Blood (0·5 ml) was collected twice weekly from rats infected with *Mycoplasma arthritidis*. W.b.c. counts, percentage of granulocytes, E.S.R., serum lysozyme, total haemolytic complement (C'H50) and C'3, increased with the developing polyarthritis. Metabolic inhibition antibodies developed only after 3–4 weeks, when the polyarthritis was already subsiding. Rats receiving salicylates (200 mg/kg twice weekly) developed a more severe polyarthritis; some of the blood changes were more pronounced.

Implantation of electrodes in the dentine of an upper canine tooth in the dog

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Electrical stimulation of the dental pulp causes predictable and characteristic pain responses in the conscious dog. Suppression of these pain responses by drugs gives an estimate of their analgesic activities (Heng & Domino, 1960; Mitchell, 1964). In the development of this technique in our laboratories it has been necessary to modify the original test, both in the surgical procedure of implanting electrodes in the dental pulp and in the method of evaluating the analgesic activities of new drugs.

A mature Beagle dog was anaesthetized with pentobarbitone intravenously. A gum flap was deflected from the base of an upper canine tooth. Two cavities were drilled approximately 4 mm apart above the gum line in the labial surface of the tooth using a round plain cut (No. 2) bur. The cavities almost reached the dental pulp and were undercut using an inverted cone (No. 37) bur. A flexible hollow probe was introduced under the gum margin and passed subcutaneously to a skin incision over the calvarium. The electrode leads were two diamel-coated stainless steel wires (external diameter 0·2 mm) sheathed in polythene tubing (external diameter 1·2 mm) connected to an Amphenol strip connector (Type 221-2), mounted on a winged, polytetrafluoroethylene base plate. The polythene tube was passed down the probe which was then withdrawn and the base plate positioned under the skin. The ends of the wires were bared, coiled and placed separately into the tooth cavities, which were then packed with amalgam (fine grain solila alloy) to form the electrodes. The gum flap and the external skin incision were sutured.

In the testing of drugs for analgesic activity the following procedure was adopted. Dogs were trained to sit in individual boxes (81·7 × 66·6 × 53·5 cm). The external electrode assembly was connected to a Palmer stimulator by leads and an Amphenol strip connector (Type 221-1). The dogs were viewed through a one-way mirror. Every 30 min, for a period of 3 h after the animals received drug or placebo by mouth, a series of transient but increasing stimuli were applied to the dental pulp. In each stimulation schedule the frequency, pulse width and duration of the stimulus remained constant at 10 Hz, 50 ms and 10 s, respectively; only voltage was varied. Increasing stimuli (0·5–30 V) were applied to the dental pulp at intervals of 30 s to determine the threshold voltages for individual reactions, for example snarling or head jerking. After the initial schedule, selected stimuli were used so that each subsequent schedule lasted for only 90 seconds. In this test the minimal oral doses of aspirin, codeine and pentazocine required to suppress pain responses in the dog were 15, 3·5 and 5·0 mg/kg, respectively. These dogs may be used repeatedly for about 6 months during which time

the normal reaction threshold remains constant. The method seems to be suitable for testing the known types of anagesic including the non-narcotic, narcotic and narcotic antagonist drugs.

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Automatic recording of the mouse abstinence syndrome

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Several attempts to understand the factors responsible for the development of physical dependence and tolerance to strong analgesics have involved experiments with mice (Maggiolo & Huidobro, 1962; Chiosa, Dumitrescu & Banaru, 1968; Way, Loh & Shen, 1968; Marshall & Grahame-Smith, 1970; Maruyama, Hayashi & Takemori, 1970; Shen, Loh & Way, 1970). The characteristic sign of abstinence in this species is uncontrollable jumping, which can be precipitated almost immediately by nalorphine or naloxone in morphine dependent mice. This response provides a convenient measure in the estimation of physical dependence capacities of prospective analgesics (Marshall & Weinstock, 1969; Saelens, Granat & Sawyer, 1971).

A simple automated apparatus which records the incidence of jumping photo-electrically will be demonstrated. Twelve mice, each housed in separate ventilated glass milk bottles (base diameter—7 cm; height—21 cm), are monitored simultaneously and 15 min print-outs enable the characterization of syndromes induced by narcotic antagonist injection or sudden drug withdrawal, respectively.

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