somewhat puzzling finding has been the absence of marked hypoglycaemia in *pertussis*-treated mice, despite very high insulin levels (Gulbenkian *et al.*, 1968; Pittman *et al.*, unpublished). This communication reports an effect of blood sampling method on the measured level of serum insulin of *pertussis*-treated mice. Female mice (HAM/ICR strain, 3–4 weeks old, 14–25 g) were treated with either, (i) *B. pertussis* vaccine (0.5 ml of 10 International Opacity Units i.p.) or, (ii) a sub-lethal dose of *B. pertussis* viable organisms (Strain 18–323, 5×10^4 colony forming units, administered intranasally under ether anaesthesia). Control mice were inoculated with the diluents. Fourteen days later, blood was removed from freely-fed mice by either heart puncture under ether anaesthesia or by decapitation without the use of ether. Serum immunoreactive insulin (IRI) was measured by the method of Hales & Randle (1963) and serum glucose was determined enzymically.

The table shows that serum IRI concentrations in *pertussis*-treated mice were not significantly different from control concentrations when blood was collected by decapitation. However, blood sampling under ether anaesthesia appears to have provided a stimulus which induced hyperinsulinaemia in *pertussis*-treated animals. Ether anaesthesia was used by Gulbenkian *et al.* (1968) and by Pittman *et al.* (unpublished). These observations appear to be consistent with the findings of Sumi & Ui (1975) that adrenaline induces marked hyperinsulinaemia in *pertussis*-vaccinated but not in control rats. Possibly adrenaline released by ether anaesthesia may have produced the hypersulinaemia in *pertussis*-treated mice.

A significant, although not severe, hypoglycaemia was found in the *pertussis*-infected but not in *pertussis*-vaccinated mice. The lack of marked hypoglycaemia in the *pertussis*-treated animals may be explained by the hyperinsulinaemia not appearing until provoked by ether anaesthesia.

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Table 1 Effect of mode of collection of blood on the serum IRI and glucose levels in *pertussis*-treated mice

	Blood collected by			
	Decapitation		*Heart puncture, ether anaesthesia*	
Treatment	*IRI (μU/ml)*	*glucose (mg/dl)*	*IRI (μU/ml)*	*glucose (mg/dl)*
Control	70 ± 10(7)	174 ± 9(7)	37 ± 7(10)	166 ± 9 (9)
Pertussis vaccine	52 ± 10(6)	148 ± 22(6)	186 ± 22** (9)	178 ± 11 (9)
Control	41 ± 13(5)	172 ± 10(5)	33 ± 6(10)	177 ± 6(10)
Pertussis infection	69 ± 8(6)	126 ± 6*(6)	160 ± 19**(10)	141 ± 7**(10)

(Values are mean ± s.e. mean. Numbers in brackets indicate number of observations. Significance of differences (control v. *pertussis*-treated) was determined by the Mann-Whitney U test. *$P \leqslant 0.05$; **$P \leqslant 0.01$)

An evaluation of hind paw oedemas in the guinea pig

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The discovery of new anti-inflammatory drugs has relied largely on the use of hind paw oedema models using the rat as the experimental animal. Ultra violet-induced erythema in the guinea pig is an exception although its relevance has never been fully understood. Other models of inflammation in the guinea pig have been reported although hind paw oedemas equivalent to those described in the rat have not been extensively evaluated. Consequently we have undertaken an investigation of the sensitivity of the guinea pig to various inflammatory mediators and irritants injected into the hind paw. Furthermore, the effects of a variety of mediator antagonists and anti-inflammatory drugs have been examined.

Male Dunkin Hartley guinea pigs (180–200 g) were used in groups of 5 throughout these experiments unless otherwise stated. Histamine and bradykinin (1–10 μg/paw) produced dose related paw oedema maximal at 15 min when injected via the subplantar (s.p.) route. 5-Hydroxytryptamine (5-HT, 10-400 μg/paw) and compound 48/80 (10–50 μg/paw) also produced a maximal oedema at 15 min but the responses were not as great as for histamine or

bradykinin. Groups of 50 animals were injected s.p. with 1 μg/paw histamine or 2.5 μg/paw bradykinin and produced normally distributed inflammatory responses (Lilefors test) at 15 min although the variation in response was considerable.

Equieffective mediator concentrations, *viz.* histamine (2.5 μg/paw), 5-HT (10 μg/paw), bradykinin (2.5 μg/paw), were used for an evaluation of mediator antagonists injected s.c. 30 min prior to s.p. injection of the mediator. Responses were recorded at 15 and 30 min prior to s.p. injection of the mediator. Tripolidine (2.5 mg/kg), a H_1 antagonist, completely inhibited the histamine induced response but was ineffective on 5-HT and bradykinin-induced paw oedemas. Cimetidine (100 mg/kg), a H_2 antagonist, significantly inhibited only the histamine oedema. Methysergide (2.5 mg/kg), a 5-HT antagonist significantly inhibited the 5-HT induced oedema but was without effect on histamine and bradykinin. Cyproheptadine (10 mg/kg), a combined histamine and 5-HT antagonist, completely abolished the histamine oedema but was without effect on the other mediators.

We have furthermore examined the effect of s.p. injection of the IgG fraction of rabbit anti-guinea pig immunoglobulin (anti-IgG, 5–200 μg/paw) in the guinea pig paw. This preparation produced a dose related oedema that peaked at 3 h. Triprolidine, methysergide and cyproheptadine all partially inhibited the anti-IgG oedema for up to 3 h. Although phenylbutazone failed to suppress the first 1.5 h of the anti-IgG oedema, it did produce significant inhibition (oral ED_{50} 33 mg/kg) of the 3 h response. Dapsone, an anti-leprotic agent that possesses anti-inflammatory activity (Williams, Capstick, Lewis & Best, 1976; Lewis, Gemmell & Stimson, 1978) inhibited both the early phase (0–1.5 h) and late phase (1.5–4 h) of the response. However, dapsone was more effective at 1.5 h (oral ED_{50} 34 mg/kg) than at 3 h (oral ED_{50} 60 mg/kg).

In summary, we have confirmed and extended existing data (Sparrow & Wilhelm, 1957) on the sensitivity of the guinea pig to various inflammatory mediators and evaluated the effects of a variety of antagonists on these responses. The large variation in the guinea pig response to these inflammatory mediators suggests that in comparison with the rat pedal oedema in the guinea pig is not an ideal model for evaluation of new anti-inflammatory drugs. Nevertheless, the use of an 'irritant' such as anti-IgG can be used in order to select and further evaluate non-steroidal anti-inflammatory drugs.

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Investigations of *Harpagophytum procumbens* (Devil's Claw) in the treatment of experimental inflammation and arthritis in the rat

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Harpagophytum procumbens (H.P.) or Devil's Claw as it is more commonly known is a herbal remedy that is advocated in the treatment of a variety of diseases, including rheumatoid arthritis (Seeger, 1973). Investigations of H.P. in animal models of inflammation have been carried out previously (Zorn, 1958; Eichler & Koch, 1970) but none have used the commonly accepted techniques of carrageenin oedema and adjuvant-induced arthritis in the rat.

Devil's Claw was provided as a dried aqueous extract of the secondary root of H.P., 1 g of powder being extracted from 2 g of root.

In the carrageenin test 30 male Wistar rats (120–160 g) were starved overnight and then dosed orally with either indomethacin (5 mg/kg) or Devil's Claw (1 g/kg). Controls received 0.5% tragacanth. One h later carrageenin (0.1% w/v in saline) was injected into the rear right foot of each animal. The volumes of both rear feet were then measured at hourly intervals by means of a mercury reservoir connected to a pressure transducer. Volumes were recorded directly from a suitably calibrated meter output of a Devices M2 recorder. All measurements were performed 'blind'. Results are expressed as the increase in volume of the right (injected) foot over the left expressed as a percentage of initial foot volume. Analysis of the results at the peak of the reaction (4 h) using Student's *t*-test showed that indomethacin produced a 63% inhibition of swelling ($P<0.001$) whilst Devil's Claw had no significant effect (−6% $P>0.1$).

Adjuvant arthritis was induced in 40 female SPF Sprag Dawley rats (120–140 g) by injection of 0.1 ml of *Mycobacterium tuberculosis* in light paraffin oil (1 mg/ml) into their rear right feet. Rear foot volumes and body weights were measured at intervals over 21 days. Drugs were administered orally every day.