tion densities that they are favoured by selection and come to form a significant proportion of the total population.

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[1] Owen, D. F., and Wiegert, R. G., *Amer. Nat.*, **96**, 353 (1962).
[2] Halkka, O., *Nature*, **193**, 93 (1962).
[3] Verdcourt, B. (personal communication).
[4] Clarke, B., *Syst. Assoc. Pub.*, No. 4, 47 (1962).

Uptake of Iodine-131 by Thyroids of Rats during Healing of Fractures

So far, the available literature is devoid of any detailed examination concerning hormonal changes which occur during healing of fractured bones.

Sixty mature male rats of about 200 g were used. The animals were divided into groups of ten. One group was left intact and served as a control. The remaining animals were subjected to experimental fractures of the left tibia by a closed method under ether anæsthesia[1]. The dates of the operations were spaced so as to obtain animals at 5, 10, 15, 21 and 29 days post-fracture. At exactly 6 h before death the rats were injected subcutaneously with 1 μc. iodine-131. They were then killed by decapitation under light ether anæsthesia. The thyroids were dissected and cleaned from adhering tissues, dried on aluminium planchets for 1 h at 90° C. The specific activities of the individual thyroids were recorded by means of a Geiger–Müller counter and expressed in terms of counts/min/mg of thyroid and the values were further corrected in relation to 100 g body-weight. The data obtained were statistically analysed using the *t* test.

The results presented in Table 1 show that thyroid activity reached its maximum two weeks post-fracture, then declined slightly but remained high during the third week and returned to the normal level by the end of the fourth week.

Table 1. Uptake of Iodine-131 by Rat Thyroid during Fracture Healing

Days after fracture	Counts/min/mg thyroid	Counts/min/mg thyroid 100 g body-weight
Control (normal)	42·67 ± 5·28	21·96 ± 3·03
5 days	44·87 ± 5·13	26·00 ± 4·56
10 days	37·78 ± 5·08	16·40 ± 2·54
15 days	105·70* ± 17·80	57·45* ± 7·17
22 days	70·59* ± 7·82	31·91† ± 3·29
29 days	47·58 ± 6·39	24·67 ± 6·48

* Significant, $P = 0·01$.
† Significant, $P = 0·05$.

One of the main actions of the thyroid hormone is to increase the basal energy metabolism of all living cells. Moreover, it is needed for the biological processes concerned with absorption, metabolism and excretion of minerals and with the formation and resorption of bone[2]. In addition, the thyroid hormone is necessary for the endochondrial bone formation and maturation of the epiphyseal cartilage[2,3].

An increased uptake of sulphur-35 was noticed at the same period of increased thyroid activity. The degree of sulphur incorporation is an indicator of sulphated mucopolysaccharides formation, an important constituent of bone ground-substance[1].

It is generally accepted that there is an increased demand for protein synthesis during repair of injuries. In this respect an increased level of thyroid hormone is considered in favour of protein anabolism[4]. The thyroid seems to play a part in binding both strontium and calcium with less labile protein of bone. When the thyroid function was blocked by administration of thiouracil, calcium and strontium were incorporated with labile protein of bone[5].

It is concluded that under normal conditions there is an increased activity of thyroid gland during the stage of cellular regeneration of callus formation, after which it drops to normal values.

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[1] Said, A. H., thesis, Univ. Ghent (1960).
[2] Reifenstein, jun., E. C., *Textbook of Endocrinology*, second ed. (W. B. Saunders Co., Philadelphia and London, 1958).
[3] Silverstein, E., Sakoloff, L., Jay, jun., G. E., and Mikelsen, O., *Amer. J. Physiol.*, **199**, 209 (1960).
[4] Hublé, D., *Brit. Med. J.*, 601 (1957).
[5] Lengemann, F. W., Wasserman, R. H., and Comar, L., *Endocrinol.*, **67**, 535 (1960).

Effect of 4,4′-Diaminodiphenylmethane against *Fasciola hepatica* in the Rabbit and in Cattle

Two drugs widely used in the chemotherapy of fascioliasis, carbon tetrachloride and hexachloroethane, show very little activity against the immature, migrating forms of the fluke. The earliest age of the fluke against which these drugs are active occurs after migration of the parasite through the liver parenchyma, when the flukes are either in, or about to enter, the bile ducts.

In rabbits, hexachloroethane at a dose of 0·66 g/kg by mouth is effective in killing the 5-week-old fluke[1] and my experiments with carbon tetrachloride (0·15 ml./kg by subcutaneous injection) against the mature and immature fluke have shown the earliest age of fluke against which this compound shows activity at this dose to be 6 weeks. Hexachlorophene, reported active against the 2-, 3-, and 4-week-old fluke in sheep and to have variable activity in rabbits[2], has shown only partial inhibition of development of the 2-, 3-, and 4-week-old flukes in our tests at the same dose (40 mg/kg dissolved in olive oil and administered orally) in rabbits. Thus, any compound effective against the immature as well as the mature forms of the parasite would be of considerable interest.

During the routine examination of a series of compounds for activity against experimental *Fasciola hepatica* infections in rabbits, it was found that 4,4′-diaminodiphenylmethane, either as the base or the hydrochloride, was active against the 1-, 2-, 3- and 4-week-old, as well as the mature 10-week-old fluke.

The methods used for testing compounds against *F. hepatica* in rabbits are based on those described by Lämmler[3], modified by Hughes[1].

The rabbits used were of either sex and varying breeds aged 3–4 months and weighing 2–3 kg. These were infected with 15 metacercariæ of *Fasciola hepatica* given orally. The compound was administered orally as an aqueous solution of the hydrochloride. The cattle used were of either sex, Ayrshire or Guernsey calves, and were aged about 2 months when infected with 300 metacercariæ administered in a gelatin capsule by means of a balling gun. The criterion for activity against the mature forms was the absence of flukes in the liver and the presence of eggs in the gall-bladder at post-mortem examination 2 weeks after dosing, and for activity against the immature forms, the absence of both flukes in the liver and eggs in the gall-bladder at post-mortem examination 10 weeks

Table 1. Effect in Rabbits of Oral Administration of 4,4′-Diaminodiphenylmethane Hydrochloride against the Immature* and Mature† Forms of *Fasciola hepatica*

Age of flukes (weeks)	Dose (g/kg)	No. cured/No. treated
1*	0·25	3/3
2*	0·1	3/3
	0·25	3/3
3*	0·25	3/3
4*	0·1	4/4
	0·25	3/3
10†	0·05	0/3
	0·075	2/2
	0·1	3/3