LETTERS TO THE EDITORS

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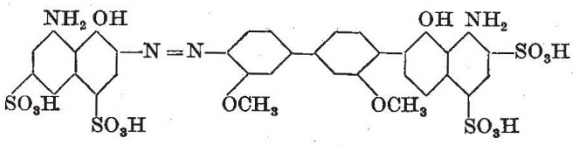
Wharton's Jelly Considered as a Conducting Path

DURING the course of experiments conducted on the sheep fœtus, dyes were injected into the umbilical cord with the object of exploring movements of substances in the cord along non-vascular pathways. The dyes used were a dis-azo dye,



related to trypan blue, and the same dye linked to serum albumin by a diazo linkage. The dye, when linked to protein in this way, cannot dissociate from the albumin, and hence acts as a tag to the protein. These substances were prepared by one of us (P.D.M.).

Fœtuses of different age periods were delivered by Cæsarean section and kept alive, with the placental site intact, and the mother alive, for periods up to five hours. The fœtuses were not allowed to breathe. 2–5 ml. of the dye solution was injected under low pressure into Wharton's jelly (avoiding the main umbilical vessels) four to five inches from the abdominal wall of the fœtus. The injection occupied approximately one minute. The injection mass passed slowly along the cord into the abdomen of the fœtus. At the end of three hours, the blue colour of the dye was well marked throughout the whole substance of the cord on the fœtal side of the injection site, over the allantois, the upper portion of the bladder, the umbilical arteries and the adjacent peritoneal reflexions. No coloration was observed along the pathway to the liver or any other site. It is clear, therefore, that the dye did not find its way into either of the three other escape routes from the cord, namely, (1) the vascular system (there are small vessels in the Wharton's jelly of the sheep as was shown by Tait); (2) the allantoic duct, in which case the dye would have appeared in the bladder; (3) the extra embryonic cœlom leading to the *inside* of the peritoneal cavity.

It is therefore evident that molecules as large as serum albumin may pass from the cord into the embryo by a pathway which is functionally and embryologically distinct from routes (1), (2) and (3) above. The molecules of albumin move at a much greater rate than could be accounted for by diffusion. There must, therefore, under the conditions of these experiments, be a bulk flow of fluid from the cord into the embryo. As the pressure available cannot have been large, the resistance to flow through the connective tissue must be small.

Tait[1] reported results of injection into the cord which are different from the results we obtained. It is possible that the differences are due to his dyes being much more coarsely particulate than those used here.

The interest in the above observations lies in the fact that the Wharton's jelly in the umbilical cord of the sheep is continuous with similar material in the cotyledons of the placenta (Barcroft and Barron), implying a path from the placenta to the fœtus other than the purely vascular one. It has yet to be discovered whether material can pass in the fœtus further than the restricted area which we have described. Clearly, if there is a continuous flow of fluid, the water at least must do so, but what sized molecules it can take with it is another question.

Further research is required to ascertain how far this non-vascular pathway in the cord is of importance in the fœtus.

We are deeply indebted to Dr. D. V. Davies for his kind advice on the anatomical problems involved.

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[1] Tait, L., *Proc. Roy. Soc.*, **24**, 417 (1875).

Production of Gliotoxin by *Trichoderma viride*

GLIOTOXIN was first described by Weindling and Emerson[1] as a metabolic product of *Trichoderma lignorum* (Tode) Harz [= *T. viride* Pers. ex Fries]. Weindling afterwards[2], on the advice of C. Thom and M. Timonin, reported that he had described the fungus incorrectly, and that instead it should be identified as a *Gliocladium*, similar to *Gliocladium fimbriatum* Gilman and Abbott. I have found that strains of *Trichoderma viride* produce gliotoxin, and I suggest that it is extremely probable that the fungus used by Weindling was not *G. fimbriatum*, but was a *Trichoderma* as he originally supposed.

In 1942 I received from Prof. H. Raistrick a culture which had been supplied to him as Weindling's strain of *G. fimbriatum*. Using the culture medium recommended by Weindling and Emerson[1], I have found this to produce gliotoxin in 4-day still cultures at the rate of about 50 mgm. per litre. Afterwards, in the course of examination of a number of isolates of *T. viride*, one isolated from a local soil (No. 211) was found to possess marked powers of antagonism to a number of bacteria and fungi. This organism was then found to produce gliotoxin in yields of about 95 mgm. per litre, that is, at twice the rate of 'Weindling's strain' under similar conditions.

Analyses (Weiler and Strauss) of the products from both fungi agree with $C_{13}H_{14}N_2S_2O_4$ as found for gliotoxin by Dutcher[3], not with $C_{14}H_{16}N_2S_2O_4$ as originally suggested by Weindling and Emerson. Data are given in Table 1.

TABLE 1.

%	Calc. for $C_{13}H_{14}N_2S_2O_4$	Gliotoxin from Strain No. 211	Gliotoxin from 'Weindling's strain'
C	47·8	47·8	47·8
H	4·3	4·4	4·4
S	19·7	19·9	19·8
N	8·6	8·3	8·6

Until I discovered the production of gliotoxin by a fungus which I considered to be an obvious *Trichoderma*, I accepted the nomenclature of 'Weindling's strain' as *G. fimbriatum* Gilman and Abbott. Since these two fungi appeared very similar in macro-