line of strike of a fault, and "plunge" with reference to sea level.

The reviewer is also glad to see a false statement, "commonly made in geological literature," sharply corrected, having once, in good faith, helped to spread it in print, *viz.*, that the angle of shear is greater than 45 degrees in "ductile" materials.

In other respects, however, the discussion of failure by rupture is open to criticism. If the angle of sheer is "always less than 45 degrees" in the direction of greatest shortening (p. 102) it is not feasible to interpret systems of rectangular joints as shear planes (pp. 126 and 127) or to say that the shear fractures are "approximately parallel" to the circular sections of the strain ellipsoid which form a strongly obtuse angle in the direction of the greatest shortening (p. 109).

In general, the strain ellipsoid is given the lip service usual among American geologists, but it is not introduced where it belongs first of all: in the explanation of the results of laboratory compression and tension tests. For such cases an obviously megascopic "imaginary sphere" is introduced inside the cylinder or square prism that is undergoing compression (p. 101). In both objects it is said to be deformed into an oblate spheroid.

This is, of course, not true in the case of the square prism. The "imaginary sphere" does not explain why the fractures form a cone in one case and a four-sided pyramid in the other. The absence of the concept of the strain-ellipsoid from so basic a discussion shows that it is not introduced at all in the truly valid sense.

Actually in this text, as in most writings of geologists who use it, the word "strain ellipsoid" stands for a two-dimensional figure of an ellipse, which is placed on the picture of a geologic structure in such a way that its axes point respectively in the directions of greatest (relative) shortening and lengthening. Into this figure diagonal lines are drawn to suit the writer's imagined needs: now intersecting at right angles (Fig. 109, p. 127) now at highly obtuse angles which face in the direction of greatest shortening, both strictly contrary to all laboratory evidence, and never, not once, in the only direction justified by the facts set forth at the start.

No wonder this devise is praised as "exceedingly useful if it is employed with discrimination." This matter obviously needs revision in the second edition.

In the discussion of the larger aspects of rupturing, of thrusts and faults, the rôle that plastic deformation, solid flow, plays in rock deformation seems to the reviewer too much neglected. Thrust sheets and fault blocks are more than lumps of inert matter that are set in motion by forces wholly outside of them. They are invariably parts of larger rock bodies every particle of which is in active upward, outward, or sideward movement, the planes of rupture representing discontinuities in the rate of movement. Seen in that light, the author's general use of the term "gravity fault" appears downright indefensible. Failure to give it the attention it deserves accounts for the wholly inadequate treatment of the structures that characterize the folding in the Swiss Alps. It also explains why the author has given over 90 lines and 8 text figures to the discussion of drag folds, while he refers in only four and a half lines to the type of minor folding that abounds in crystalline limestones and schists.

Further recitations of differences in bias or emphasis between the reviewer and author would tend to obscure the basic fact concerning this book: It is a text-book of high merit, written in simple language, easy to read (being printed in large type), forthright in its approach to the concrete matters of terminology and basic principles, methods and technique in structural geology which are indispensable as a foundation for practical work.

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SPECIAL ARTICLES

BIOLOGICAL EFFECTS OF A TOXIC AND A SENSITIZING SUBSTANCE ISOLATED FROM PARAFFIN OIL EXTRACT OF DEAD TUBERCLE BACILLI[1]

IT is a well-known and remarkable fact that killed tubercle bacilli retain many important properties characteristic of the living organism. The nature of the lesions which develop at the site of inoculation and the sensitization to old tuberculin (an almost infallible test of infection) which it confers on animals, has always shown clearly that the dead bacilli have the same specificity of action as that of living ones.

The effects of dead tubercle bacilli become quite comparable to those of living organisms with regard to lesions and sensitization if the dead bacilli are suspended in paraffin oil instead of saline solution. The experiments of Hagan and Levine,[2] Opie and Freund,[3] Coulaud,[4] Saenz[5] and Noel Rist[6] established clearly

[1] This study was carried on under a grant from the Josiah Macy Junior Foundation.

[2] Hagan and Levine, *Jour. Am. Vet. Med. Asn.*, 8: 728, 1932.

[3] E. Opie and J. Freund, *Jour. Exp. Med.*, 66: 761, 1937.

[4] Coulaud, *Rev. de le Tub.*, p. 850, 1934.

[5] A. Saenz, *Revue d'immunologie*, p. 530, 1937.

that the inoculation of paraffin oil suspensions of heat-killed tubercle bacilli produce a sensitization to old tuberculin (O.T.) at least as intense as that given by living virulent bacilli (and much more intense than that given by the same amount of dead bacilli in saline solution). The oil suspensions also provoked the appearance of lesions far from its site of inoculation, whereas suspension in saline gives merely local lesions. All workers agree that pure paraffin oil alone does not produce these effects.

In spite of achieving such results, approaching more and more closely to those induced by living bacilli, workers in the field were still of the opinion that the whole organism was necessary to produce the effects. This opinion was strengthened by the numerous unsuccessful efforts to sensitize normal animals to O.T. with substances extracted from tubercle bacilli.

In attempting to answer the question as to the nature of the mechanism by which paraffin oil enhances the effects of dead bacilli, it occurred to me that it might consist of the removal of substances from the bacilli by the oil. In such a case one should be able to find an active principle in oil which had been in contact with the dried dead (killed by autoclave) bacilli.

Such oil was subjected to prolonged centrifugation, which separated it from the suspended bacilli. The resulting oil differed from the pure oil in viscosity, absorption spectra and specific fluorescence. Moreover, biological controls, after centrifugation at 80,000 r.p.m. for 24 hours, confirmed the fact that this oil was free of bacilli.

I have been able to show that this oil extract contains an active antigen which precipitates with tuberculous rabbit serum. The inoculation of this oil stimulated the formation of antibodies in rabbits and produced a definite sensitization to O.T. in guinea pigs.[7] For the first time, therefore, it was possible to sensitize normal animals to O.T. without using the whole dead or living organism.

In attempting to find the material responsible for this sensitization, a toxic substance was extracted from the oil. A precipitate was first obtained from the oil with the aid of dioxane. This precipitate, P, was submitted to extractions with many organic solvents.

Among these, the dried chloroform extract, inoculated into guinea pigs intraperitoneally in paraffin oil, was found to be very toxic, 2 gamma, the smallest dose tried, being sufficient to produce lesions in the lungs and usually killing the animal.[8] The biological results were supervised by Dr. Alfred Boquet, head of the department of tuberculosis at the Paris Pasteur Institute.

The toxic substance proved to be acid-fast and highly birefringent. It shows beautiful colorations in polarized light. Microanalysis of the toxic substance showed it to be free of nitrogen and phosphorus.[9] Hydrolysis with 10 per cent. potassium hydroxide in alcohol separates it into sugars and an acid alcohol which appears to be very similar to the mycolic acid isolated by J. R. Anderson.[10] But neither mycolic acid nor these sugars alone have shown such biological toxicity. It is possible that the toxicity of this polysaccharide is due to an impurity of a protein nature not discernible in the microanalysis. In this case, such an impurity must be active in amounts as small as 0.01 gamma.

The work which had been carried on in Paris (Institut de Biologie Physico-Chimique) was interrupted in June, 1940, by the war. It was resumed at Cornell University Medical College (Dr. Morton Kahn's laboratories) in the spring of 1942. The nature of the sensitizing substance contained in the oil was still unknown as well as the amount necessary to produce sensitization.

From 8 grams of dried human tubercle bacilli (all that was at first available) of the strain H_{37} (single cell, Dr. Morton Kahn) which is of a low virulence, it was not possible to extract the toxic substance in significant amounts. However, from this material, it was found possible to extract a substance which sensitized normal guinea pigs to P.P.D. and also O.T. with a single 1/10 mg injection. The inoculations were made intraperitoneally, the substance being suspended in paraffin oil. It was later possible to sensitize normal animals with the same amount of substance suspended in saline. All these results were supervised by Dr. Morton Kahn.

It was interesting to determine the relative proportion of toxic and sensitizing substances in two different strains of different virulence. Cultures were made with the strains H_{37} (Dr. Kahn) and a strain PB_{15} of a higher virulence isolated by Dr. Florence Seibert on Corper's medium and cultivated by us on Long's medium. It was found that the precipitate, P, from PB_{15} was richer in toxic substance and poorer in sensitizing substance than the precipitate from H_{37}.

Of the animals (8 out of 10) which revealed sensitization to P.P.D. and O.T. five weeks after receiving a single injection of 0.1 of mgr of the sensitizing substance, 5 remained sensitized 10 months later. Three of them were sacrificed to assure us that they were not tuberculous. The two others, as well as three who were no longer sensitized, and five controls then re-

[6] Noel Rist, "L'Allergie conferée par le bacille morts." These de Paris, 1938.

[7] Nine Choucroun, *Compt. Rend., Acad. des Sci.*, 208: 1757, 1939.

[8] *Ibid.*, 210: 511, 1940.

[9] *Ibid.*, June, 1940.

[10] R. G. Anderson, *Jour. Biol. Chem.*, 85: 339, 1929.

ceived (February 9) H_{37} live bacilli. All the animals died before May except the two which were still sensitized. These are still living and in good health. This experiment was only an indication that the sensitizing substance may act as a protective one. Further experiments, now under way, involving 46 animals, appear to confirm this impression.

The sensitizing substance may, therefore, be able, if separated from the toxic material which accompanies it in the whole bacilli, to protect animals against tuberculosis.

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AN INOCULATED PENICILLIN DRESSING

CONCENTRATED and purified penicillin are not available to civilians except in extreme circumstances. For intravenous administration it is desirable to use the purest and most potent product obtainable. There are conditions, however, in which it is possible to use advantageously penicillin of less potency. Wounds, furunculosis, sinus infections, gonorrhea and other infections of the skin or mucous membranes might be so treated.

In order that patients may have the benefits of penicillin treatment not otherwise available we have explored some of the possibilities of the use of the crude product.

The Florey or Oxford Unit is defined as "the amount of penicillin which, when completely dissolved in 50 ml of meat extract broth, just inhibits completely the growth of the test strain of *Staphylococcus aureus*."[1] Thus a solution containing one unit per cc represents a bacteriostatic agent against the staphylococcus diluted 50 times. The average production from Czapek's synthetic medium is about 4 units.[2]

Since, in the accounts of the therapeutic use of penicillin, the continuous exposure of the infecting organism to the penicillin is stressed, it seemed possible to us that in surface infections the substance might be produced in contact with the lesion. A dressing 5 cm × 5 cm composed of eight layers of gauze was placed in a Petri dish and saturated with a medium containing 1 per cent. yeast extract, 2 per cent. dextrose, 2 per cent. corn starch and 2 per cent. glycerine. This was autoclaved and inoculated with penicillium. After two days at room temperature 1 cc of sterile human plasma was allowed to flush underneath the dressing to simulate as well as possible its application to an open wound. At intervals, shown in the protocol below, the Petri dish was tipped so that the small amount of liquid would drain away from the gauze. This was titrated by the ring test and dilution method. Fresh plasma was substituted under the dressing for that withdrawn. (See Table 1.)

TABLE 1

TITRATION OF PENICILLIN PRODUCED ON INOCULATED DRESSING

Days after inoculation	Diameter of ring test	Units of ring test	Dilution of complete inhibition	Units by dilution method
3	30 mm	5+	.....	...
4	22	.75	.....	...
6	24	1.0	1:200	4
7	..	...	1:200	4
8	21	.75	.....	...
10	10	.25	1:10	.20
3	25	1.5	.....	...
Control washed with salt sol.				

It is impossible to say that these *in vitro* tests represent the exact conditions which would result in the application of the dressing to a lesion, yet the tests demonstrate that a fair amount of penicillin is produced over a period of 4 or 5 days and a bacteriostatic condition would be maintained at the point of contact with the lesion.

Clinical application of the penicillium inoculated gauze dressings and the crude liquid penicillin was made, employing patients who had not been relieved by other acceptable forms of therapy.

One patient had an acute osteomyelitis and periostitis of the right humerus of two weeks' duration. A previous wide incision had been made over the site of the lesion and sulfonamides were prescribed without relief. An inoculated gauze dressing was planted over the wound. Within three hours there was less pain, and in ten days the patient was discharged from the hospital clinically well.

Another patient who had a large furuncle on the back of his neck was treated by injecting the crude liquid penicillin into the open crater and by the local application of an inoculated gauze dressing. Three days later the patient was relieved of all discomfort and the wound was granulating.

A third patient had multiple soft tissue abscesses over his lower back and sacral region. This infection has been recurring regularly for three years. The infecting organism was a *Staphylococcus aureus*. His last period of hospitalization under accepted methods of therapy has been of six months' duration. Crude liquid penicillin was injected into the abscesses and their sinuses and penicillin inoculated gauze dressings were placed over the larger abscesses. This patient is remarkably improved and is still under treatment.

Two other cases of chronic osteomyelitis and periostitis of the femur are being treated with the crude liquid penicillin and the inoculated penicillin gauze

[1] H. W. Florey and M. A. Jennings, *Brit. Jour. Exp. Path.*, 23: 120, 1942.

[2] E. P. Abraham and E. Chain, *Brit. Jour. Exp. Path.*, 23: 103, 1942.