cyst was formed during the meningitis and was entirely unrelated to the hemiplegia, the occurrence of which would then be unexplained. As for the infection itself, one can only regard it as a fortuitous event which proved to be the last straw for the patient.

The occurrence of these three clinical entities—subarachnoid haemorrhage, intracerebral haemorrhage, and meningitis—in any one patient is such a rare event that it is interesting to speculate what the odds against their happening in an identical twin are—an astronomical figure, surely! That the case should have occurred at all is an example of the interesting possibilities that sometimes materialize during the course of medical practice.

I should like to express my thanks to Dr. Ronald Jones for permission to publish this case as well as for his criticism and advice, and to Dr. Eric Biddle for the use of his post-mortem notes on the subject.

UREA AND ITS EFFECT ON TUBERCLE BACILLI

BY

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Urea has been shown to have a marked beneficial effect in the treatment of septic wounds as well as to possess certain physiological properties in regard to proteins. Spiro has been quoted in relation to the latter, but I have not been able to have access to his paper, dated 1900. Ramsden, in 1902, showed that it acted as a "*substance sensibilisatrice*," rendering proteins more prone to zymolysis, conversion into acid- or alkali-albumin; as a protective substance, since coagulable proteins are not heat-coagulable in its presence but reacquire their coagulability when the urea is removed by dialysis; and as a solvent. He added that "in a saturated urea solution no putrefaction ever takes place."

Symmers and Kirk (1915) made a powerful claim for treatment of septic processes by crystalline urea. Kirk, after giving striking examples of its successful application, pointed out, however, that the wounds should be kept tightly closed by covering the urea with some dry protective material such as oiled silk or by suturing, as a "dry dressing on top of the urea absorbed the solution and prevented its action on the tissues." Symmers, dealing with the problem from the bacteriological point of view, showed that strong concentrations of urea were bactericidal and bacteriostatic. He showed, further, that urea would kill bacteria in the presence of blood and other protein substances.

One of Symmers's experiments—a very striking one—may, however, have given rise to some misunderstanding and deserves to be carefully considered. He took two tubes of tuberculous sputum. To one of these he added urea and the other he left as a control. From the tube treated with urea a culture was made after 15 minutes from which only 3 colonies grew. From a further culture put up after 30 minutes there was only one colony. From the control tube there was abundant growth on agar. Anyone reading this account in a hurry might imagine that it was intended to convey that tubercle bacilli had been killed, but this was not the fact or the intention. The tuberculous sputum had been chosen because it afforded a good example of a badly contaminated sputum. Its culture after 15 minutes and half an hour showed that the urea had sterilized it or at least had gone very far towards sterilizing it in a very short space of time, whereas a culture from the control sputum gave an abundant growth on agar. The experiment was not intended to prove the sterilizing effect of urea on tubercle bacilli, but to show its effect on putrefactive organisms.

The Experiment

It occurred to me, therefore, to try the effect of urea on the tubercle bacillus itself as exemplified by a pure culture. Two

cultures were obtained from Prof. W. H. Tytler of the Welsh National School of Medicine. One of these failed to grow either with or without urea, and was therefore put aside as useless for the tests. The other, labelled "Pleural Fluid 22924" and dated Nov. 8, 1941, was emulsified in sterile water to a dilution of about 5,000 million bacilli per c.cm., the number being judged by the opacity of the fluid but not counted.

On Dec. 30, 1941, in each of 4 sterile test-tubes was placed 1 c.cm. of this suspension of tubercle bacilli, urea being added as follows:

Tube I :	Sat. sol. urea	..	..	1 c.cm. of tubercle suspension
" II :	" " " /2	..	..	1 " " "
" III :	" " " /4	..	..	1 " " "
" IV :	" " " /8	..	..	1 " " "

At the same time 1 c.cm. of tubercle suspension was put up with 1 c.cm. of distilled water, two test-tubes being thus suspended so as to have two "controls."

All 6 tubes were then transferred to the incubator at 37° C. and left for 48 hours. At the end of this time each tube was removed and 0.5 c.cm. of the contents placed on a "bottle" of Löwenstein-Jensen medium, the screw cover being well fixed and the bottles placed in the incubator at an angle close to the horizontal. After a week they were replaced vertically, the surface being dry.

On Feb. 9, 1942, the culture tubes were examined and found to show growth of tubercle bacilli as follows:

Tube I :	Sat. sol. urea	..	T.B. susp.	..	No growth
" II :	" " " /2	..	" "	..	"
" III :	" " " /4	..	" "	..	+
" IV :	" " " /8	..	" "	..	++
Control :	Aq. dest.	..	" "	..	+
"	" " "	..	" "	..	++

It should be recalled that the saturated solution of urea had been diluted in each tube by an equal volume of bacillary tubercle suspension, so that the final cultures were made with half the strength in each tube.

Conclusions

The experiment shows that urea in dilutions of half saturation and one-fourth saturation completely kills off the tubercle bacilli from a thick emulsion in 48 hours. In an eighth and a sixteenth dilution, however, it is powerless to kill, though it is significant that the growth was much less on Tube III than on Tube IV. The phenomenon seems to be just the same as that noticed by W. J. Wilson (1906) with coliform and other bacteria.

Seeing that urea either in the pure state or in saturated solution is harmless to the tissues and that it not only kills tubercle bacilli in very large numbers but also destroys septic secretions and ordinary saprophytes as well as pathogenic germs, it would appear very suitable as a dressing for tuberculous ulcers and even, perhaps, for cavities close to the pleural surface where adhesions have made these accessible or small tuberculous empyemata. In the treatment of tuberculous ulcers, however, where the crystalline urea was being used, it should be protected from absorption by the dressings by the interposition of oiled silk or some similar material between the urea and the dressings.

It is to be noted that Stonham (1941) reported favourably on urea in the treatment of septic wounds and that Muldavin and Holtzmann (1938) obtained with it excellent results in infected cases.

Good accounts of the physiological and therapeutical uses of this substance may be found in articles by Gurchot and McCawley (1940) and Holder and MacKay (1939).

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