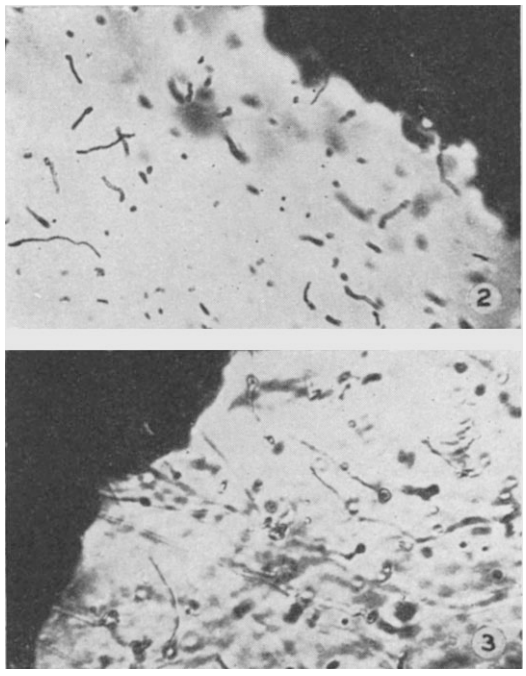

Figs. 2 and 3. (2) Limited germination in the spore–agar inoculum after three days in contact with an unwounded root surface (right) (× *c.* 330). (3) Extensive germination and mycelial development in the same inoculum shown in Fig. 3 after two days in contact with a lateral gash on the main root. Note marked tropic response towards the wounded surface (left) (× *c.* 330)

spores from the three treatments were examined after twenty-four hours, it was apparent that germination had been markedly stimulated in proximity to the wound in comparison both with the control and with the intact root surface. Moreover, there was a definite inhibition of spore germination, as compared with the control, by the intact root surface. This observation is in striking contrast to the recent report of Jackson[9] that germination of spores of *Fusarium solani* was stimulated by the presence of intact seedling roots. A chromatographic analysis of the materials diffusing from injured banana roots revealed that the factors stimulating *Fusarium* germination and multiplication are amino-acids and, of these, glutamine appears to be the most important.

The observations reported in this article strongly suggest certain conclusions which may be of importance in future studies of Panama disease. In the first place, the current tendency to disregard the main roots as important infection sites must be re-examined in the light of clear evidence of the penetration of these organs when they have been injured. Secondly, the role of injury in Panama disease infections must be considered in all future investigations, not only as a condition making penetration possible but also as a source of influences which bring about a stimulation of the germination of *Fusarium* spores, thereby increasing the likelihood of successful penetration. In studies now in progress it is hoped to provide a critical evaluation of the importance of injury in the penetration of lateral rootlets by the fungus. Moreover, it will be necessary to determine the applicability of the observations reported here to banana plants growing in different circumstances and particularly under field conditions. The frequent occurrence of serious wounds in banana roots in the field, not only on lateral rootlets but on main roots as well, is certainly compatible with the concept of injury as a major factor in Panama disease infections.

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THE REARRANGEMENT OF EPINEPHRINE

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THE study of the enzymatic alteration of a metabolite logically starts from the knowledge of the nature of its electronic configuration and an appreciation of the chemical susceptibilities of the molecule. Such information provides a rational avenue for an investigation into the metabolic pathway. When this approach was applied in a study of the metabolic degradation of the catechol amines, an interesting possibility for a channel of metabolism emerged. I wish to report a rearrangement of epinephrine and norepinephrine of the pinacol–pinacolone type, leading to the formation of 3,4-dihydroxyphenylacetaldehyde. Since this aldehyde is a direct intermediate of 3,4-dihydroxyphenylacetic acid, one of the metabolites which has been reported to be a product from the incubation of norepinephrine with liver slices[1], this rearrangement may represent a chemical model for a further biochemical pathway of catechol amines.

Rearrangement of epinephrine and norepinephrine to 3,4-dihydroxyphenylacetaldehyde. To 200 mgm. of epinephrine or norepinephrine was added 3 ml. of 85 per cent phosphoric acid. (The reaction also proceeds with other strong acids such as 20 per cent hydrochloric acid.) The reaction mixture was heated rapidly to 125° C. for no more than 20 sec. and poured into 30 ml. of water. This solution was extracted twice with 10 ml. of ethyl acetate and the extract was washed with 5 ml. of water. The ethyl acetate of the extract was removed by evaporation with a stream of nitrogen. The residue (62 mgm.) was a clear, highly viscous oil which did not crystallize in the cold. This material was used for making derivatives.

The 2,4-dinitrophenylhydrazone of 3,4-dihydroxyphenylacetaldehyde was recrystallized from ethanol (melting point found, 169–70° C.; melting point lit. (ref. 2), 169–70° C.; analysis for $C_{14}H_{12}N_4O_6$ requires C, 50·60 per cent; H, 3·61 per cent; N, 16·86 per

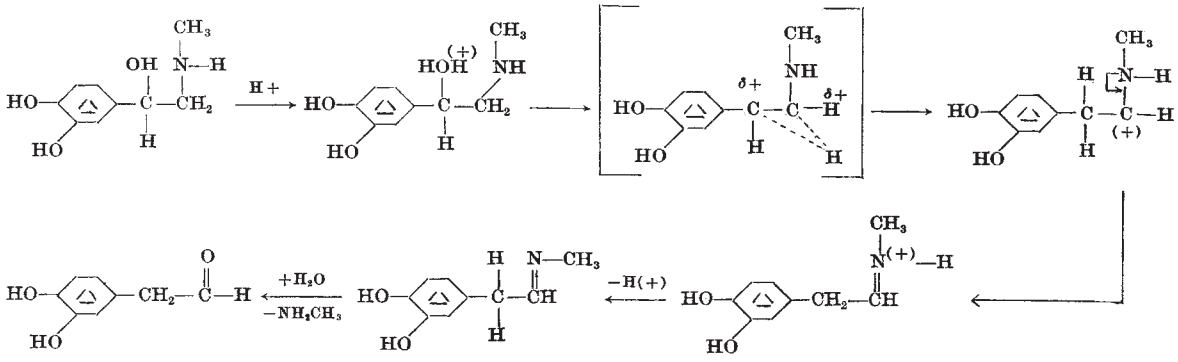

Fig. 1

cent: found C, 50·58 per cent; H, 3·76 per cent; N, 16·60 per cent.). The semicarbazone of 3,4-dihydroxyphenylacetaldehyde was recrystallized from ethanol/water (melting point found, 198–200° C.; melting point lit. (ref. 2), 199–200° C.).

Properties of 3,4-dihydroxyphenylacetaldehyde. This aldehyde appears to be quite stable when stored at − 15° C. It is very unstable in alkaline solution, rapidly turning brown then black to form complex polymeric products. It can be chromatographed on Whatman No. 1 paper in acid solvent, *n*-butanol/1·0 *N* hydrochloric acid, having an ascending R_F of 0·70. The catechol aldehyde exhibits the expected absorption peak in the ultra-violet at 280μ.

The effect of 3,4-dihydroxyphenylacetaldehyde on the isolated rabbit ileum and on the isolated uterus of the rat was determined using the methods described by Burn[3]. It was about 500–1,000 times less active than epinephrine in these systems. With 0·025–0·1 mgm. of the aldehyde per ml., marked relaxation of the isolated ileum and an inhibition of the contraction of the isolated rat uterus induced by acetylcholine was observed.

Holtz *et al.*[4] claimed that when urine, shown to contain oxytyramine, was incubated with tissue in the presence of oxygen a material was produced which had a depressor effect on blood pressure. They assumed that the depressor agent was 3,4-dihydroxyphenylacetaldehyde.

The material, prepared as described above, was tested for its effect on the blood pressure of a dog. The mean arterial blood pressure was determined with a mercury manometer connected to the cannulated femoral artery of animals anæsthetized with 'Nembutal'. Injections of as much as 24 mgm. 3,4-dihydroxyphenylacetaldehyde per 10 kgm. body-weight of the dog had no effect whatever on the dog's blood pressure.

From my observations on the lability of this material it is very unlikely that Holtz *et al.*[4] could have obtained it directly from incubation mixtures under the conditions which they described.

Rearrangement of ephedrine to phenylacetone. 100 mgm. of ephedrine sulphate was treated with 3 ml. of 85 per cent phosphoric acid at 130° C. for 2 min. The sweet odour of phenylacetone was readily apparent. The reaction mixture was poured into 30 ml. of 0·1 per cent 2,4-dinitrophenylhydrazine in 2 *N* hydrochloric acid. The derivative begins to form immediately. The precipitated hydrazone of phenylacetone was recrystallized from ethanol (melting point, 152–53° C. uncorrected; melting point lit. (ref. 5), 152–53° C.).

In 1860, Fittig[6] discovered that when the 1,2-glycol, pinacol, was treated with sulphuric acid, it underwent rearrangement to a ketone, pinacolone. Since that time a large number of substituted 1,2-glycols have been shown to undergo this conversion and reactions of this general type have become known as the 'pinacol–pinacolone rearrangement'.

The mechanism of this rearrangement has been extensively investigated and much has been learned about the aptitude of the various groups to migrate, the nature of the intermediate transition state of the molecule, and the effect of the character of substituent groups on the migrating species.

From the product of the acid-catalysed rearrangement of epinephrine, of norepinephrine, or of ephedrine, one may deduce that a similar mechanism will account for the carbonyl compounds formed.

In this case, as in the general pinacol–pinacolone rearrangement, a proton is added to the hydroxyl-group, which is thus eliminated as a water molecule, leaving a residual positive charge in the form of a carbonium ion. Simultaneously with its formation, the vicinal hydrogen is attracted, producing a positive charge on the adjacent carbon from which the hydrogen has migrated. This carbonium ion attracts electrons from its electronegative neighbour, the amino-group, to form, with a loss of a proton, the unstable imino-group. Hydrolysis of this group to the carbonyl-group takes place as shown in Fig. 1.

A similar explanation for the rearrangement of D-1,2-diphenyl-2-amino,1-anisyl ethanol has been advanced by McKenzie and Mills[7].

In the case of ephedrine either the hydrogen- or the methyl-group could migrate. Since phenylacetone alone was formed in this reaction it is clear that it was the hydrogen that migrated. This is consistent with the observations of other workers that the migratory aptitude of hydrogen is greater than that of any other group[8].

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