	16	4
Texas		8		1	4	117	20
Mountain		**38**		**1**	**6**	**118**	**1**
Montana		7		1	3	10	
Idaho		9				7	
Wyoming		4					1
Colorado		6			1	15	
New Mexico		3			2	81	
Arizona		1				5	
Utah		8					
Nevada							
Pacific	**1**	**129**		**1**	**8**	**77**	**1**
Washington		14				4	
Oregon	1	14					
California		101		1	8	73	1
Alaska		4				1	
Hawaii					1		

[1] Including cases reported as streptococcal sore throat [2] Including cases reported as salmonellosis.
Anthrax: California, 1 case. *Psittacosis:* New York City, 2 cases.

FOREIGN REPORTS

CANADA

Reported Cases of Certain Diseases—Week Ended Oct. 20, 1951

Disease	Total	Newfoundland	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia
Brucellosis	6					2	3				1
Chickenpox	609	5		11	4	144	212	22	35	66	110
Diphtheria	8				3	5					
Dysentery, bacillary	10					3					7
Encephalitis, infectious	2							1	1		
German measles	78	3		2		20	11		1	25	16
Influenza	20			17			3				
Measles	518	3		15	2	102	89	12	9	126	160
Meningitis, meningococcal	7	1				1	1	1			3
Mumps	278	3		8	3	42	145	10	22	13	32
Poliomyelitis	74			4	4	17	32	6	3	4	4
Scarlet fever	258	2			1	56	32	32	16	19	100
Tuberculosis (all forms)	343	[1] 101		7	23	100	17	6	8	34	47
Typhoid and paratyphoid fever	8				1	5				2	
Venereal diseases:											
Gonorrhea	301	8		6	21	49	58	28	17	37	77
Syphilis	81	1		5	4	42	15	2	3		9
Primary	6					3	2	1			
Secondary	7				1	5		1			
Other	68	1		5	3	34	13		3		9
Other forms	1										1
Whooping cough	227			1		93	70	9	11	32	11

[1] Includes cases discovered in a recent survey.

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

The following reports include only items of unusual incidence or of special interest and the occurrence of these diseases, except yellow fever, in localities which had not recently reported cases. All reports of yellow fever are published currently.

Smallpox

Cameroon (French). For the period October 1–10, 68 cases (22 deaths) of smallpox were reported in the Benoue Region.

Ceylon. During the week ended October 20, nine cases of smallpox were reported in the Western Province as compared with four for the previous week.

French West Africa. For the period October 11–20, Dahomey and Ivory Coast reported 49 and 12 cases of smallpox, respectively.

Tanganyika. During the week ended October 13, nine cases of smallpox were reported in the seaport of Dar-es-Salaam.

Togo (French). During the period October 1–10, nine cases of smallpox were reported in Anecho.

Typhus Fever

Iraq. For the week ended October 27, two cases of typhus fever were reported in Baghdad.

Japan. One case of typhus fever was reported in Japan for the week ended September 15.

Turkey. Four cases of typhus fever were reported in Turkey for the week ended October 27.

Yellow Fever

French West Africa. The suspected case of yellow fever previously reported in Bembereke, Dahomey, was not confirmed.

Gold Coast. On September 5, one case of yellow fever was reported in Suhum. A fatal suspected case was reported in Tarkwa on October 12. The fatal suspected case reported in Accra on September 19, was not confirmed.