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implant when transplanted to the uterus of an untreated pseudopregnant foster mother (experiment 1*b*).

Although these results suggest that the serum impaired the viability of the eggs, further experiments showed that this was not so. Blastocysts from serum-treated mice will develop satisfactorily when transplanted to the testes of untreated hosts (experiment 1*c*). Furthermore, blastocysts taken from untreated donors will develop beneath the kidney capsule of mice treated with serum (experiment 3).

It seems then that neither the sensitivity of the uterus nor the viability of the egg is adversely affected by the treatment. Presumably the serum has interfered with the mechanism whereby the blastocyst initiates the decidual response, a *sine qua non* of implantation in the uterus but not in extra-uterine sites. Eggs transplanted from treated donors to the pseudopregnant uterus of non-treated hosts (experiment 1*c*) must be explained by a local action of the serum carried across on the surface of the egg. A similar argument has been used by Guttmann *et al.*[14] to account for the prolonged survival of renal allografts in rats when only the donor had been treated with anti-lymphocytic serum.

The way in which the serum inhibits the induction of a decidual reaction by the egg is unknown. Its action may be non-specific; it may damage the uterine tissues or interfere with the hormones required for implantation. The findings are also consistent with the view that the serum has inhibited an immunological interaction between blastocyst and uterus.

Tyler[15] first postulated that "implantation itself may involve interactions that are of antigen–antibody type". The following recent findings may be interpreted as lending support for this idea. (*a*) The mouse egg expresses transplantation antigens. (*b*) There is selection of blastocysts of particular genotype at implantation in the mouse[7] and rat. (*c*) Antigen contained in the blastocoelic fluid of the rabbit blastocyst is also found in the uterine lumen and uterine stromal cells just before implantation[16]. (*d*) At implantation the antimesometrial uterine epithelium cells in the rat show a marked ability to transfer substances even of high molecular weight to the sub-epithelial space[17]. (*e*) In the sub-epithelial space in the mouse there is an accumulation of lymphocytes and other white blood cells around the site of, and at the time of, egg implantation[18]. (*f*) Only the blastocyst, not other objects similar in size, is able to induce a decidual reaction in the mouse[19]. This suggests that the reaction is induced by something more than the physical presence of the blastocyst. If implantation requires the recognition of antigens displayed by the egg, there is some evidence to suggest that they may be tissue specific[20] and/or strain specific[7].

Further work is needed using purified haemagglutinating and thymocyte antisera to determine the cause of these results.

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Pharmacology of the Mechanism of Certain Effects of Reserpine in the Rat

TWENTY minutes after receiving large doses of reserpine (5 mg/kg, given intraperitoneally), rats develop a myohypertonic-hypokinetic-cataleptic state, showing generalized tremor, piloerection, diarrhoea, ptosis and cutaneous hyperalgesia. In such a state rats do not move, but allow themselves to be dragged by the tail. The ptosis is reversible during the first 40 min after its appearance and then irreversible (compare refs. 1 and 2). We have found that the symptoms remain unaltered for 24 h, and then gradually subside to a practically normal state after 48 h. When the forelimbs of the animal under the influence of reserpine were placed on the edge of a table, and the rat held by the tail, it remained still in this position, unlike normal animals which would climb quickly onto the table. Rats placed on the edge of an open cage on their abdomen behave similarly; they do not climb or jump down as normal rats would do. The animals treated with reserpine find it difficult to swim in water and do so in an oblique (or sloping) position, and they cannot get themselves out of the water bath. Normal rats swim quickly in a near horizontal position and get out of the water easily.

An identical state can be produced by injecting the rats intraperitoneally with large doses of serotonin or tryptamine (30 mg/kg). In the case of serotonin, however, such a state is observed only in a second phase. During the first phase (between 2 and 40 min after injection) rats show total flaccid paralysis with analgesia, but with the rest of the sensory system apparently undisturbed. The second phase after injection of serotonin (after 40 min) is identical with the state observed after an injection of reserpine. The serotonin effect disappears gradually after 2 h. When tryptamine is given there is only one phase of reaction; the animals show the same symptoms which reserpine produces immediately (2 min) after injection and these effects last for 1 h.

Doses of 2 mg/kg of adrenergic agents (adrenaline and noradrenaline) produce a different depressive state, with myohypotonia, analgesia and semiptosis.

Pharmacological assays have shown us that there is more than a casual similarity between the effects of reserpine and those of serotonin and tryptamine. We can summarize the results of our experiments as follows. (*a*) The antiserotoninic drug methysergide injected intraperitoneally in a dose of 5 mg/kg 50 min before the administration of reserpine postponed the appearance of its effects by 45 min. A second dose of methysergide if given 10 min after reserpine completely blocked the effects of the reserpine. The effects of serotonin and tryptamine were inhibited by one dose of methysergide injected 50 min before the administration of these drugs, and the animals remained in a completely normal state. LSD and BOL (bromolysergic acid diethylamide) (2 mg/kg) only delayed the appearance of the effects of reserpine for 40–60 min. None of these drugs depress catecholamine.

(*b*) Adrenergic blocking agents (10 mg/kg of phentolamine, 5 mg/kg of dihydroergotamine and 1 mg/kg of propanolol) administered in the same way did not affect the symptoms produced by reserpine and serotonin. They also had no effect on catecholamine depression.

(c) Centrally active anticholinergic drugs (atropine and benactyzine, in doses of up to 30 mg/kg) showed no effect on the symptoms produced by reserpine and serotonin, nor did they affect catecholamine depression.

(d) The antihistamine drugs ('Phenergan' and 'Benadryl', in doses of up to 30 mg/kg) had a sedative effect, but were without effect on the symptoms produced by reserpine, serotonin or catecholamines.

(e) The inhibitors of monoamine oxidase (iproniazid in a dose of 100 mg/kg, nialamide in a dose of 50 mg/kg or tranylcypromine in a dose of 30 mg/kg) delayed the second phase of the effects of serotonin and reserpine, but did not inhibit them. Iproniazid injected 24 h before reserpine and serotonin delayed their effects for 4 h; nialamide injected 24 h before, and tranylcypromine injected 1 h before, delayed the appearance of the effects for 35 min. The serotonin paralysis of the first phase was markedly reduced by these drugs; the flaccidity was less pronounced and the animals tried to move with some success. No effect on catecholamine depression was observed.

(f) Injection of 500 mg/kg of dopa 20 min earlier postponed the effect of reserpine by 4 h, inhibiting the action of serotonin and tryptamine completely; 200 mg/kg had no effect on the effects of reserpine, but blocked the tryptamine symptoms and the second phase of the serotonin effects.

(g) Clinical antidepressive drugs, such as imipramine, desmethylimipramine, amitryptiline and nortryptiline, in doses of up to 50 mg/kg similarly retarded the appearance of the effects of serotonin and reserpine without blocking them. Catecholamine depression was not modified in any way by these drugs.

(h) Antiparkinson drugs ('Tremaril', 'Diparcol' and 'Parsidol'), in doses of up to 30 mg/kg, completely inhibited the effects of reserpine and serotonin. 'Aturban' had no effect. None of these drugs had any action on the symptoms produced by catecholamines.

(i) Phenylethylamine and methylamphetamine, in a dose of 10 mg/kg, inhibited the effects of reserpine and serotonin and those of catecholamines (compare ref. 3).

It is interesting that dopa postponed the effects of reserpine and inhibited those of serotonin and tryptamine, but it is difficult to see this as evidence that a depletion of catecholamines is the cause of the effects of reserpine, unless the same mechanism also applies to the effects of serotonin and tryptamine. The situation is similar with regard to the temporary blocking action of inhibitors of monoamine oxidase.

The inhibition of the effects of both reserpine and serotonin by the antiserotoninic drug methysergide argues in favour of the hypothesis of Brodie and Shore[4] that reserpine acts by releasing serotonin, at least as far as the effects observed by us are concerned. Nevertheless, tryptaminic mechanisms would also fit in with our results. There are further implications in the complete inhibition of the effects of reserpine and serotonin by antiparkinson drugs while other central anticholinergic drugs were inactive in this respect.

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Neuro-interstitial Junction in a Gastropod, *Glossodoris*

On the basis of ultrastructural observations, we have suggested a unified "glio-interstitial" cell-system in the Mediterranean sea-slug *Glossodoris*[1]. This system includes the glial cells described in the central nervous system of several gastropods[2-3] and the "interstitial cells" associated with the peripheral nervous system. The later non-neuronal elements resemble the "interstitial cells of Cajal" in the peripheral nervous system of vertebrates[4] in their relationship with nerve plexuses and smooth muscle fibres, in their morphology and in their staining properties (ref. 5 and my unpublished results). A special type of junction between nerve fibres and interstitial cells has been found in an electron microscope study of the foot of *Glossodoris tricolor* (Cantraine).

This junction is formed by an apposition of membranes with morphological polarization and differentiation, as in a regular nervous synapse. Fig. 1 shows nerve fibres lying in close contact with the interstitial cell. In two places the membranes are thickened and densely stained (differentiation) and the intercellular cleft is reduced to 120 Å. The nervous side of the contact shows a striking accumulation of vesicles (polarization) which are the same size as "synaptic vesicles" (300–800 Å), but some of them have an electron-dense core (200 Å) separated from the outer membrane by a clear space. This second type is similar to the vesicles in the vertebrate nervous system[6] which are thought to contain catecholamines.

Fig. 1. Arrows indicate synaptoid contacts. *c*, Collagen; *g*, interstitial granules; *n*, neurite; *nu*, nucleus of the interstitial cell.

Both the differentiation and the polarization suggest that these contacts represent the site of special exchange between the nerve fibre and the interstitial element, apparently directed from the nerve process toward the interstitial cell. The structure of the neuro-interstitial junction is similar to that of the neuromuscular junction