In the severer cases in which several injections were required the patients were kept in bed for forty-eight hours; then forced flexion, sitting and standing were practiced to note improvement. The interval for injections following the first one was variable, and I think no advice need be ventured on this point, except to state that it is safe to give the injections from twenty-four to seventy-two hours apart, and in equally close succession for as many injections after that as may be necessary. The largest number in a given case was five. Individual conditions should, I think, prevail in the matter of reinjections. Tenderness may persist at the point of puncture for several days.

In the earlier cases objective sensory changes in the distribution of the nerve were examined for, but none were noted that could be relied on, because of the predominating "subjective" pain.

The prognosis, if the reports of Lange, Bum, Umber, Alexander, Kellersman, Grossman, Schlesinger, and several others are to be credited, is exceedingly good.

Lange states that of his 56 cases 13 were acute, and among this number treated there was 1 complete failure and 1 recurrence after six months. In the 11 subacute cases, 1 patient remained uncured, 2 were improved, and there was 1 recurrence in four weeks. There were 32 chronic cases, with 4 patients uncured, 4 improved and 4 recurrent. The total of 56 cases showed 15 per cent. of complete failures, 10 per cent. recurrences, 10 per cent. improvements—which is intended to mean that his method accomplishes cures in approximately 65 per cent. of all the cases.

Bum¹² has treated 81 patients who had sciatica with injections of 100 c.c. of an 8 per cent. sodium chlorid solution, and records 63 per cent. complete cures and 21 per cent. improvements.

Schlesinger¹³ treated 42 patients, with a total of 51 injections, with excellent results. The percentage of cures, improvements, recurrences and failures in my own cases corresponds very closely to that of other observers who had access to more abundant material. I have had occasion to inject refrigerated normal salt solution in a case of herpes zoster for the severe root pain which long outlasted the eruptive skin lesion, and have used it in a case of intercostal neuralgia. In both instances, which I shall report more fully at another time, the control of pain was marked and lasting.

COMMENTS

1. The deep infiltrating perineural injections palliate the pain of sciatica.

2. The acute, subacute and chronic types of sciatica lend themselves to this treatment, and whereas the number of injections required varies, immediate notable relief is afforded by the first injection in nearly all cases.

3. The treatment is most indicated and effective in the non-symptomatic cases, but is also of value in the symptomatic variety.

4. Normal salt solution of varying temperature and quantity, or the beta-eucain solution of Lange, is to be preferred to other anesthetic or mordant solutions. Alcohol is harmful and contraindicated.

5. The sciatic nerve may be reached deep in the ischio-trochanteric hollow (its peroneal branch lower down at the capitulum fibulae), but it is more surely

and safely reached directly after its emergence from the notch.

6. The point for puncture and penetration to the nerve is best determined by drawing a line between the postero-external border of the great trochanter and the sacro-coccygeal joint; at the junction of the inner third and outer two-thirds of this line is the spine of the ischium. A thumb's breadth to the outer side of this spine lies the sciatic nerve. Cadaver experiment and clinical experience lead me to endorse this landmark above all others.

7. The method requires a syringe (preferably metal) with a capacity for 30 to 60 c.c. or more, a needle of desirable length (8 to 12 cm.) directly attachable to the syringe.

8. Accidents of any consequence almost never occur. Unpleasant effects and complications are few and insignificant.

9. The prognosis in the sense of a cure is good if the facts suffice—namely, that in the large number of cases observed for from one to four years many patients have been entirely free from pain during that long an interval. Improvement is common. Recurrences are not the rule, and failures are the exception.

103 State Street.

THE DURATION OF THE ACTIVELY INFECTIOUS STAGE OF TUBERCULOSIS *

ROBERT N. WILLSON, M.D.

AND

RANDLE C. ROSENBERGER, M.D.

PHILADELPHIA

The object of this study has been primarily to render a rich field of tuberculous material of practical value from both the clinical and laboratory viewpoints. Scant benefit accrues to humanity at large from scientific knowledge that can not be applied to its betterment or protection. We have endeavored through scrutiny of the secretions and excretions of tuberculous subjects to arrive at definite conclusions: 1, with regard to the possibility of transmitting the disease during its earliest stages; 2, as to what means, and through what media, infection of human beings by other individuals may and does occur; and, 3, as to how far and how thoroughly under the ordinary circumstances of daily life Nature provides for the destruction of infectious tuberculous material, subsequent to its excretion from the human body.

It has been, and as the result of this investigation still more certainly is, our conviction that tuberculous infection may and does not infrequently occur through the semen; whether or not by means of the spermatozoön as the host and carrier of the tubercle bacillus remains to be determined. Such a mode of infection does not, of course, require the immediate appearance of a symptom-complex of tuberculosis, as we know it clinically. That the disease may be implanted prior to birth needs as witness only the occasional congenital caseous pneumonia, included in the experience of every pathologist of ordinary wide opportunity. Veterinarians and plain farmers add a homely proof also in the not infrequent dropping of a tuberculous calf by a tuberculous cow, evidence to the same effect from the

12. Wien. klin. Wchnschr., 1907, No. 49.

13. Deutsch. med. Wchnschr., 1908, No. 6.

*Read before the International Congress on Tuberculosis, Washington, Sept. 28, 1908.

lower animal kingdom. John R. Williams¹ cites a case of almost certain placental transmission. Harbitz² has recently reported five cases of congenitally tuberculous twins, and has demonstrated the presence of latent bacilli. Kraemer³ relates a number of instances in which the father is tuberculous, and all the children die of the disease, the mother remaining perfectly well. Every physician knows of at least one such occurrence. It is, in fact, our unhesitating belief that many if not most cases of so-called predisposition, or postnatal infection, with tuberculous parentage, are illustrations of latent tuberculosis—the result of intrauterine infection. Such transmission, whether maternal or paternal, reveals its secrets in response to only one line of investigation, and this offers difficulties and leads to conclusions that are not by any means clear-cut nor final.

There have come to us during the past four months eight opportunities for autopsy on men dying in the Philadelphia General Hospital from tuberculosis in advanced stages. From each of these subjects the testicles and two inches or more of each vas deferens were removed as soon as possible after death. The duct was carefully dissected from the surrounding tissues, and by sterile scissors cut across about one inch from its junction with the testicle. By gentle pressure from the testicle outward along the duct were expressed from one to two small drops of clear semen, which was at once applied to clean glass slides, spread, and stained for tubercle bacilli, decolorized and differentiated with Papanheim's solution of rosolic acid in alcohol. The fresh specimen was first examined for live spermatozoa, but in no instance were they found in motion. In all fifteen specimens of semen were examined (from eight subjects).

CASE 1.—General tuberculosis. The testicles and epididymis appeared normal. The semen from the right testicle and duct showed no bacilli. The semen from the left side was also negative.

CASE 2.—Tuberculosis of lungs; cavity formation. The testicles and ducts appeared normal. The semen from both sides failed to show bacilli.

CASE 3.—Empyema. Caseous pneumonia of left lung. Right lung less involved. Sputum full of bacilli. The semen from the right testicle and tube yielded one typical tubercle bacillus. The semen from the left side showed no bacilli. The testicles and duct appeared normal.

CASE 4.—Chronic ulcerative pulmonary tuberculosis. Tuberculous enteritis, ulcerated mucous membrane of appendix. One testicle only was present. The semen from the normal-appearing testicle and duct yielded three typical tubercle bacilli.

CASE 5.—Chronic ulcerative tuberculosis of the lungs. The semen from the normal-appearing right testicle and duct showed a few typical tubercle bacilli. No bacilli were found in the semen from the left side.

CASE 6.—Caseous pneumonia. Tuberculous enteritis and cystitis. The testicles and ducts appeared normal. The semen from the right side showed one tubercle bacillus. There was none in the semen from the left side. The testicles appeared normal, also the ducts.

CASE 7.—Chronic ulcerative tuberculosis of both lungs. Caseous pneumonia of left lung. The testicles and ducts appeared normal. No tubercle bacilli were found in the semen from either side.

CASE 8.—Case from insane wards. The *Amoeba coli* was present in the stools. There was a tuberculous cavity in the right lung and pneumothorax; tuberculous ulceration of intestines and feces full of tubercle bacilli. One tubercle bacil-

lus was found in the semen from each side. There was no macroscopic involvement of testicles or tubes.

Thus in a series of eight cases tubercle bacilli were found by simple staining methods in five instances, and in the semen from five out of fifteen testicles. The fact that the bacilli were usually found, if at all, in the semen from only one side, would rather give force to the belief that there was local tuberculosis of the corresponding organ or duct, though not macroscopically evident. This fact would not, however, affect the question of the infectiousness of the semen, and the danger to the woman, and the fetus. The fact that the semen was directly from the testicle points to the blood as its vehicle from the point of inoculation.

Inoculation and impregnation of laboratory animals with testicular semen from tuberculous subjects had been projected, is now being carried out, and will be reported on subsequently. The semen from the seminal vesicles has been used for inoculation of the lower animals by a number of investigators, and has frequently produced tuberculous infection. Karlinski⁴ at times found the semen from the seminal vesicles swarming with tubercle bacilli. In other cases he has found it impossible to demonstrate one bacillus, until inoculation experiments enabled their demonstration in the test animals. He has also injected bacilli into the testicle of a healthy goat, then has brought about coitus with the female, and studied the tuberculous progeny (five out of nine) from a healthy mother. He has noted the dropping of a tuberculous calf by a healthy cow, impregnated by an infected bull; and proved his results by autopsy.

We know of no one other than ourselves who has used the semen obtained directly from the testicle and the first portion of the vas deferens, and shall therefore complete this study when the opportunity presents. The discovery of the tubercle bacillus in testicular semen not only establishes the possibility, but the likelihood of frequent transmission of the disease by the male to the fetus. It also aids in establishing the more important fact that congenital tuberculosis is likely to be apparent at birth proportionately to the susceptibility of the maternal element and the developing fetus to the influence of the bacillus and its toxin. Provided they are resistant and fully or overnourished until term, there may be no indication of the latent infection.

There is no need to dwell on the possibility of infection by means of sputum. Practical interest seems to us to center rather in the demonstration of the bacilli in other excreta of the body, to which human beings are constantly and ignorantly exposed for new or reinfection. Important also are the time of earliest infectiousness of these excreta, and their tenaciousness of virulence under favorable and adverse circumstances within and without the body.

EARLY APPEARANCE OF TUBERCLE BACILLI IN SECRETIONS AND EXCRETIONS

It is a matter of common knowledge among medical men that tubercle bacilli may be determined by staining methods in the sputum from a bronchial tuberculosis long before the chest yields definite and localizing signs. It is equally well known that the intestine may swarm with tubercle bacilli from a rectal ulcer before the presence of the ulcer has been suspected.

A case in point has been studied recently by us in a man who was admitted to the wards of the Philadelphia

1. Probable Placental Transmission, THE JOURNAL A. M. A., April 6, 1907, xlviii, 1184.

2. Untersuchungen über Tuberkulose, Christiania, 1905.

3. Beitr. z. Klin. d. Tuberk., 1908, ix, No. 2.

4. Ztschr. f. Thiermed., 1905.

General Hospital supposedly suffering from uremic intoxication. He was comatose and his breathing stertorous; there was no cough, no considerable sputum, no symptom attracting attention to the lungs, and no diarrhea. A tiny speck of sputum was once expectorated and was found full of tubercle bacilli. The feces were then studied and showed scattered tubercle bacilli. When later the urine could be obtained the bacilli were also demonstrated in the sediment. There had been no suspicion of tuberculosis prior to the examination of the stray mite of sputum and the feces. The patient was infectious to others without doubt for days, perhaps for weeks and months, prior to the detection (accidental or routine, as one will) of the causal germs.

Although not by any means a new finding, the fact has not been generally recognized by the practitioner that in the feces and urine of most, if not all, tuberculous patients is contained infectious material and that in these excreta the bacilli may be demonstrated with great frequency and regularity by tinctorial methods, and often by animal inoculations when the former fail. The full knowledge of the value of this procedure led us to a tinctorial study of the sputum, urine and feces, in a large series of cases known to be tuberculous; and also to a series of inoculations of animals with tuberculous material, especially such as no longer showed the bacillus by tinctorial methods.

Our first step was the exhaustive examination of specimens of sputum, urine, and feces, from 100 patients known by the examination of the sputum to be actively tuberculous. In all instances the smears were made on new and thoroughly clean glass slides, long immersed in alcohol, ether and nitric acid, then washed with soap and distilled water, and dried over the flame. Urinary sediments were usually centrifugated and washed three times with distilled water prior to fixing on the slide. When only a small quantity of urine was obtainable (1 to 2 c.c.) the washing was dispensed with and the entire quantity of urine was placed in the center of a slide and allowed to dry in as small a space as possible, being stirred in the beginning with a tiny portion of egg albumin. The sediments were all obtained from eight ounces of the evening urine, allowed to settle over night, and from this precipitation was pipetted off into distilled water a small tube full of deposit.

We mention in passing the great difficulty experienced by us and by all students of urinary sediments in fixing the latter on a glass slide. After many failures we found that two methods would invariably succeed: 1, the coating of the smear, after fixing in the flame, with a thin solution of ether celloidin; and, 2, the use of a minute quantity of egg albumin on the slide before applying the urinary sediment. The single objection to the ether celloidin rests in its thickness, and consequent overdeep staining with the counter-dye. Even with the albumin fixation one precaution is necessary, namely, that the smallest possible quantity of albumin should be used in order to avoid the difficulty in decolorizing the albumin, and the albumin-fixed specimen by Pappenheim's fluid. Once these precautions are observed, no further sediments should be lost.

The smears from the feces were in some instances prepared by dissolving a little of the stool in a test-tube of distilled water, and smearing this semipaste in a thin, even layer on a slide. Occasionally it was sufficient to rub a small portion of the interior of the stool into a drop of sterile distilled water already on the slide. There seemed to be little advantage in one method as

compared with the other, though the latter affords economy of time and glassware, and was finally adopted as the method of choice. The slower method was held in reserve as slightly more thorough, to use in the event that no bacilli were found by the first procedure.

In all cases the smears were stained with cold carbol-fuchsin in covered jars, for at least fifteen minutes, and then decolorized and counter-stained in Pappenheim's solution of rosolic acid and alcohol about twenty minutes. A number of specimens were allowed to remain in the rosolic acid and alcohol for twelve to eighteen hours, without decolorization of the tubercle bacilli.

The following record will show the startling frequency of the presence of the tubercle bacillus in the urine and feces of admittedly tuberculous subjects in advanced stages of the disease:

Of 100 patients, male and female, from the tuberculosis infirmary of the Philadelphia General Hospital, the sputum of all chosen for experiment showed considerable numbers of tubercle bacilli. The entire 100 also showed tubercle bacilli in the feces, a few in considerable numbers; many more showed but few in scattered microscopic fields; several in such scarcity as to admit of discovery only after painstaking search. Thirty-eight of the 100 also showed the bacilli in the urinary sediments, never in considerable numbers, but, on the contrary, usually discovered after tedious study of the specimen. All negative specimens were examined for at least one hour before being considered free from tubercle bacilli. Several specimens, at first considered negative, were searched repeatedly and after several hours yielded one or two bacilli.

There seemed to be no direct relation between the number of tubercle bacilli in the sputum, the feces and the urine of a given patient. Occasionally the sputum appeared richly infested, and only the last field examined would disclose a lone organism in the fecal or urinary preparation. As far as possible in this series we avoided patients with renal or intestinal tuberculosis, and the patients that came to inspection at autopsy usually bore out our judgment in their freedom from active involvement of these organs. One patient in the insane ward, already referred to, had been studied for a considerable time as an instance of ameba infection. The stools showed tubercle bacilli in such numbers as to suggest tuberculous sputum rather than feces. This patient died suddenly of tuberculous pneumothorax, no lesion having been suspected in the lungs, cough and sputum being absent. At the autopsy the lower bowel was found to be riddled with ulcers of a nondescript type, from the floor, of which, however, we obtained many tubercle bacilli.

We had also the opportunity of examining the excretions from a number of patients with supposed tuberculosis (pulmonary) who had found their way into the tuberculosis wards, and yet had never yielded tubercle bacilli in the sputum. In not one of these cases in which the examination of the feces and urine indicated an absence of tuberculosis, did the autopsy prove the case one of active tuberculous infection.

One of us (Rosenberger) has during the past few years examined the feces in 1,104 cases of all kinds (including 71 instances of known tuberculous infection) with a percentage of 26.6 of positive finding of the tubercle bacillus. Excluding the 71 instances of recognized tuberculosis, there remain specimens examined from 1,033, of which number 21.5 per cent. were positive. These examinations were mostly of specimens

from patients with maladies resembling tuberculosis, such as typhoid states, or even malaria. A number were from apparently healthy individuals. To make sure that the tubercle bacillus alone was being dealt with, old and young cultures (six days' and six weeks' growths) of the butter bacillus, of the bacillus of Rabinovitch, of Grassberger, of the grass bacilli of Korn and of Moeller, the horse-dung bacillus, mist bacillus, the margarin bacillus, the bacillus of nasal secretion, and the smegma bacillus, were mixed with feces. Spreads were then made in the ordinary manner (after the organisms had been left in the feces for from one to twelve days) and it was found that all these organisms would decolorize completely in twenty minutes. Control preparations made of sputum or feces kept in Pappenheim's solution, showed the tubercle bacillus still retaining the red stain of the carbol-fuchsin after 116 days' exposure to the rosolic acid alcohol. Sections of tissue containing the bacillus lepræ, stained with carbol-fuchsin and then placed in Pappenheim's solution, showed the bacillus still retaining the stain up to the fourteenth day. Another organism that apparently was as acid-fast as the tubercle bacillus was that of Johnes' disease in cattle. This resisted Pappenheim's solution for sixty days. The spread was then removed from the fluid by some one's error, and further study was interrupted.

The foregoing studies have led us to the following conclusions:

1. In all cases of active tuberculosis, not only in cases in which they can be demonstrated in the sputum or urine, tubercle bacilli are present in the feces.

2. The urine of all actively tuberculous subjects probably contains tubercle bacilli, even though in small numbers. The average scarcity in a given specimen renders the study of the urine impracticable as a routine procedure. In many specimens they are stumbled on only when the examiner is about to give up the search, and it becomes necessary to class the specimen among the positive by virtue of the last field examined. Certainly it would seem that former publications reporting higher percentages of urines as positively containing tubercle bacilli, have included smegma bacilli among their findings. These can be differentiated, either by careful catheterization or by the use of rosolic acid and alcohol in decolorizing, or, if necessary, by obtaining the urine directly from the bladder at autopsy, as in the animals examined in our Experiments 4 and 5, reported in this study.

Thus Flick and Walsh⁵ report a series of 60 patients examined, the urine of 44 of whom showed supposed tubercle bacilli, by tinctorial methods, and yet out of five animals inoculated with the urinary sediment not one developed tuberculosis. In the presence of actual and living tubercle bacilli the tuberculous urinary sediment should prove infectious for susceptible animals, as shown by Bloch,⁶ who used, in many instances, urinary sediments in which the bacilli could not be demonstrated by tinctorial methods, and yet therewith successfully inoculated guinea-pigs with tubercle. His method was to crush the tiny inguinal glands between his fingers, and to inject the urinary sediment in the neighborhood of the trauma, in the likelihood that this area would be infected.

3. The question still remains *sub judice* whether scattered tubercle bacilli may not be found exceptionally in

the feces and urine of normal subjects. It would seem rational to believe that the feces would contain occasional tubercle bacilli, carried into the mouth with the food or air, and thence into the digestive tract, without infecting the patient. Our investigation of apparently healthy subjects has in no instance led to the discovery of the tubercle bacillus. We have knowledge, however, of at least two cases in which we have found bacilli in the feces, and in which at autopsy (made by others) no macroscopic lesions of tuberculosis could be detected throughout the body. This does not mean, of course, that the patient may not have had an actual infection by tubercle bacilli at the time of examination of the feces, and the discovery of the bacilli. Nor does it even imply that microscopic lesions may not have been abundant, no histologic study of the organs having been made. The recent experiments of Ravenel and Reichel,⁷ as well as those of many other laboratory workers, have shown how little lesion the bacilli may cause in an intestinal wall on passage through the latter to cause a bacteriemia, and it may well be that the instances that seemed at first glance to be accidental bacilli were, instead, the only evident expressions of a latent tuberculosis.

We have also studied the spinal fluid, the fluid from thoracic effusions, and ascitic fluid from a number of patients suspected of being tuberculous. In many instances we have demonstrated the tubercle bacilli, in others not. In one man for whom we had despaired of relief from an over-refilling ascites, accompanying a dilated heart, incision was made and to our surprise numbers of tubercle bacilli were found in the fluid. The patient practically recovered after the incision, and the fluid failed to return. In the remarkable case, to which we have already referred, of the patient supposedly dying of uremia, with no known or recognized pulmonary lesion, and no cough, clinical recovery ensued, but the patient continued to evacuate bacilli in feces and urine up to the time he was lost to view.

The following cases are of decided interest in this connection:

CASE 9.—*Patient*.—C. S., Philadelphia General Hospital. Bacilli could not be demonstrated in the sputum or urine, and yet were easily shown in the feces. On physical examination this patient showed a small area of doubtful consolidation at the extreme right apex.

CASE 10.—*Patient*.—A. W., a negro, with signs suggestive of meningitis, showed a few tubercle bacilli in his spinal fluid and very many in the feces. There were no signs of pulmonary or intestinal involvement and there was no diarrhea, and no increase of sputum.

CASE 11.—*Patient*.—J. K. presented a slight and probably early involvement of the right pulmonary apex. No tubercle bacilli could be found in the sputum, but they were present in large numbers in the feces.

CASE 12.—*Patient*.—S. C., an Italian, with an indefinite febrile condition, no signs of meningitis other than a slight stiffness of the nucha. The spinal fluid yielded tubercle bacilli, also the feces. There was no indication of intestinal implication.

CASE 13.—*Patient*.—J. M. had apparently a pulmonary congestion, slight fever, both bases flat on percussion, no cough, no sputum, no diarrhea. The abdominal muscles were rigid, and tubercle bacilli were found in the feces. This man recovered and was discharged from the hospital, still passing tubercle bacilli from the intestinal canal.

We have also in the past year had the opportunity of studying four cases of acute miliary tuberculosis of

5. Tr. Path. Soc., Philadelphia, April, 1903.

6. Berl. klin. Wchnschr., xlv, No. 17.

7. Jour. Med. Research, March, 1908.

other portions of the body than the intestines, in which tubercle bacilli were demonstrated in the feces. Autopsy showed an intestinal tract free from ulceration in each case.

One patient with cervical adenitis, on the way within the last month to the operating table, presented tubercle bacilli in the feces, and no other suggestion of tuberculosis throughout the body.

The foregoing cases emphasize at least three points of interest to the practitioner and to the pathologist:

1. Instances are not infrequent in which tuberculosis of parts other than the pulmonary and digestive tracts may be demonstrated by examination of the feces.

2. Tubercle bacilli may be sometimes shown in spinal fluid, or ascitic or pleural fluid, in cases of early and localized tuberculosis other than that of the pulmonary system, and in these cases the bacilli may be and usually are excreted in the urine and feces.

3. Incipient pulmonary tuberculosis may show considerable numbers of tubercle bacilli in the intestinal excretions, even in the absence of cough and obtainable sputum.

Of the infectiousness of incipient pulmonary tuberculosis there can be no doubt, even in instances in which neither cough nor sputum is apparent, provided such patients excrete tubercle bacilli in urine and stool. A number of cases have come to our attention that still further emphasize the need of supervision and care of the incipient disease. Two such may be mentioned in bare outline:

CASE 14.—Miss B. was reported in a former series of cases of incipient tuberculosis. She had then a slight involvement of the right apex. The nature of the onset and the physical signs left little room for doubt as to the nature of the process. There was slight cough, no sputum.

CASE 15.—The sister of Patient 14 slept with her during her convalescence, and developed a similar though more extensive involvement. Both of these patients recovered and are perfectly well.

CASE 16.—Simultaneously with the recognition of the second case the cook in the house, who cared for Patient 15 during these months as maid, and with whom Patient 15 had constant dealing as housekeeper, developed an active apical lesion. No other source of infection than Patient 14 could be discovered for the latter two patients. The feces of all three contained tubercle bacilli. There were many opportunities of infecting the hands in disposing of the urine and stools of Patient 14.

CASE 17.—Miss L. was a young girl presenting an early and very slight involvement of the right apex posteriorly, in conjunction with an appendicitis, which operation and pathologic study proved to be tuberculous. Tubercle bacilli could not be found in the sputum. The sister of the patient, who had not been well, was her bedfellow, and soon developed an active tuberculosis of the left lung and pleura, which is not yet under control. There was no apparent opportunity common to both for the infection. Moreover, the cases seemed strikingly successive and similar in course and type. The feces of both contained tubercle bacilli.

If these are true instances of infection of healthy persons by infectious material transmitted from supposedly non-infectious cases of tuberculosis, whether through inappreciable particles of pulmonary or bronchial material or through contamination of hands or food by moist or dry fecal or urinary soiling or dust, then it would appear that care must be exercised in a new and more active fashion in throwing safeguards around those who live with a patient who has even incipient tuberculosis. Seen in this light, at no date in the history of a case of infection is a rigid oversight begun too early

from the standpoint of the welfare of others. Such a conclusion, apparently well grounded, requires only the fact already stated of the presence and discovery of tubercle bacilli in the semen, and the consequent likelihood of frequent latency of tuberculosis, to render the possibility of infection of a healthy mother or family by a newly-born tuberculous infant not only a possibility but a matter of concern. Especially will this be true in a case in which the father is known to be tuberculous and the mother appears to be free.

We have had neither the opportunity nor the time as yet to study the milk from nursing tuberculous mothers. The frequency of infection of milk from tuberculous cattle leaves little occasion for hope that a different state of affairs obtains in the human secretion.

The knowledge that pregnancy and the ordeal of child-bearing tends to light up a sluggish or dormant tuberculous condition in the mother would also lead us to believe that the tuberculous mother is above all other times then likely to secrete and excrete tuberculous waste products.

INFECTIOUSNESS OF OLD SECRETA AND EXCRETA

We have been interested to note in passing the duration of virulence of the tubercle bacillus in sputum, urine and feces under natural conditions favorable to and unfavorable to their life. We have met with results that vary to the last degree. On June 1, 1908, six specimens each of urine, sputum and feces, all containing virulent tubercle bacilli, were set aside in vessels covered with large-meshed gauze and exposed for about twelve hours daily to sunlight and air. On July 1 and August 1 the bacilli in the sputum could be demonstrated without difficulty and proved specifically toxic for guinea-pigs. They took the stains readily in the urinary sediments also and in the dried fecal mass rubbed up with distilled water and smeared as usual. The specimens were then saved for further study. A few days later the bacilli could no longer be shown in two of the specimens of sputum. With material from one of these sputa a guinea-pig was inoculated (Experiment 3) hypodermically, and within a few days tubercle bacilli were demonstrated in its feces, not having been present there up to that time.

In contradistinction to this finding one of us (Rosenberger) has preserved virulent tubercle bacilli in tap water, exposed to sunlight and diffuse daylight for a full year, then has produced tuberculosis in a guinea-pig by inoculation and recovered the bacilli from the animal. There seems to be no rule possible for the calculation of the viability of the germ under a given environment. There seems to be some doubt, moreover, whether in process of time tubercle bacilli must necessarily die out in any or all excreta, the time being indeterminate and impossible of regulation except by immediately destructive methods. Certainly we must conclude that the organism may persist in a non-stainable form in any or all known media and retain its virulence for use on a favorable occasion.

It may still be that from the tubercle bacillus we shall learn the secret of perennial youth. In a recent paper Dixon⁸ has discussed the action of direct light and eosin on the tubercle bacillus. He seems a little more optimistic in regard to the bactericidal influence of drying and of the sun's rays than appears to us warranted

8. Dixon, Samuel G.: May Not Drinking Water, When Polluted with Sewage, Be One Medium of Dissemination of the Tubercle Bacillus? *THE JOURNAL A. M. A.*, Aug. 1, 1908, II, 380.

in the light of our experiments. There is no doubt that certain infected sputa are rendered innocuous by Nature's and by simple artificial means. It is our knowledge, and we believe that it will be of service to the practitioner if he is brought to understand that under favorable conditions, or even when exposed to air and strong sunlight, the bacillus may attain a virulent old age. The most dangerous feature of its persistence, as shown by our Experiment 3, is its occasional survival in a form that requires tedious culture and refuses demonstration by tinctorial methods.

There opens up an endless series of queries as to the actual presence or absence of bacilli in excreta on which a negative laboratory report is made and in which neither cultural nor inoculation tests are made to determine the doubt. This masked battery will decimate more than one generation and defy defeat and silencing unless some more certain method be discovered of promptly demonstrating the silent forms of the tubercle bacillus. The almost unlimited life of the bacillus in butter, and its frequent occurrence therein, has been dwelt on with force by Schroeder and Cotton.⁹ They have shown that after four and one-half months the bacilli were as virulent as at the start, the fatty nature of the butter probably protecting them from destructive influences. This may also lend a hint as to the length of life of bacilli even in dried secretions and excreta, in certain of which enough of fatty matter is perhaps maintained to allow of their existence, while in a few or even many the fat content is low and the bacilli easily destroyed.

ORIGIN OF THE BACILLI IN URINE AND FECES

There need be no discussion of instances in which local tuberculous lesions are present in either the urinary (kidney to urethral meatus) or digestive tracts. With regard to the appearance of bacilli in the urine of patients with tuberculosis of the glands of the neck, or of the lungs, or of the peritoneum even, there need be little hesitation in turning to the acknowledged bacteriemia for the explanation. With regard to the presence of bacilli in the feces in similar cases the answer must not be so precipitate.

In the first place they may be swallowed with food or water, or with sputa in instances of tuberculosis of the bronchi or lungs. On the other hand, our animal experiments do not lead us to believe that many bacilli introduced by the mouth become demonstrable in the feces until several days after their introduction into the stomach with the food. Experiments in which the bacilli have been introduced by us in the form of native sputum have led us to doubt whether they are carried into the intestines in a form that will accept the stain when swallowed by the patient as his own sputum. Certainly such a possibility must be considered. Of all the explanations, however, it now appears to us the least satisfactory.

Longcope¹⁰ and others have shown the frequency of tuberculosis of the thoracic duct and the involvement of its lymph with tubercle bacilli in cases of general tuberculosis. Here we find at least one explanation both of the presence of the bacilli in the intestine and of the scattering abroad from the digestive tract. The final means of transmission, however, whether one medium be the lymph and another the tissues themselves, must be the blood, if all the requirements and demands of the known

facts are to be met. Once granted, as we must, that bacilli administered in soup to animals reach the heart blood in four to five hours, as Besanti and Panisset have shown in a number of experiments, we need no further explanation of the transportation of tubercle bacilli from local lesions far distant to the manufactory of the fecal mass.

EARLY APPEARANCE OF TUBERCLE BACILLI FOLLOWING INOCULATION OF GUINEA-PIGS

It has also been our aim through the inoculation of guinea-pigs by various methods, and by careful scrutiny of their physical signs, their secretions and excretions, both prior to and subsequent to inoculations, to determine the earliest probable period of infectiousness in a given case of tuberculosis.

In order to arrive at as practical results as possible we not only fed to one guinea-pig tuberculous sputum spread on cabbage leaves, but into others injected tuberculous sputum in distilled water either hypodermatically or intraperitoneally.

EXPERIMENT 1.—On Aug. 8, 1908, a large male guinea-pig, weighing 420 gms., was fed on 8 c.c. of tuberculous sputum from a patient in the tuberculosis infirmary. The urine and feces were examined on the day prior to the inoculation, and on each day thereafter. On the day prior to the feeding a few micrococci and fungi were found in the stools and urine. On the third day after the feeding for the first time a few scattered tubercle were found in the feces, together with many tiny diplococci. The urine also contained many diplococci on the third day and thereafter, but no tubercle bacilli were discovered in the urine until the seventh day. They were constantly present in the feces from the time of the first appearance, and were occasionally found in the urine up to the time the search was discontinued. An autopsy was performed on this pig on Sept. 16, 1908. The lungs showed several small foci of caseous deposit. No other macroscopic change was evident.

EXPERIMENT 2.—On Aug. 18, 1908, a large brown and white male guinea-pig weighing 530 gm. was inoculated hypodermatically about an inch from the tail with tuberculous sputum from a woman in the infirmary. The feces and urine were examined daily before and after the inoculation. Tubercle bacilli appeared first on the fifth day in the feces, and on the eighth day in the urinary sediment. The search was then discontinued. Autopsy showed widespread tuberculous involvement of the lungs. The intestines showed no ulceration.

EXPERIMENT 3.—On Aug. 18, 1908, a large male guinea-pig, weighing 490 gm., was inoculated with a solution in 1 c.c. of distilled water of a dried tuberculous sputum which had been exposed to air and sunlight for over two months, and in which the tubercle bacilli were no longer tinctorially demonstrable. The feces and urine showed no bacilli on the day of inoculation or thereafter until the sixth day, when they were detected in small numbers in the feces. They were at no time found in the urine. Autopsy showed tuberculous involvement of the lungs. The intestines showed no ulceration.

EXPERIMENT 4.—On Sept. 1, 1908, a large male guinea-pig was inoculated intraperitoneally with 2 c.c. of tuberculous sputum and distilled water aa . It died of septicemia on the third day. The urine and feces were examined on the day of inoculation and no tubercle bacilli were found prior to operation. The peritoneal cavity at autopsy showed a large quantity of pus and lymph. There were also scattered miliary pus foci in the lungs. The peritoneum was thickened and everywhere covered with purulent exudate. A smear from the peritoneal pus showed a very few cocci and myriads of eosinophiles. The bladder was full of urine containing pus (2 c.c.). This was fixed and dried with egg albumin on a slide and stained. A single colony of eight tubercle bacilli was found in the preparation. They were also present in the feces obtained directly from the cecum.

EXPERIMENT 5.—On Sept. 1, 1908, a large male guinea-pig was inoculated with the same sputum and similarly to the

9. Circ. 127, Bureau of Animal Industry, U. S. Dept. Agric.
10. Bull. 3, Ayer Clin. Lab., 1906.

last one. It died on the fourth day, from septicemia. The urine examined before inoculation showed no tubercle bacilli. The feces also gave no bacilli. The autopsy gave the same findings as in the preceding animal, except that the suppurative process was not so far advanced. The lungs were congested, but showed no purulent metastases. A smear from the peritoneal pus gave myriads of small diplococci and no tubercle bacilli. The bladder contained urine, which showed in the dried and stained specimen a few scattered tubercle bacilli. The feces also contained scattered single tubercle bacilli.

CONCLUSIONS

1. Intrauterine tuberculous infection of the ovum through the semen is probably a frequent event.

2. Tubercle bacilli are present in the feces and in the urine of many, and probably all cases of active local and systemic tuberculosis of the human being.

3. Tubercle bacilli appear in the feces and urine of tuberculous subjects within the first few days following an acute infection, and in certain instances long prior to the appearance of physical signs.

4. The only likely means of rendering tuberculous excreta (sputum, feces, urine) innocuous is the direct and effectual application of heat. They can not be expected certainly to overgrow or die out or surely to succumb to sunlight or drying.

5. Excreta from which formerly demonstrable tubercle have apparently disappeared may still prove destructive to animal life, and the bacilli again be recovered from the test animals in a demonstrable form, both by culture and by tinctorial methods of examination of the excreta.

6. The routine examination of the stools for tubercle bacilli should be more invariable even than that of the sputum. It more often yields a positive result. In occasional instances the microscopic field is as thickly spread with the bacilli as any sputum. Often the search must be painstaking and extended until a few scattered bacilli have been detected.

7. The examination of the urinary sediment for tubercle bacilli is not adapted to the use of the general practitioner. It should be resorted to whenever necessary to a thorough confirmation of suspected and doubtful or local (genitourinary) infection. The inoculation of guinea-pigs with the urinary sediment is a surer though slower method of demonstrating the bacillus, provided the test animal escape early death from mixed infection.

8. Probably all infections will open up to similar methods of study their causal organism when once we have determined upon specific stains and differential methods. There appears to us to be little doubt that every bacterial infection is a bacteriemia, and it seems not improbable that in every bacteriemia the causal organism is excreted through the urine and the feces.

SIGNIFICANCE OF THE FOREGOING

The import of this and of similar studies by other investigators is at once vital in its bearing on society at large. The physician is confronted with the certainty that he has no more than begun the crusade against tuberculosis. He has perhaps even overestimated the possibility of its complete ultimate control. Without the slightest desire of uttering a pessimistic word, and with the knowledge that in the clearest understanding of the truth lies the best hope of ultimate accomplishment—on the basis of this study we feel dubious as to the extinction of the disease by human means. No more likely is it that the discharges from the typhoid or cholera or dysenteric patient will always

or even usually (except in hospitals) be effectually destroyed, and thus prevented from polluting the air we breathe and the drinking supply, than that tuberculosis shall more than be inhibited in its spread. Granting as we now must that the infection is scattered broadcast for days and weeks, and perhaps months, before signs and symptoms demand a study of the case, it will be seen at a glance into what a labyrinth wanders the quest for its extermination and control.

Urine, sputum and feces are virulent, whether wet or dry, and for an indefinite time, the very indefiniteness of which renders them positively antagonistic to the health of the community until the bacillus or some equally positive destructive force places the sufferer under the sod.

The studies of Lord¹¹ have shown us that one fly-speck may contain as many as 5,000 tubercle bacilli; further, that thirty infected flies deposit in three days from 6,000,000 to 10,000,000 tubercle bacilli. We are, therefore, starting some centuries late in the destruction of flies.

Friedmann has injected tubercle bacilli into the vagina of a guinea-pig just after coitus, and later demonstrated the bacillus in the embryo. We, therefore, not only have on our hands the destruction of insects, but the prevention of marriage among the tuberculous. And yet, in spite of this knowledge that urine and feces and sputum and semen all carry, under favorable conditions, the certainty of a spread of the disease—in future rather because than in spite of this—there will be disinfected many an otherwise ignored or neglected source of contagion.

In so far as we arrive a step nearer a comprehensive realization of the armament, the subtlety, and the ubiquity of the tubercle bacillus; in just the proportion that our effort at control is relentless and systematic; in just that measure will we render a dayspring of true health conceivable, and lighten with hope this toilsome burden of man.

ANEMIAS OF INFANCY *

JOHN LOVETT MORSE, A.M., M.D.

Assistant Professor of Pediatrics, Harvard Medical School; Assistant Physician at the Children's Hospital and at the Infants' Hospital; Visiting Physician at the Floating Hospital

BOSTON

The blood of infants under 2 years differs normally in certain of its characteristics from that of adults. The hemoglobin, relatively high for a time after birth, rapidly falls to a minimum of 55 or 60 per cent. in the first three weeks, then gradually rises to 70 per cent. at about six months, where it remains during the rest of infancy. There are, moreover, normally great variations in different individuals and in the same individual at different times. The number of red corpuscles is somewhat larger than in adults, averaging between 5,500,000 and 6,000,000 per c.mm. During the first few weeks of life there is more or less variation in the size and shape of the red cells, and nucleated forms, are not very unusual during the first few days.

11. Pub. Mass. Gen. Hosp., 1906, 1.

* Read in the Section on Diseases of Children of the American Medical Association, at the Fifty-ninth Annual Session, held at Chicago, June, 1908. Owing to lack of space, the article is here abbreviated by omission of the portion relating to leukemia. The complete article appeared in the Transactions of the Section and in the author's reprints.