the air. The bag and pad methods are not suitable for determination of the sodium content of sweat.

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Oestrogen and Gonadotrophin in the Blood of Dogs during Bone Fracture Healing

Previous reports have dealt with variations in the activity of thyroid glands[1] and changes in the levels of androgens, follicle-stimulating and luteinizing hormones[2] as a result of bone fracture. The present investigation is concerned with changes in oestrogens and gonadotrophic hormones (FSH and LH) in the blood of dogs during the healing of bone fractures. Twenty-five mature anoestrous non-pregnant female dogs were used. Mid-diaphyseal fractures of the left radius were made by an open technique. Animals were anaesthetized using chloropromazine hydrochloride and thiopental sodium. The radius in the dog was firmly fixed at its proximal and distal extremities to the ulna, which was left intact and acted as a natural splint.

At weekly intervals after fracture, 50 ml. of blood was collected by jugular venipuncture from each of 5 animals. The animals were afterwards killed and the uterus and ovaries were examined to exclude pregnancy and cyclic ovarian activity. The blood was allowed to clot, and sera belonging to animals of the same group were pooled. Groups of animals were examined at one, two, three, four and six weeks after fracture.

Oestrogenic substances were separated[3] and assayed biologically[4]. The methods used for the isolation and assay of gonadotrophic hormones were as described earlier[2]. The results obtained, which are shown in Table 1, were analysed statistically. The standard error of the mean was computed and '*t*' tests were performed to detect differences between groups.

Significantly high levels of oestrogenic substances were observed by the end of the second week after fracture and were continued until the end of the sixth week. This early rise in serum oestrogen, which was not preceded or accompanied by appreciable changes in either FSH or LH, favours the hypothesis of the existence of extra-ovarian sources for oestrogen, such as the adrenal cortex. Adrenal corticotrophic hormone is shown to induce the production of relatively small amounts of oestrogen by the adrenals[5]. However, the changes in serum FSH and LH detected in the subsequent stages of the healing process could be explained on the basis of the findings which showed that oestrogen increased the synthesis and release of LH. At the same time, it induced a drop in FSH content in the blood and in the pituitary gland[6]. This was the case during fracture healing, where increased oestrogen formation elevated serum LH without significantly affecting serum FSH.

Table 1. Oestrogens, Luteinizing (LH) and Follicle Stimulating (FSH) Hormones in the Serum of Bitches during Bone Fracture Healing

Weeks after fracture	Oestrogen (mouse uterus wt., mg/100 g body-wt.)	LH (No. of corpora haemorrhagica per mouse)	FSH (wt. of mouse ovary, mg/100 g body-wt.)
Normal	63·50 ± 2·25	0·31 ± 0·170	37·14 ± 2·36
One	73·37 ± 5·66	0·20 ± 0·140	32·95 ± 3·28
Two	94·29† ± 4·16	0·10 ± 0·002	31·84 ± 2·57
Three	79·90† ± 2·36	1·27* ± 0·250	38·52 ± 3·32
Four	81·98† ± 2·15	1·36* ± 0·430	42·35 ± 3·13
Six	79·34* ± 3·50	0·50 ± 0·260	39·06 ± 2·80

± Standard error.
* Significant at 95 per cent confidence level.
† Significant at 99 per cent confidence level.

It is generally accepted that bone resorption takes place during the early stages of fracture healing[7], this coincides with the period when the rise in serum oestrogen was insignificant. The increased level of oestrogens during the second week favours an increased bone formation[8] and mineral deposition[9]. Oestrogenic substances are known to possess a general metabolic action on bone[10]. It is believed that oestrogen possesses a specific stimulating effect on osteoblasts which in turn form protein matrix on which calcium and phosphorus are deposited as hydroxyapatite to form normal bone. Animal experiments have shown that ovariectomy decreased callus formation and the breaking strength of bone[11]. On the other hand, the extraneous administration of oestrogens hastened fracture healing[12].

It could be concluded that a rise in oestrogen level takes place in the blood of dogs after the lapse of one week following bone fractures, and that this hormone is physiologically essential for the normal process of fracture repair.

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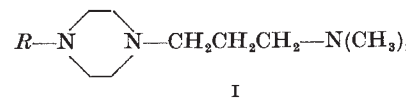
PHARMACOLOGY

N^4-substituted N^1-(3-Dimethylaminopropyl)-piperazines : a New Series of Compounds active against *Trypanosoma cruzi* Infections in Mice

Recent reviews[1–3] on the treatment of *Trypanosoma cruzi* infections (Chagas's disease, South American trypanosomiasis) in man emphasize the lack of a satisfactory mode of therapy.

We wish to report the synthesis and biological evaluation of a series of compounds of the general structure:



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