Stimulation of the presynaptic cell elicited a steady train of spikes which resulted in the appearance of small depolarizing potentials in the postsynaptic cell. The interaction was one way. Hyperpolarization of the postsynaptic cell by 50–60 mV greatly increased the amplitude of the potentials indicating that the latter are excitatory postsynaptic potentials (EPSP's). In Figure 2A the strict one for one relationship between the presynaptic spikes and the EPSP's can be seen. There was a delay of 20 msec between the presynaptic spike and the onset of the EPSP. The duration of the EPSP was between 200 and 250 msec. The amplitude of the EPSP was 1 mV at a membrane potential of −100 mV.

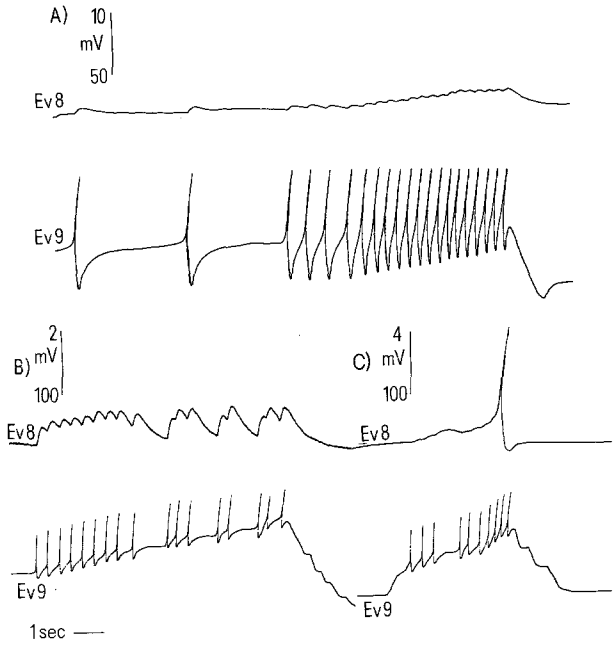

Fig. 2. Responses recorded in the postsynaptic cell (upper traces) when the presynaptic cell (lower traces) is stimulated to fire spikes. A) Each presynaptic spike gives rise to 1 EPSP. EPSP's summate if they are evoked close enough together. B) Facilitation and summation of EPSP's produced by a train of presynaptic spikes. C) EPSP's summate to cause the postsynaptic cell to fire an action potential.

The one for one relationship was maintained as the frequency of firing in the driver cell was increased (Figure 2A). The EPSP's began to summate as soon as the frequency of firing in the driver cell was increased to 2 spikes per sec. Figure 2A shows summation of the EPSP's depolarized the membrane by 5 mV. During the depolarization individual EPSP's could be seen clearly. Often, summation of EPSP's caused the postsynaptic cell to fire an action potential (Figure 2C). With repetitive stimulation of the driver cell the EPSP's were facilitated as well as summated (Figure 2B). After prolonged periods of firing in the driver cell, EPSP's increased in both amplitude and duration. Unitary PSP's reached an amplitude of 2 mV and increased in duration to as long as 1 sec from an initial duration of 200 msec. The delay between stimulation and response remained constant at 20 msec.

The results suggest that the input onto the follower cell is monosynaptic. Preliminary investigations have suggested that acetylcholine or glutamate could be the transmitter compound released by the presynaptic cell onto the follower cell[6]. It therefore appears that the presynaptic cell is an interneurone. Experiments show that it receives an excitatory input from the anal nerve[6].

This system requires further investigation into the monosynaptic nature of the synapse, but already promises to be useful for the study of cell-cell interactions.

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Ultrastructural Changes in the Dorsal Root Ganglia Evoked by Thalidomide in Rabbits[1]

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Summary. Administration of the teratogenic drug thalidomide to pregnant does produces ultrastructural changes in foetal ganglion cells, Schwann cells and axons in the posterior root ganglia corresponding to forelimb segments deformed by the drug. Ultrastructural changes in ganglia appear on the 13th day of gestation, i.e., preceding the appearance of limb malformation.

Among teratogenic substances capable of producing deformities in the major systems of the human body, the maximum activity is exhibited by thalidomide[3,4]. Nevertheless, the various mechanisms of dysmorphogenesis and in particular thalidomide teratogenesis are poorly understood. McBride[5,6] reported that thalidomide toxicity is associated with derangement and decreased numbers of ganglion cells of the dorsal root and postulates that it is the diminution in number of sensory nerve fibres which interferes with peripheral organ development.

To seek confirmation of this hypothesis, the ultrastructure of sensory neurons of the dorsal root ganglia of New Zealand White Rabbits deformed by thalidomide was compared with that of untreated controls. Sensory neurons were examined on the 13th, 15th, 17th and 21st days of gestation because these days correspond to important stages in development of limbs: on day 15 digital tissues begin to condense in the forepaws and by day 17 separation has occurred of the digits of the forepaws, as well as complete reduction of the webbing. Day 21 marks the end of organogenesis in the rabbit (Edwards[7]).

[1] This work was supported by a grant from Foundation 41.

[2] We are grateful to Miss C. Ellis and Mr. P. Westphal for technical assistance.

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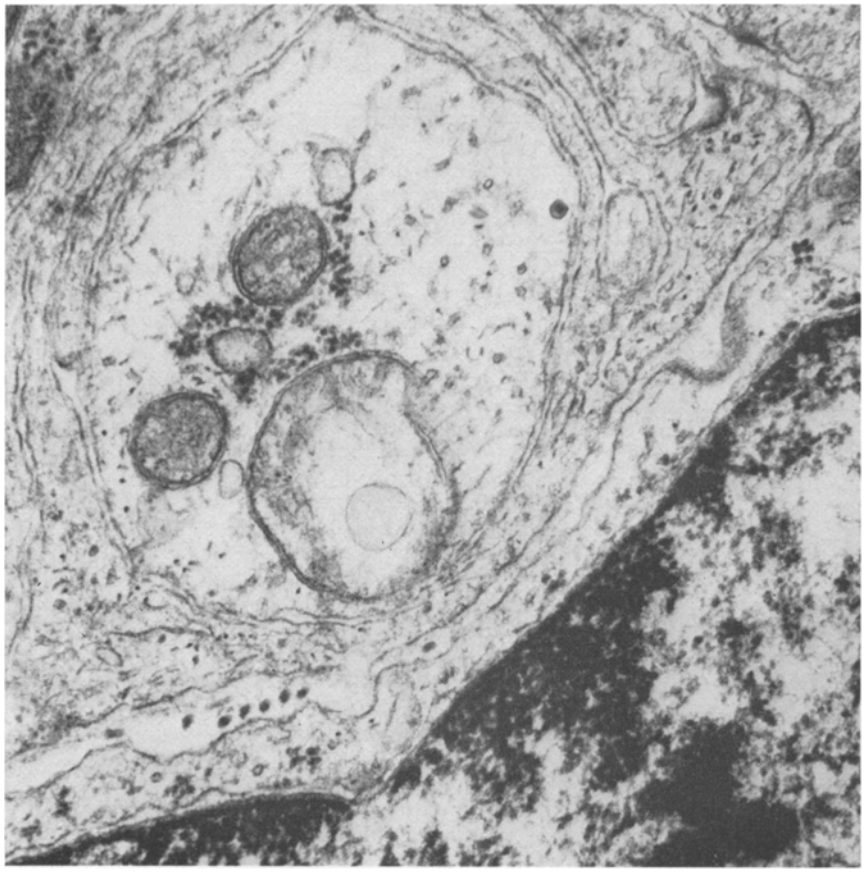

Fig. 1. Axon showing decreased numbers of microfilaments and microtubules together with abnormal vacuolation of a mitochondrion. Uranyl acetate and lead citrate. × 60,000.

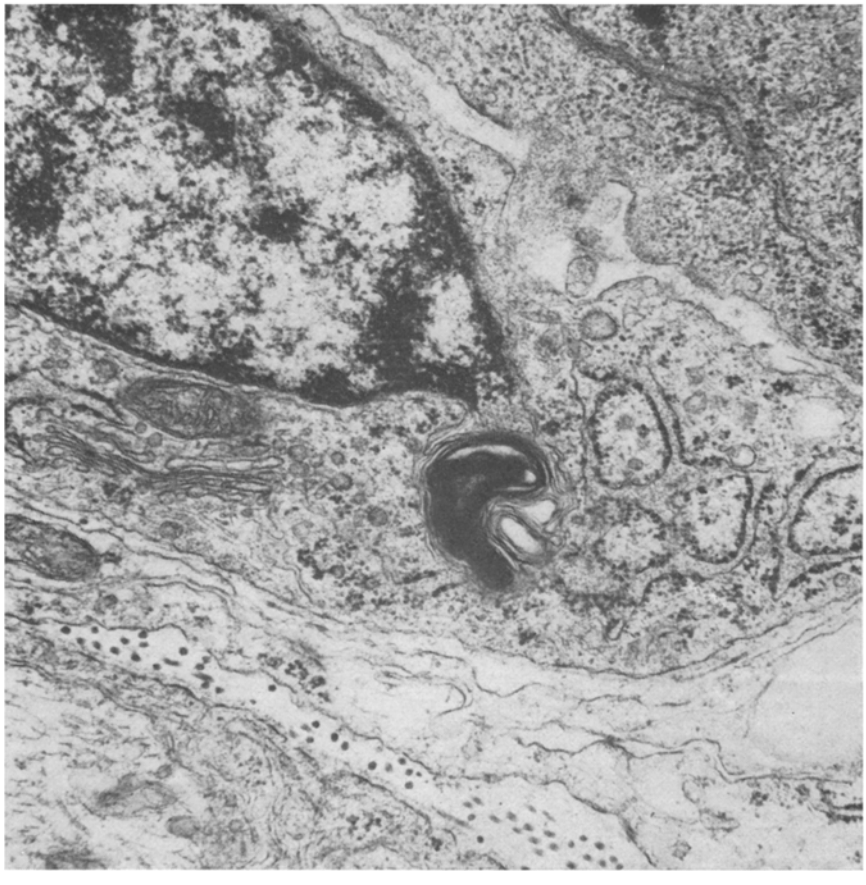

Fig. 2. Tightly whorled electron-dense 'myelin figure' associated with a Schwann cell. Uranyl acetate and lead citrate. × 20,000.

Fourteen adult New Zealand White does (3–5 kg body weight) were randomly allocated to either control or experimental groups. One doe was mated per day; she was taken to the cage of the buck and removed immediately after copulation. The time of mating was considered as 0 h of pregnancy. The experimental group was treated daily with thalidomide (α-phthalimido glutarimide) in a dose of either 150, 200 or 250 mg/kg from the 8th to 12th day inclusive. Immediately before administration, the drug was suspended in 10 ml 0.5% carobxymethyl cellulose and 5% glucose by vigorous agitation for 1–3 min at room temperature and given by gavage. Control animals were given 10 ml of the suspending medium on the corresponding days of gestation.

Animals were killed on day 13, 15, 17 and 21. Each doe was anaesthetized with i.v. sodium pentobarbital, the abdomen opened and the foetuses and membranes exposed in utero. The numbers of viable, dead and resorbed foetuses were recorded. From each foetus in turn, the membranes were removed and Karnovsky's combined aldehyde fixative injected into the subdural space at the base of the skull. The cervical vertebral column including the intact spinal cord and ganglia, were excized without delay and agitated in Karnovsky's solution overnight at 4 °C. The dorsal root ganglia at the level of C6 and C7 were then dissected away from the vertebral column and spinal cord and transferred to 0.1 *M* cacodylate buffer pH 7.4. The ganglia were post-fixed in 2% osmium tetroxide for 1 h and then embedded in Spurr's epoxy resin. Sections were cut with a LKB ultramicrotome, stained with uranyl acetate and lead citrate and examined with a Philips 300 electron microscope.

Six control does produced a total of 49 viable foetuses of which none were deformed but there were 5 resorptions. 3 does treated with 150 mg/kg thalidomide produced 9 resorptions and 15 foetuses, of which 6 were malformed. 3 does treated with 200 mg/kg produced 6 resorptions and 17 foetuses, of which 9 were deformed. 2 does treated with 250 mg/kg produced 5 resorptions and 12 foetuses, one of which was dead and 6 were malformed.

Ultrastructural changes were found in axons, Schwann and satellite cells as well as ganglion cells of cervical posterior root ganglia in 15-, 17- and 21-day-old foetuses exposed to thalidomide which exhibited marked reduction deformities of the relevant dermatomes, as well as in 13-day-old foetuses from treated does. Abnormalities of axons were the commonest lesions which included loss of microfilaments and degeneration of microtubules, together with vacuolation and distension of mitochondria (Figure 1). More severely damaged axons were represented by irregular whorls of laminated, electron dense configurations or 'myelin figures', many of which were related to either the cytoplasms of Schwann cells or to immediately adjacent axons (Figure 2). Ganglion cells exhibited only minor abnormalities, comprizing an overall increase in number of mitochondria and free ribosomes, but without concomitant increase in endoplasmic reticulum. The nuclear envelopes of ganglion cells at 13 days and to a significantly and progressively lesser extent in 15-, 17- and 21-day-old foetuses were irregularly indented.

Ultrastructural changes are therefore present in relevant cervical posterior root ganglia at 13 days, i.e., preceding the appearance of thalidomide-induced fore limb malformations and subsequently with increasing frequency and concomitant with progressive maldevelopment. It is therefore likely that these changes represent the primary lesion evoked by thalidomide and are not secondary atrophic neural changes resultant from deformity of the peripheral segments.

Pseudomonas aeruginosa Causes Epidemic Disease in the Milkweed Bug, *Oncopeltus fasciatus* Dallas (Insecta, Heteroptera)

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Summary. *Pseudomonas aeruginosa* was recognized as the causative organism of an epidemic disease occurring in a laboratory breed of *Oncopeltus fasciatus*. The infection probably occurs peroral and is favoured by high temperature and humidity. *Pseudomonas aeruginosa* destroys the fat body of the bug.

Oncopeltus fasciatus has become a widely used laboratory animal[2]. Therefore the occurence of a severe epidemic disease, as observed in this and other laboratories, seems of interest. The illness breaks out rather suddenly and unpredictably affecting almost exclusively animals of the 5th (last) larval instar, never imagines. If the sickness appears in a culture jar, within 1 to 3 days almost all bugs of the 5th and – to a lesser degree – 4th larval stage are killed. Dead bugs have dark blue to black swollen abdomens and spread a characteristic unpleasant odor, which reminds one of trimethylamine. First signs of the illness are hard to diagnose, since dark gut content shining through the cuticle can be mistaken with the onset of the pathological abdomen darkening. If the symptoms, i.e. discoloration of extended body areas and paralization, are clearly recognizable, the animal perishes normally within 24 h; recovery was never observed.

Light and electron microscopic studies on specimens from independently diseased populations revealed that bacteria were present in the hemocoel, together with tissue debris, and extra- and intracellularly in the fat body, obviously dissolving it (Figure 1). Other tissues seemed intact and never invaded by bacteria. In several experiments, at least 5 different strains of bacteria (Pl 3, Pl 4, Pl 5, Pl 11, Pl 1/12) were isolated. It is highly probable that the majority of the strains is derived from gut content[3], for despite careful preparation of the fat body a damage of the gut could not always be avoided. To establish the disease causing bacterium, young 5th larval instars were punctured with a needle contaminated

[1] For her interest and discussion I thank Dr. G. Hausner. Miss I. von Graevenitz and Miss H. Schilling gave techincal support.

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