Induction of implantation in the rat by iproniazid*

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Summary. Rats were bilaterally ovariectomized on Day 3 post coitum and treated
daily with progesterone. Iproniazid, an inhibitor of monoamine oxidase, on Day 8
induced implantation in all rats. Indomethacin treatment prevented this effect.

Introduction

The involvement of prostaglandins (PGs) in decidual cell development (Castracane, Saksena &
Shaikh, 1974) and implantation (Lau, Saksena & Chang, 1973; Castracane et al., 1974;
Kennedy, 1977) in laboratory animals has been clearly shown. Iproniazid, a potent monoamine
oxidase inhibitor recommended as having therapeutic value in mental depression (Koelle,
1970), has an abortifacient action which is mediated through an increased endogenous
production of PGs (Chatterjee, Biswas & Pal, 1974). We therefore studied the ability of
iproniazid to induce implantation in rats, and also whether indomethacin, a potent inhibitor of
PG biosynthesis and release (Vane, 1971; Ferreira, Moncada & Vane, 1971; Rankin, Ledford,
Jonsson & Baggett, 1979), can reverse the implantation-inducing effect of iproniazid.

Materials and Methods

Animals. Inbred albino rats weighing 150–170 g were used. They were kept in light controlled
conditions of 14 h light/24 h. Pro-oestrous females were caged with males of proven fertility and
mating was confirmed by finding spermatozoa in the vaginal smear (Day 1 of pregnancy). Bilateral
ovariectomy was performed on Day 3 under light ether anaesthesia. Care was taken to
avoid damage to the oviduct. All the rats were killed on Day 12 and the number of implantation
sites was recorded.

Drugs and treatments. Iproniazid phosphate, donated by the F. Hoffman La Roche & Co.
Ltd, Basle, Switzerland, was dissolved in distilled water and administered subcutaneously (s.c.) as
a single injection (0·2 ml) at a dose of 150 mg/kg body weight on Day 8. Progesterone (Proluton
Dep: Schering, India) was diluted in olive oil and injected s.c. at a dose of 5 mg/rat/day from
Day 3 to Day 11 p.c. Indomethacin (I.D.P.L., India) was dissolved in olive oil and administered
s.c. at 2·5 mg/kg (0·2 ml) on Days 7, 8 and 9.

Results

As shown in Table 1 daily injections of progesterone were not able to induce implantation, but a
single injection of iproniazid to the progesterone-treated animals was successful. Concomitant
administration of indomethacin inhibited the iproniazid-induced implantation.

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Table 1. Effect at Day 12 of iproniazid on implantation in rats bilaterally ovariectomized on Day 3 of pregnancy

<table>
<thead>
<tr>
<th>Treatment (day of pregnancy)</th>
<th>No. of rats</th>
<th>No. with implantation sites</th>
<th>Mean ± s.e.m. no. of implantation sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progesterone (Days 3–11)</td>
<td>6</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Proniazid (Day 8) +</td>
<td>7</td>
<td>7</td>
<td>6.66 ± 0.55</td>
</tr>
<tr>
<td>Progesterone (Days 3–11)</td>
<td>6</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Proniazid (Day 8) +</td>
<td>6</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Progesterone (Days 3–11) +</td>
<td>6</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Indomethacin (Days 7–9)</td>
<td>6</td>
<td>0</td>
<td>—</td>
</tr>
</tbody>
</table>

Discussion

PGF-2a treatment in the mouse prevents the inhibitory effect of indomethacin on implantation (Lau et al., 1973). Iproniazid acts by interfering with the metabolism of catecholamines (Koelle, 1970) which can stimulate the release of prostaglandins in the spleen (Ferreira et al., 1971). Moreover, indomethacin blocks the conversion of arachidonic acid to endoperoxides (Flower & Vane, 1974).

Cyclic AMP is also able to induce implantation (Webb, 1975) and β-adrenergic catecholamine can stimulate adenylate cyclase in pigeon erythrocytes (Davoren & Sutherland, 1963). Endometrial adenylate cyclase is also known to be stimulated by PGE-1 and PGE-2 (Bhalla, Sanborn & Korenman, 1972). The formation of cAMP by cyclo-oxygenase in uterine decidual tissue is inhibited by indomethacin (Rankin et al., 1979).

References


Kennedy, T.G. (1977) Evidence for a role of prosta-

Koelle, G.B. (1970) Drug acting at synaptic and neuro-


Webb, F.T.G. (1975) Implantation in ovariectomized mice treated with dibutyryl adenosine 3'5' mono-

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