Fig. 2. The same region sectioned at a more proximal level. A, Nerve terminals; Ax, axons; T, thickened muscle membrane; G, Golgi apparatus; Nft, neurofilaments; Mf, myofilaments.

tions as seen, for example, in developing chick somatic muscle¹, with the exception that basement membranes were not apparent.

The morphology and state of preservation of the terminal regions shown in Figs. 1 and 2 are inconsistent with the view that they represent surviving remnants, after 7 days in culture, of neuro-muscular junctions present in the muscle before explantation. Furthermore, axons can be traced towards them from the bundle growing out from the confronting explant of spinal cord. We therefore suggest that neuro-muscular junctions may form *de novo* in appropriate *in vitro* conditions, and that they may do so within a brief period of culture. Appearances of this kind have so far been observed in six preparations.

It is known that after weeks or months *in vitro* explants of already connected spinal cord and muscle may establish electrophysiological communication indicative of synaptic relationship². We cannot at present conclude that the junctions we describe are in this sense functional, although their morphology suggests that this may well be the case. If they prove to be so, their identification may be of value for future studies of the development of relationships between nerve and muscle, with particular reference to any specificities that may exist.

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Premature Birth induced in Mice by Salicylate

ANIMAL experiments have provided a great deal of information about the interaction of drugs early in pregnancy. Little, however, is known of drug action in the late stages of pregnancy^{1,2}. In our previous studies on the damaging effect of sodium salicylate on the foetus, a tendency to premature birth was observed in the mouse when this substance was given on the seventeenth gestation day³. We have therefore investigated the effect of some other anti-inflammatory drugs on the gestation time.

Sixty-one pregnant primiparous A/Jax mice were used. They were mated overnight and the day when a vaginal

plug was observed was denoted as the zero day of pregnancy. On the seventeenth day of gestation, at 1000 h, the mothers were given a single intramuscular injection of 0.1 ml. per 20 g body-weight of the appropriate solutions (Table 1), while the controls were left uninjected. Chloroquine-phosphate and sodium salicylate were dissolved in distilled water. Immediately after injection the mice were placed on wire nettings in separate cages. Daily inspections, at 1000 h, revealed the day of birth. Newborns were not examined or counted.

After injection of sodium salicylate half of the animals delivered on the seventeenth day (Table 1). No other female, injected or uninjected, gave birth before the eighteenth day. The most frequent days of delivery, except in the salicylate group, were the nineteenth or twentieth day.

Pharmacological induction of premature birth in the human, for therapeutic reasons, is mostly performed by administration of oxytocin⁴. Formerly quinine was used to induce labour⁵, but in this experiment chloroquine did not affect the duration of pregnancy. Salicylate has been suspected to cause abortions although this has not been proved satisfactorily⁶. It is interesting to note that of the substances tested only the teratogen sodium salicylate induced premature birth. Neither cortisone, a potent teratogen in the A/Jax strain of mice, nor *p*-hydroxybenzoic acid, a non-teratogen, induced premature birth^{7,8}. The mechanism behind the foetal damage induced by sodium salicylate is not known. There have been very few reports of experimentally induced premature birth, but our findings support the view that the teratogenic tests of different substances should be extended to include tests for foetal damage induced late in pregnancy, for example, premature birth.

Table 1. EFFECT OF ANTI-INFLAMMATORY DRUGS ON THE LENGTH OF GESTATION TIME

Treatment	No. of females giving birth on gestation day				
	17	18	19	20	21
Uninjected	0	3	6	1	0
Saline	0	3	3	4	0
Sodium salt of salicylic acid 100 mg/ml.	5	2	3	0	0
Sodium salt of <i>p</i> -hydroxybenzoic acid 100 mg/ml.	0	3	6	1	0
Chloroquine phosphate 10 mg/ml.	0	1	4	5	1
Cortisone acetate* 25 mg/ml.	0	1	4	4	1

* 'Cortodrine' ®, Astra, Sweden.

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