Corresponding results were obtained from other experiments, where the penicillin concentration varied from 1 down to 0·05 unit per ml. From these experiments it is possible to say that absorption of penicillin, if any, probably amounts to less than ten molecules per bacterium.

The work is continuing, and further details of it will be published elsewhere.

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Effect of Antibacterial Analogues of Vitamin K on *M. tuberculosis*

I would like to record some experiments made three years ago and recently repeated with a different technique. During a search for chemically defined growth-factors for *M. tuberculosis*, it was decided to investigate vitamin K. The role of vitamin K in bacterial metabolism has not been determined; but this vitamin is present in many organisms and is probably of nutritional importance[1,2,3]. Anderson has isolated from a laboratory strain of human tubercle bacillus a pigment, 'phthiocol' (2 methyl 3 hydroxy 1 : 4 naphthoquinone), which has vitamin K-like activity[4,5]. It has been postulated that phthiocol is derived from vitamin K during the extraction of the bacteria[6]. For many years it has been known that *M. paratuberculosis* when freshly isolated will grow only on media containing extracts of other acid-fast bacteria, notably *M. phlei*. The claim has been made that phthiocol and 2 methyl 1 : 4 naphthoquinone can replace *M. phlei*[7]; but the stimulant action is not so marked, and hence it does not follow that the *M. phlei* growth-factor and these compounds are the same. *M. tuberculosis* var. *hominis* can also have its growth accelerated by extracts of other acid-fast bacteria, and for these reasons this investigation was undertaken. Reports in the literature on the action of phthiocol and 2 methyl naphthoquinone are not consistent[8,9], but naphthoquinone derivatives have been claimed as inhibitory[10]. In the accompanying table compounds 1 and 2 are water-soluble synthetic vitamin K derivatives and both inhibit growth.

As recently isolated virulent strains of *M. tuberculosis* require complex media of unknown composition, an indirect approach to the problem was sought by the use of antibacterial analogues of the vitamin K series. Such compounds have been made by McIlwain[3], and their effect is shown in the table. The results are parallel to those obtained with other organisms, and I have obtained similar but not identical results with different culture substrates. The phenazine derivatives are of interest because of their relation to the bacterial pigments pyocyanine and chlororaphin, and iodinin itself is obtained from *Chromobacterium iodinum*. Compound 10 is non-toxic to guinea pigs and mice, and *in vivo* tests are now in progress.

Thus the original hypothesis that vitamin K-like compounds are necessary for the nutrition of *M. tuberculosis* has not been proved; but the results listed do suggest that similar substances play some part in the metabolism of the organism. Recent advances in vitamin K research may have an application to this problem[11,12,13].

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Medium: Long's plus Tween 80, 0·01 per cent; bovine plasma fraction V, 0·2 per cent. Inoculum: 1 mgm. virulent *M. tuberculosis* var. *hominis*

	Compound	Amount causing inhibition at eight days	
		Molarity	Parts per million
1	4 Amino 2 methyl 1 naphthol hydrochloride	10^{-5}	3
2	Tetrasodium 2 methyl 1 : 4 naphthohydroquinone diphosphate	4×10^{-4}	166
3	Quinoxaline di N-oxide	2×10^{-4}	33
4	2 Methyl quinoxaline di N-oxide	5×10^{-4}	80
5	Methyl pentyl quinoxaline di N-oxide	10^{-4}	25
6	2 Hydroxy quinoxaline	5×10^{-2}	1000
7	1 : 2 : 3 : 4 : Tetrahydrophenazine di N-oxide	2×10^{-4}	20
8	1 : 2 : 3 : 4 : Tetrahydrophenazine	5×10^{-4}	100
9	Phenazine mono N-oxide	10^{-4}	25
10	Phenazine di N-oxide	5×10^{-6}	1
11	Dihydroxy phenazine di N-oxide (iodinin) (impure preparation)	10^{-5}	2

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Dicumarol Poisoning and Vitamin K Deficiency in Relation to Quick's Concept of the Composition of Prothrombin

In 1943, Quick[1] published some experiments which were taken as evidence for the multiple nature of prothrombin. In the same paper Quick expressed the opinion that the hypoprothrombinæmia in vitamin K deficiency might be due to the disappearance of the same constituent of prothrombin as that which is lacking in dicumarol poisoning, namely, the component which is relatively stable during storage.

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