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AUTHORITY

SMUFD d/a ltr, 8 Feb 1972

TRANSLATION NO. 853

DATE: July 1963

DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

p

Jul 63

LABORATORY INFECTIONS ESPECIALLY WITH TYPHOID BACILLI

/Following is a translation of an article by Walther Schäfer, of the Hygiene Institute of the University of Munich (Director: Prof. Kisskalt), in the German-language periodical Archiv für Hygiene und Bakteriologie (Archive of Hygiene and Bacteriology), Vol 132, 1950, pages 15-32./

Kisskalt (3 and 4) reported on laboratory infections with typhus bacilli in 1915 and 1929 in response to an inquiry by the testing offices. In 1939 this collection was extended by Draese (2) (of the Hygiene Institute of the University of Munich) in response to another inquiry. A total of 191 cases of laboratory infection with typhus bacilli were brought together in the three articles.

As a result of this survey it was shown among other things that the lethality of the cases in which the infection had demonstrably come from pure cultures was definitely higher (8 of 51 = 15.7%) than that of the cases in which the manner of infection was not really clear and therefore not only cultures but also infectious material for examination (feces, blood, etc.) must be considered as possible sources of infection (10 of 114 = 9%). In explanation of this considerable difference Kisskalt pointed out the probably larger dose of infection in the cases of culture infections. This assumption seemed to him to be confirmed by the reduction of the incubation period below 14 days in more than a third of these cases, which was in agreement with Knorr's findings (5) concerning the lengthening of the incubation period in waterborne epidemics, where the infection dosage is generally low.

The age of the strains had no detectable influence on the course of the infection. Even strains kept for a long time on artificial nutrient media were still highly pathogenic. — No relation could be proved between pathogenicity for man and either poisonousness to the experimental animal (virulence) or agglutinability; strains of no great viru-

lence to animals brought about fatal illnesses and conversely after exposure to very virulent bacilli illness failed to develop. — In some cases one and the same strain in repeated infections led to disease patterns of similar seriousness, but in other cases the course of the second illness deviated quite markedly from that of the first, so that such observations are inadequate for evaluating the rôle of the virulence factor.

For more precise evaluation of protective vaccination, too, the material on hand seemed not extensive enough. Still it could be seen that of the patients that had been vaccinated fewer died than of those that had not been vaccinated.

It therefore seemed indicated to send around a new inquiry and get together additional cases of laboratory infections, in order among other useful observations to study the influence of vaccination on the consequences of infection, on the basis of a body of material now grown somewhat larger. For as against ordinary cases of infection, laboratory infections in which the time of the infection is known offer the rare opportunity of pinning down the length of the incubation period fairly exactly and hence pursuing the question of the effect of previous protective vaccination on the length of the interval before the appearance of the first symptoms of disease. The most important question as to the value of protective vaccination, — how often an infection is overcome without any disturbance of the health, — cannot of course be answered precisely with the laboratory infection material, for we must reckon with the fact that most such infections in the laboratory run their course unnoticed. Only the subsequent onset of the disease will often enough in retrospect show up the importance of a perhaps otherwise inconspicuous "accident on the job" in dealing with bacteria cultures in its proper light. All that is left to do is to take as our starting point the clinical evaluation of the course of the disease in the cases where illness does occur, and estimate the advantage of vaccinated over unvaccinated laboratory personnel according to the varying gravity of the aspect of the disease.

In the spring of 1949 Privy Councillor Kisskalt sent out a questionnaire worded as follows to the testing offices and bacteriological laboratories known to us:

1. Have you had cases of infections with pure cultures of typhus or paratyphus bacilli or other bacteria or viruses?

2. Was infection by a bacteria culture proved, or did other possibilities of infection exist at the same time, e.g. with infectious feces or blood (or dust and the like)?

3. Have laboratory infections occurred without its being possible in retrospect to reconstruct the mode of infection, but which are nevertheless to be regarded as laboratory infections?

4. Age? Sex? Season of the year? Disease of the digestive system, malnutrition, or other non-specific infection (cold, or the like) prior to exposure to the bacilli?

5. How did the infection occur? How many hours after a meal?

6. Were many bacilli presumably taken in? — What was done after the infection?

7. How long was the incubation period? — What was the condition of the patient up to the onset of the disease?

8. Had the patient been vaccinated? — How long before? How many times?

9. What was the course of the disease? light? serious? — How were the bacilli being grown? What was their agglutination titer?

10. Is the origin of the pure culture well known? — Was it started from feces, from the spleen, etc.? — Was the culture from a case whose clinical course (light, serious) is precisely known?

11. Special characteristics? slightly, strongly agglutinable?

12. How long was it on artificial nutrient medium before the infection? On what medium? Had it been often reinoculated?

13. Are other cases known to you? — Who can give information about them?

14. Are cases known to you in which in spite of typhus bacilli being taken into the mouth no illness followed?

15. Do you particularly desire that the case be kept

anonymous?

16. Have other persons been infected from this case?

17. Are cases known to you of intentional criminal infection with bacteria strains? — What cases?

18. What measures and/or regulations do you recommend for the prevention of laboratory infections?

We cordially thank our 72 colleagues who took the trouble to answer. The institutes and laboratories of the East Zone did not participate in answering the questionnaire.

The cases reported are classified on the following basis:

Group 1: Date and manner of the infection known

Group 2: Manner of infection unexplained

Group 3: Probable infection without resulting illness.

A. Infection with Typhus Bacilli

Group 1: Incontestable Infection from Bacteria Cultures

Case 1. — Infected with blood containing typhus bacilli when a cut injury occurred at a minute vein June 1945. 4. Age 46, female, previously healthy, poorly nourished, overworked. — 5. Two hours after breakfast. — 6. No disinfection. — 7. About 3 weeks. Occasional headache and fatigue. — 8. No. — 9. Of average severity; blood culture positive. — 12. Fresh strain. — 16. The office nurse of the Infectious Diseases Department also took typhus (exact source of infection unknown).

Case 2. — Infected by swallowing water containing typhus bacilli while using an unstopped pipette. — 4. Age 22, female, reduced state of nourishment. — 6. Rinsed mouth with dilute hydrochloric acid, drank dilute hydrochloric acid and schnaps. — 7. Exactly 14 days. — 8. Vaccinated several times, the last time half a year before the infection. Had been sick with typhus once before. — 9. Medium severity, blood culture and Widal reaction positive. — 10. Laboratory strain of the Behring plant at Marburg. — 11. Readily agglutinable. — 12. Old laboratory strain. — 14. The same person had ingested bacilli in the same way half a year before

without becoming ill. — 16. No.

Case 3. — Infected in sucking a culture up in a pipette, October 1947. — 4. Age 60, female, previously healthy. — 5. Two hours after breakfast. — 6. Rinsed mouth with pepsin and dilute hydrochloric acid; vaccinated immediately after infection. — 7. No complaints for 9 days; went to work as usual. — 8. Decades earlier, and just after infection (cf. 6). — 9. Light. Moderate fever several days. Diarrhea one time. Blood culture positive. No bacteria detectable in feces and urine. — 10. The culture was derived from feces of a person with a light case. — 12. Fresh strain.

Case 4. — Infected from cadaveric material. — 4. Age 21, female. — 7. About 10 days; headaches. — 8. No. — 9. Very severe.

Case 5. — Infected while using a pipette. — 4. Age 25, female, poorly nourished. — 5. Five hours after breakfast. — 7. Fourteen days; condition normal. — 8. Not definitely ascertainable. — 9. Fatal. — 10. No.

Case 6. — Infected while using a pipette, August 1947. — 4. Age 32, female, poorly nourished, otherwise in good health. — 5. Five hours after the noon meal. — 6. Oral disinfection with alcohol and dilute hydrochloric acid; swallowing of hydrochloric acid. — 7. Fourteen days; no complaints. — 8. Several times, the last time 6 weeks before infection. — 9. Very severe. — Fresh strain from blood culture.

Case 7. — Infected with a pure culture. — 4. Age 20. — 8. No. — 9. Very severe; two recurrences. — 10. No.

Case 8. — Infected in making agglutination test. — 4. Age 38, male. — 5. Two hours after breakfast. — 6. Usual disinfection. — 7. Seventeen days; no complaints. — 8. Several times, the last time half a year before infection. — 9. Very severe, with intestinal bleeding and relapse. Bacilli in feces and blood. — Strain derived from a group illness of 20 cases of moderate severity. — 11. Highly virulent, readily agglutinable. — 12. Fresh.

Case 9. — Infected in setting up the Widal test; no safety pipette. Spring of 1947. — 4. Age 20, female. — 6. Oral disinfection. — 7. Twenty-one days. — 8. Half a

year before. — 9. Light. — 10. Strain 2-3 months old, quite agglutinable.

Case 10. — Infected while using a pipette during the Widal test, spring of 1946. — 4. Age 25, female, reduced nourishment. — 5. Empty stomach. — 6. Mouth rinsing and drinking of dilute hydrochloric acid and alcohol. — 7. Slow onset after 8 days. — 8. Half a year before. — 9. Very severe. Blood culture positive. No bacilli found in feces and urine. — 10. Cultured shortly before from bile.

The incubation period in these ten cases was:

	9	10	11	12	13	14	15	16	17	18	19	20	21	days
vaccinated	1					2			1				1	
unvaccinated		1											1	

In case 3 the vaccination was "decades" before. Immediately after the infection another vaccination was performed. After 9 untroubled days the patient became slightly ill with no intestinal symptoms. Considering her relatively advanced age of 60 years one is tempted to assume a connection between the mild course of the illness and the effect of the protective vaccination. The relatively short incubation period of 9 days might also be thought of as a result of vaccination, since Otto and Schäfer (6) in their animal experiments with Breslau infections were able to observe a shortening of the lifetime of the animals by injections of killed bacteria (= vaccination) simultaneous with or shortly after the infection.

In case 5, which ran a fatal course, there was an incubation of 14 days. Since it could not be ascertained in retrospect whether a protective vaccination had been attempted earlier, the case drops out of consideration for our problem. Likewise case 8, in which the length of the incubation period was no longer known.

From the earlier compilations of laboratory infections by our institute (Kisskalt, Drasse) 44 cases could be found in which data on incubation time and the presence or absence of a protective vaccination were available. Including the above cases we find the following incubation periods in the vaccinated and unvaccinated groups:

Days:	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
19 vac.							1	1		1		7	2	1	2		1		2	1
32 unvacc.	1		2	1		2	2	3	2	2	2	6	1	1	1	1	1	1	2	1

At first glance it is evident that in a considerable part (about half) of the unvaccinated cases the incubation period is shorter than the average figure of 13-14 days, as was emphasized earlier by Kisskalt. In the vaccinated cases this part is considerably smaller and in most cases (about 5/6) the incubation period was 14 days and longer. (We omit to adduce any mathematical comparison factor here in consideration of the rather small number of cases.)

The dependence of the incubation time on the quantity of bacilli taken in was pointed out by Knorr (5) in connection with the drinking-water epidemic in Pforzheim. In cases of laboratory infections the infection dose must have happened in certain cases to be quite exceptionally high, but these variations affect the vaccinated and unvaccinated groups in the same way. The effect of prior protective vaccination still suggests itself strongly as an explanation of the unequal incubation period. It is obvious that a vaccinated organism can sometimes deal with the invading germs longer than an unvaccinated one without loss of its health. We know from many other infectious diseases that with increasing incubation time the prognosis becomes more favorable. Perhaps in typhus, too, the lengthening of the incubation period indicates a better average prognosis for those who develop the disease in spite of having been vaccinated. — This would also fit in with the observations of Bertram (1) at the time of the Paris epidemic of 1941, when after partaking of an infected food about 610 persons became ill. In half the cases the incubation time could be precisely learned. It was found that in general the shorter the incubation period the more severe the course of the disease.

Group 2: Infection Not Satisfactorily Observed

Case 11. — Source of infection not determined. Lunch was warmed up in the steriliser, in which there was also infectious material. March 1946. — 4. Age 20, female, reduced nutrition. — 8. Several times before, the last time 2 months before infection. — 9. Case of medium severity. Bacilli in feces and blood.

Case 12. — SI (source of infection) unknown. Fall of 1945. — 8. Vaccinated earlier. — 9. Medium severity? (Data

incomplete.) No bacilli found.

Case 13. — SI unknown. May 1948. — 8. Several times, the last two years earlier. — 9. Atypical, but not mild. No diarrhea.

Case 14. — SI unknown. Winter of 1947-48. — 4. Age 28, male, average state of nutrition. — 8. Last vaccination five years before. — 9. Medium severity. Blood culture positive.

Case 15. — SI unknown. Summer of 1948. — 4. Age 20, male, average state of nutrition. — 8. Last vaccination four years before. — 9. Severe. Relapse. Blood culture positive.

Case 16. — SI unknown. Received incoming material. Summer of 1948. — 4. Age 30, female, average nutritional condition. — 8. Three months before. — 9. Mild. Bacilli in blood and urine.

Case 17. — SI unknown. Winter of 1946-47. — 4. Age 22, female, average nutritional condition. — Shortly before becoming ill. — 9. Mild, uncomplicated. Bacilli in feces and blood.

Case 18. — Infected from washing inadequately disinfected test tubes that had contained feces and urine. — 4. Age 36, female, reduced nutritional condition. — 7. Headaches; after 14 days, fever. — 8. Half a year before. — 9. Severe relapse. Bacilli found.

Case 19. — SI unknown. Possibility of infection outside the laboratory. September 1946. — 4. Age 57, female. — 8. Half a year before. — 9. Medium severity. Bacilli in feces.

Case 20. — SI unknown. Like 19. October 1947. — 4. Age 22, female. — 8. Earlier and 3/4 year before. — 9. Average.

Case 21. — Infected while doing bacteriological work, probably with pure cultures. Summer of 1945. — 4. Age 55, female. — 7. Nausea, headaches. — 8. No. — 9. Severe. Bacilli in feces, blood, and urine.

Case 22. — Like 21. Winter of 1946. — 4. Age 25, male, poor nutritional state. — 8. Earlier and shortly before illness. — 9. Average severity. No bacilli found.

Case 23. — Like 21. March 1946. — 4. Age 28, female, poor nutritional state. — 8. Unknown, probably not. — 9. Blood culture positive.

Case 24. — Like 21. Summer of 1944. — 4. Age 40, male. — 8. Yes. — 9. As memory serves, rather severe.

Case 25. — Possibly infected while gathering bacilli from agar for regeneration. March 1946. — 4. Age 18, female, medium nutritional state. — 8. No. — 9. Severe, but without complications. No bacilli found.

Case 26. — Employed in cleaning the glassware. Possibility of outside infection, however. May, 1946. — 4. Age 21, female, medium nutritional state. — 8. No. — 9. Light, no bacilli found.

Case 27. — SI not ascertainable. Employed in setting up the Widal test. — 4. Age 41, female. — 8. No. — 9. Severe. Bacilli found.

Case 28. — SI unknown. — 4. Age 38, female, good nutritional state. — 8. Six years before. — 9. Medium severity. No bacilli found.

Case 29. — SI unknown. November 1947. — 4. Age 22, female. — 8. Two years before. — 9. Medium severity. Bacilli in blood.

Case 30. — SI unknown. Summer of 1946. — 4. Age 37, female, poor nutritional state. — 8. Sixteen years before. — 9. Medium severity. No bacilli found.

Case 31. — SI unknown. — 4. Age 34. — 8. Half a year before. — 9. Medium severity. Blood culture positive.

Case 32. — SI unknown. — 4. Age 49. — 8. Half a year before. — 9. Medium severity. Blood culture positive.

Case 33. — SI unknown. Employed in washing glassware. — 4. Age 21, female. — 8. Several times, the last time three weeks before. — 9. Mild. Bacilli found in blood and feces.

Case 34. — SI unknown. Like 33. — 4. Age 28, female. — 8. Several times, the last time six weeks before. — 9. Fatal within 10 days.

Case 35. — SI unknown. 1945. — 4. Age 22, female. —

8. No. — 9. Mild.

Case 36. — SI unknown. 1946. — 4. Age 33, female. — 8. No. — 9. Mild.

Case 37. — SI unknown. — 4. Age 20, female. — 8. Twelve months before. — 9. Mild.

Case 38. — SI unknown. — 8. No. — 9. Severe.

Case 39. — SI unknown. — 8. Yes. — 9. Mild.

Case 40. — SI unknown. — 8. Yes. 9. Severe.

Case 41. — SI unknown. — 4. Age 28, female. — 6. 23 days? — 8. Several times, the last time three months before. — 9. Severe. Blood culture positive.

Case 42. — SI unknown. June 1948. — 4. Age 36, female, good nutritional state. — 8. Most recently 3/4 year before. — 9. Very mild.

Case 43. — SI unknown. — 4. Age 30, female. — 7. headaches. — 8. No. — 9. Severe. Blood culture positive.

Case 44. — SI unknown. — 4. Age 25, poor nutritional state. — 7. Headaches. — 8. No. — 9. Severe. No bacilli found.

Case 45. — SI unknown. — 4. Age 25, poor nutritional state. — 7. Icterus. — 8. No. — 9. Severe. No bacilli found.

Case 46. — SI unknown. — 4. Age 35, male. — 8. Yes. — 9. Medium severity.

Case 47. — SI unknown. — 4. Age 45, female. — 8. No. — 9. Medium severity.

A total of 37 cases of typhus among laboratory personnel were thus reported to us without its having been possible to find out the time or manner of infection in the respective cases. Counting in the ten cases in which the infection process was known, we have a grand total of 47 cases of laboratory infection with typhus reported to us. That nearly a third (15 persons) were unvaccinated seems to us surprisingly high for present conditions, i.e. 20 to 30 years after typhus vaccination by reducing the rate of illness during the first

World War had convincingly demonstrated its prophylactic effect, and the high rate does not seem to us quite excused by considering the difficulties of the war and post-war years. The deficient hygienic situation of many makeshift laboratories during that time should have been all the more reason for carrying out protective vaccination meticulously.

In evaluating the influence of protective vaccination on the course of an illness that broke out in spite of it, the data from the earlier compilations of Kisskalt and Draese (113 cases) were also included. In connection with the attempt to classify the cases in various groups according to the appraisal of their clinical severity it hardly needs to be mentioned that in view of the heterogeneous make-up of the material the subjective factor of clinical evaluation has broad play. Nevertheless the attempt seems defensible, since this subjective factor affects both the vaccinated and unvaccinated groups approximately equally. The course of the typhus infection in the 92 unvaccinated and 66 vaccinated patients is shown in the following table:

Vaccinated	total	fatal	severe	medium	mild
within the last year	32	1	7	11	13
more than a year before	34	1	12	12	9
unvaccinated	92	12	41	21	18

The mortality of the unvaccinated patients was somewhat higher than the usual average of 11-12%. The mortality of the vaccinated patients was definitely below this figure (2 of 66).

Among the unvaccinated the disease was severe in half the persons (omitting the fatal cases) (41 of 80). Among the vaccinated a severe course of the disease was reported in less than a third (19 of 64) of the cases. That the protection of vaccination declines with increasing time from the date of the last vaccination is also suggested in our small amount of material. The persons who regularly had a vaccination not more than a year behind them came out better than those that let several years go by. — A mild case was more frequently reported among the vaccinated than the unvaccinated.

Since our material, gathered as it was in many ways, cannot be evaluated without certain qualifications, let us abstain from drawing too great conclusions from the differences in the course of the disease as between vaccinated and unvaccinated patients. No unprejudiced person will be able to avoid the impression that besides the lower mortality the

course of the disease was also milder on the average. As is well known, this is a question on which the opinions of the clinicians differ rather widely (cf. Schäfer (7) page 81). Part of the authors do not recognize any mitigation of the character of the disease in cases that break out in spite of vaccination. In not a few individual cases this observation may in fact not hold good; how far it may be generalized seems questionable. This uncertainty shows up, too, in the balance of our table, although it concerns only two relatively small groups of patients.

In any case there is no doubt that for the personnel of bacteriological laboratories without exception regular typhus vaccination (TAB vaccine) should be required at intervals of one year at the longest. Besides the latent aborting of infections that take place, a more favorable outcome of "accidents on the job" is to be expected from this.

The limits of vaccination protection are clear from the second cases that continue to be observed occasionally, and for which there is particular opportunity among laboratory personnel because of the continuing danger of exposure. When the immunity after recovery from the disease proves good only for a limited period, then vaccine prophylaxis, too, can provide higher resistance only temporarily or to an inadequate degree. It is in this light that we should regard case 2, where after recovery from an earlier case of typhus and in spite of repeated vaccinations the disease still recurred.

B. Infection with Paratyphus Bacilli

I. Paratyphus A

Case 48. — Infection in all probability with a pure culture while differentiating the strain. January 1947. — 4. Age 38, female, poor nutritional state. — 7. About 8-10 days. — 8. Not vaccinated. Typhus 11 years before (also a laboratory infection. — 9. Medium severity. No bacilli found. — 10. The culture was derived from a patient who was seriously ill. — 11. Stated to be not readily agglutinable. — 12. About two weeks on agar.

Case 49. — Infection probably while setting up the Widal test. — Age 22, female. — 8. Yes. — 9. Mild case. Blood culture positive. There was a mixed infection with A and B. — 11. Readily agglutinable. — 12. Three to four months old.

Case 50. — Source of infection unknown. — 4. Age 33, female, poor nutritional state. — 8. Several times. Typhus 13 months before (also a laboratory case). — 9. Mild.

Case 51. — SI unknown. Winter of 1945. — 4. Age 35, male. — 8. Several times. — 9. Severe.

Case 52. — SI unknown. — 4. Age 24, female. — 6. Nothing. — 8. Nine months before. — 9. Mild. Bacilli found in feces. — 10. From a group illness in which all cases were mild. — 11. Readily agglutinable, fresh strain.

Case 53. — Infected with a pure culture while working at strain collection. — 4. Age 23, female. — 6. Nothing. — 7. At least 10 days, perhaps longer. — 8. Several times, the last time a month before. — 9. Mild. — 10. Fairly fresh strain (see 52).

It is interesting that two of the cases of paratyphus A infection were preceded by a typhus illness — also contracted in the laboratory — occurring in one case 11 years and in the other 1 year before (cases 48 and 50). — As in the 10 cases previously reported (Kisskalt and Dresse), no fatality occurred among these 6 cases.

II. Paratyphus B Schottmüller

Group 1: Mode of Infection Certain

Case 54. — Infected while setting up the Widal test (unstopped pipette), fall of 1941. — 4. Age 34, female. — 6. Mouth rinsing. — 8. Yes. — 9. Mild. Blood culture positive.

Case 55. — Infected from a pure culture while using a pipette. — 4. Age 24. — 8. Yes. — 9. Mild. — 10. Strain several years old. — 11. Readily agglutinable.

Case 56. — Infected from a pure culture while using a pipette, November 1945. — 4. Age 46, female. — 8. Yes. — 9. Mild.

Case 57. — Infected from a pure culture by swallowing while using a pipette, 1941. — 4. Age 42, female. — 5. Two hours after breakfast. — 6. Nothing. — 8. No. — 9. Mild.

Case 58. — Infected by swallowing a pure culture (rather large quantities). — Age 46, female, medium nutri-

tional state. — 7. Four to five days. — 8. Two years before. — 9. Of medium severity. Bacilli were found.

Case 59. — Infected when a broth was spilled. — 4. Age 25, female, poor nutritional state. — 7. About 14 days. — 8. Half a year before. — 9. Mild. Bacilli were found.

Case 60. — Infected while setting up the Widal test. (No safety pipette.) Summer of 1945. — 4. Elderly T.A. /Probably Technischer Assistent; technical assistant./ — 8. No. — 9. Rather severe. — 10. Strain 2-3 months old, readily agglutinable.

Case 61. — Infected in the same way as 60. — 4. Age 19, female. — 6. Oral disinfection. — 7. About 14 days. — 8. Half a year before. — 9. Very mild. — 10. Same as 60.

Case 62. — Infected while sucking up a culture in setting up the Widal test, summer of 1946. — 4. Age 24, female. — 6. Oral disinfection. — 8. Regularly at intervals of 3/4 year. — 9. Mild. Bacilli were found.

Group 2: Mode of Infection Unclear

Cases 63 and 64. — SI unknown. — 8. Earlier. — 9. Bacilli found in feces.

Cases 65, 66, 67. — SI unknown. — 8. No. — 9. Severe.

Cases 68, 69, 70. — SI unknown. — 8. Yes. — 9. Two severe, one mild.

No fatality occurred among these 17 cases of Paratyphus B Schottmüller infection.

In 7 cases the infection could be proved to have occurred by sucking up cultures while setting up the Widal test. The same mode of infection may have been present in a considerable part of the so-called unclear cases. Of course that is basically the way things are when it comes to infections with typhus strains. Pipetting with live cultures must in the technique of bacteriological-serological typhus diagnosis be regarded as in practice the chief source of laboratory infections. This is the more difficult to understand in that here in contrast to many unnoticeable possibilities of infection (unpacking incoming material, etc.) we are dealing with a readily understood work process. The best-intentioned pre-

ventive prophylaxis (protective vaccination) does not achieve its end if it is not complemented by an equally conscientious exposure prophylaxis. Pipetting, to be sure, is unavoidable, but safety precautions can — and, the balance of our survey compels us to say, must — be taken that are capable of reducing the danger of infection. That this is possible without making the carrying out of laboratory work even in a "big business" essentially more difficult has been demonstrated. Such precautions include: 1. The use of killed cultures instead of live cultures in setting up the Widal test, and 2. the use of safety pipettes or at least closed pipettes in setting up the Grube test (serological differentiation of strains).

1. For setting up O agglutination a heat-killed strain (one hour at 100° C) is generally as good as a pure O strain.

For setting up H agglutination cultures killed with formol (0.3–0.5%, 24-hour sterility test) are as a rule as good as live cultures. The agglutinability of the test strains is hardly affected at all. In rare cases inadequate titration differences could always be re-tested with live cultures. In the overwhelming majority of cases the Widal test with formalinized cultures gives a sufficiently clear result for diagnosis. For routine serum diagnosis it may be designated as the preferred method.

2. Apart from special cases calling for nicety of discrimination, the use of formalinised cultures in the Grube test, too, achieves the purpose. When live cultures are used, working with safety pipettes or at least closed pipettes should in her own interests be as much a matter of course to the technical assistant as, say, plunging everything into a disinfectant solution afterwards. The use of rubber caps or balls is often felt cause a slowing down of the tempo of the work and should therefore be avoided as far as possible out of convenience. Trying to compel their use no longer seems promising.

It will never be possible to avoid laboratory infections entirely by precautionary measures and training, but reducing their frequency lies well within the range of possibility. We present below the proposals of several laboratory directors in response to our question about measures for preventing laboratory infections. Posting of official regulations is taken for granted.

Regular vaccinations are recommended by Hofmann, Werner, Maassen, Wehrrig, Ernst, Gaertner, and others. — The personnel should be kept in an adequate nutritional state (Zulagen).

Working with killed Widal cultures is advocated by Hofmann, Zeitlmann, Werner, Steinemann, Fehr, and others. Gaertner rejects this method, since "such work would be based neither on bacteriological ability nor on biological thinking." — Safety pipettes are demanded by Werner, Reploh, Jötten, Steinemann, Loderkämper, and others. Haas recommends rubber-capped pipettes when working with live cultures. The need of special caution in agglutination on the microscope slide is pointed out.

The necessity of strict care that nothing shall be washed that has not been sterilized in the autoclave is pointed out by Hofmann, Steinemann, and others. Werner considers it necessary to admonish the technical assistants that serum is infectious too. Schmidt-Lange, Gaertner, and others consider it important that agglutinations be carried out only by particularly experienced technical assistants.

Adequate laboratory spaces are called for and most laboratory infections attributed to cramped quarters (Löns, Liebermeister, Pothmann, Leonhard, R. Müller). Windows should be screened (Gaartner and others). Zimmermann attaches special importance to floors without cracks (linoleum, terrazo). For working with Rickettsia tightly sealed face masks are recommended (Siegert). Strict care should be taken that there is no eating and no smoking in laboratory spaces (Maassen, Schütz, and others). Jötten and Gaertner remind us of the necessity of checking disinfectant solutions.

Question 17, on cases of intentional, criminal infections was answered as follows:

A secret notice concerning acts of sabotage discovered during the war was circulated among the consulting hygienists.

Two nurses in Kharkov are said to have become fatally ill with typhus after eating purposely infected foods (Loderkämper). — Rumors attributed the death of a member of the Wehrmacht in Poland to an intentional infection (Zeitlmann). — In 1944 a waiter poured a broth culture of typhus bacilli in beer (Hofmann). — Probably the typhus epidemic in December 1941 among those who ate at a Paris soldiers' home, in the

course of which a total of 610 persons were taken ill, was a case of this kind (Bertram, 1).

Group 3: Infection Without Subsequent Illness

A total of 25-30 cases were reported in which in spite of obvious contact with cultures (usually in pipetting by sucking up with the mouth) no illness occurred. Typhus, paratyphus A and B, Breslau, and dysentery bacilli are represented among these cases. The information about whether the persons had been vaccinated is too incomplete to evaluate the material from that standpoint. Undoubtedly the frequency of such instances of infection is considerably higher still. A part of these cases are kept secret "when everything turns out all right," and in some other cases the occurrence is not even noticed.

How troublesome the limited pathogenicity can sometimes be is shown by a case in which a twenty-year-old because of misfortune in love drank the rinsings from a Schottmüller culture, in consequence of this suicide attempt was put into the psychiatric clinic and then transferred to the infectious disease section, and in the end did not get sick at all (reported by Jötten).

C. Other Laboratory Infections

I. Swine Erysipelas

Case 1. — The infection occurred in mopping up a spilled culture after cutting a finger with a splinter of glass. — 4. Age 29, female. — 6. Disinfection of the wound. — 7. Twenty-four hours; no complaints or distress. — 8. No. — 9. Mild. Well after three days (immune serum). Bacilli found. — 12. Four-month-old strain.

Case 2. — Infected by a wound during dissection. — 4. Age 37, male. — 7. Twenty-four hours. — 8. No. — 9. Mild.

Case 3. — Infected in dissecting a hog after injuring a finger. — 6. Swelling on the third day. — 8. No. — 9. Mild.

II. Bang's Disease

Probably infected while doing dissection. — 4. Age 35, male. — 7. About 8 days; fatigue. — 9. Severe. Recovery after 3 weeks. Vaccine therapy.

III. Enteritis Breslau

Infected by accidentally sucking up rinse water from a bacilli culture. Spring of 1937. — 4. Age 33, female. — 5. Three hours after a meal. — 6. Oral disinfection. — 7. Three days. No complaints. — 8. No. — 9. Medium; diarrhea and chills. — 10. Fresh strain, readily agglutinable.

IV. Spotted Fever

Case 1. — Infected in inoculating a chicken embryo. 1939. — 4. Age 24. — 7. About 8 days. — 8. Yes. — 9. Medium severity.

Case 2. — Possible infection by dust (animal caretaker). 1945. — 4. Age 33. — 8. Yes. — 9. Medium severity.

Bieling reported 17 cases (written communication). Fifteen of these were infected from cultures and two by lice.

25-30 cases of laboratory infections have occurred at the Lemberg institute (Haas). A report on 7 cases in a group illness from spotted fever among hospital employees who had infected themselves in the laboratory is to be found in A. Wo. /probably Aerztliche Wochenschrift; Doctor's Weekly/ 1947, page 441 (Hormann). In some of these cases droplet infection /Tröpfcheninfektion/ must have taken place; in others the infection came about through louse bites.

Other cases of laboratory infections are reported by Eyer et al. (Zeitschrift für Hygiene (Journal of Hygiene), Vol 122, 1940, page 702), Ciuca and Ionescu-Mihaesti, Löffler and Mooser (Schweizerische Medizinische Wochenschrift (Swiss Medical Weekly), 1942, page 755), and others.

V. Q Fever (Balkan Influenza)

The technical assistant was working with blood samples from patients suffering with Balkan influenza. The infection may have taken place when a minute vein was opened by the prick of a needle. — 7. Twelve days. — 9. Diagnosis unsure. Typhus was thought of, but there was neither bacteriological nor serological support for this.

Detailed data on a group illness from Q fever in the laboratory are given by Hauk and Weyer in DMW /Deutsche Medizinische Wochenschrift; German Medical Weekly/, 1949, page

198 (where a bibliography on other cases is to be found). There were 6 certain and 5 undetermined cases. Two persons were engaged in working up the strains and one person fed the infected lice. The others attacked lived in the same barracks but had nothing to do directly with the Rickettsia laboratory. Cockroaches were the only possible — and very unlikely — insect carriers. The danger of laboratory infection in working with R. burneti is described as extraordinarily great (high resistance in the dried state). The illnesses for the most part occurred only after a long period of working in the laboratory.

Seven cases occurred during the winter of 1948/49 at the Paul Ehrlich Institute at Frankfurt. Four persons were engaged in growing Rickettsia in chicken cultures and animal passages. In the case of the other three, dust infection is assumed. — 4. Two to three weeks; in one case exactly 27 days. — 8. No. — 9. Two severe, 2 medium, 3 mild. — 11. Considerable pathogenicity in the guinea pig. — 12. About four weeks in animal passages.

VI. Volhynia Fever

Two infections while feeding lice (reported by Bieling). — Haas observed about 100 cases at the Lemberg Institute.

Rickettsia infections are often practically unavoidable in the laboratory. They seem to occur still more frequently than infections with typhus and paratyphus bacilli. The additional possibility of transmission by the inhalation of infectious dust apparently plays a considerable part.

VII. Yellow Fever

Bieling mentions two probable cases resulting from infection with strain 17 D.

VIII. Epidemic Hepatitis

Ten cases are reported. One of these died of an acute yellow atrophy of the liver.

IX. Field Fever

Infected with a pure culture while immunising rats. Spring of 1947. — 4. Age 55, male. — 7. About 14 days. —

10. Strain Malleradorf II.

X. Tuberculosis

Case 1. — SI unknown. There was a possibility of infection with material for analysis. — 4. Age 25, female. — 9. Began with pleurisy. After 1/2 year, tuberculosis of the genital organs. Bacilli found in menstrual blood and by animal experimentation.

Case 2. — SI unknown. Worked with tuberculous material. — 4. Age 30, female. — 9. Bacilli in sputum. Recovery after one year.

Case 3. — SI unknown. — 4. Age 64, fem. — 9. Mild.

Case 4. — SI unknown. — 4. Age 51, male. — 9. Bacilli in sputum. Recovery after one year.

Case 5. — SI unknown. — 4. Age 25, male. — 9. Mild.

XI. Diphtheria

Four cases, evidently infected by the same bacilli carrier, who was employed in the laboratory. — 9. Three illnesses of medium severity, one mild. Strain of Type II in all cases.

Case 6. — SI unknown. — 4. Age 26, female. — 9. Severe. Type gravis.

Case 7. — SI unknown. — 4. Age 20, female. — Mild.

XII. Pyocyaneus

In consequence of a laboratory infection a pyocyaneus sepsis developed of which the patient died. (Reported by Schmidt-Lange.)

XIII. Leaping Ill

Two cases are reported by Mieling in Klinische Wochenschrift (Clinical Weekly), Vol 18, 1937, page 652 and Deutsche Archiv für Klinische Medizin (German Archives of Clinical Medicine), Vol 182, 1938, page 451.

A case of laboratory infection with the Lansing strain,

which ran a peculiar course, is described in detail by Beller in Zentralblatt fUr Bakteriologie (Central Journal of Bacteriology), I, Vol 155, 1949, page 269.

Summary

In answer to general inquiries made at bacteriological laboratories, numerous reports have been received regarding infections of laboratory personnel during the past years (altogether 200 cases). While in the past bacteria eberthella typhi and salmonella were the cause of most laboratory infections, Ricketsiaceae are now numerically prevailing wherever work is done with them.

Approximately seventy new cases in which infections were caused by bacteria eberthella typhi and salmonella have become known to us. In comparing the progress of infection of vaccinated individuals with that of unvaccinated individuals the cases previously published by Kisskalt and Draese have been included. As far as a survey of 156 cases permits of any conclusion, the incubation period is longer with vaccinated persons while at the same time the illness itself is less severe and lethality less frequent.

In order to reduce the probability of infection of laboratory personnel it is recommended among other suggestions that killed organisms be used when making the Widal test. The use of safety pipettes is also recommended once more. ()

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CSO: R-3293-D/b