

without mass term, the result will be a transformation into new types of particles with finite rest mass and spin $\frac{1}{2}$. This theory, however, will be much more complicated, since the interaction terms of the vector field ϕ and the spinor field ψ are of the third order (type $\phi(\psi\psi)$). One has to apply perturbation theory, and it is well known that this has so far always led to infinite values of the self-energy. But recent investigations carried out by Dr. H. W. Peng, in my Department, have shown that this is due only to insufficient mathematics. Therefore it can be expected that Peng's method of secular perturbations will allow the mass problem to be tackled as sketched here.

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Excretion of Penicillin in Man

PENICILLIN is rapidly eliminated from the human body, and 40–99 per cent of an injected dose can be recovered from the urine within four hours in normal cases. There is some evidence that the drug is actively secreted by the renal tubules^{1,2}. In cases of severe azotæmic nephritis, penicillin has been demonstrated in the blood for so long as ten hours after a single injection, although in a normal person after a dose of 25–50,000 units it would have disappeared in three hours.

There were recently admitted to this Hospital two patients, both of whom had had incomplete abortions at the sixteenth week of pregnancy and both of whom developed extreme oliguria directly afterwards. In each case this condition lasted for ten days before recovery began, and during this period such urine as was passed consisted of a glomerular filtrate with evidence of little tubular function. This is shown by Table 1, from which it may be seen that even at high blood urea levels there was only a low urea concentration in the urine (cf. extrarenal azotæmia, in which urinary urea may reach 4 per cent), that chlorides were not retained even though the plasma values were far below normal (560–620 mgm. sodium chloride per 100 c.c.), and that creatinine was concentrated to a small extent compared with the 'normal' ratio of about 100³.

TABLE 1. CONCENTRATIONS ARE GIVEN IN MGm. PER 100 ML., AND THE DAYS REFER TO THE NUMBER OF DAYS OF OBSERVATION.

	Case I		Case II	
	2nd day	10th day	2nd day	10th day
Urine vol. (ml.)	15	180	165	150
Urea in blood	174	530	255	320
Urea in urine	170	600	800	600
Chlorides (as NaCl) in plasma	590	360	400	320
Chlorides (as NaCl) in urine	160	255	215	305
'Apparent' creatinine in plasma	8	18	8	12
'Apparent' creatinine in urine	6	9	67	50

These temporarily self-nephrectomized persons provided an opportunity of observing the fate of injected penicillin, for physiological as well as therapeutic reasons. 45,000 units of a preparation issued by the Therapeutic Research Corporation were injected intra-muscularly, and bacteriostatic assays were made upon serum samples at intervals after-

wards. Bacteriostasis was measured in slide-cells, using the Oxford standard strain of *Staphylococcus aureus* as test organism. The results are given in Table 2.

TABLE 2.

+ = bacteriostasis.
± = partial bacteriostasis compared with control.

Hours after injection	Serum dilution					
	1/1	1/2	1/4	1/8	1/16	1/32
Case I. 3	+	+	+	+	—	+
7	+	+	+	+	±	+
18	+	+	+	+	—	—
26	+	+	+	+	—	—
32	+	+	±	—	—	—
45	+	+	—	—	—	—
72	+	±	—	—	—	—
107	+	—	—	—	—	—
131	—	—	—	—	—	—
Case II. 1	+	+	+	+	+	+
6	+	+	+	+	+	+
20	+	+	+	+	±	—
26	+	+	+	+	—	—
48	+	+	+	+	—	—
68	+	±	—	—	—	—
92	+	—	—	—	—	—
116	+	—	—	—	—	—
116 (with penicillinase)	—	—	—	—	—	—

In both cases urine samples collected during the test periods were assayed for penicillin by the ring test⁴, but none contained detectable amounts.

The second patient was given a further injection of 47,500 units five days after the first. The 24-hour urine volumes on the succeeding days were 150, 480, 600 and 1,260 c.c. Her serum, taken three days after this injection, still caused complete inhibition of growth of staphylococci at a dilution of 1:1, and partial inhibition at 1:2 (effect abolished by penicillinase). On this occasion the urine excreted during the twenty-four hours following injection caused inhibition of growth in the ring test corresponding to $\frac{1}{2}$ –1 unit of penicillin per c.c., but subsequent specimens caused negligible inhibition.

The failure to recover penicillin from the urines (pH 6.8–7.6, and preserved with toluene) of case II must have been due both to grossly impaired glomerular and tubular function. As judged by creatinine values, however, concentration of the urine by tubular reabsorption of water was still occurring to the extent of at least five times, although chloride reabsorption and urea excretion were greatly deficient. If penicillin were concentrated in the urine solely by reabsorption of water, it seems probable that it would have been sufficiently concentrated in the urine to have been detected in the ring test. However, such evidence for active tubular secretion is suggestive only.

The main conclusion to be drawn from these two cases is that in the absence of significant renal excretion of penicillin this drug is slowly inactivated in the body, but will nevertheless remain detectable for five days.

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