respiratory arrest, whereas the latter symptom is the first to appear after large doses of amidone.

In animal experiments the respiratory depressant activity in these compounds parallels analgesic activity, so that, broadly speaking, in effective compounds a given degree of analgesia is accompanied by a similar degree of respiratory depression.

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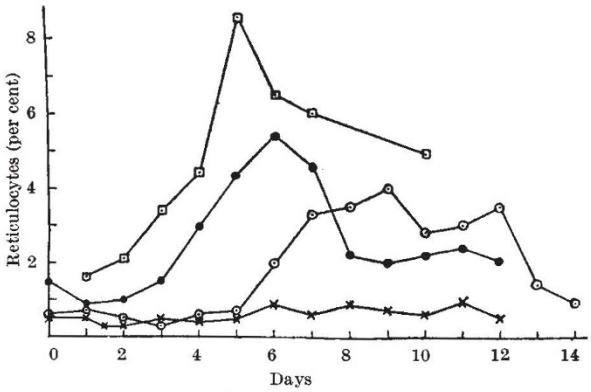
Thio-thymine (2-Thio-5-Methyl-Uracil)

Spies *et al.*[1] have reported the value of 5-methyl-uracil (thymine) in the treatment of pernicious anæmia. Jacobson and Williams[2] have suggested the use of splenectomized rabbits for the assessment of anti-anæmic factors, and Bavin and Middleton[3] have shown that thymine causes a reticulocytosis when injected into such splenectomized rabbits. We have used a similar method for the study of the hæmopoietic activity of various thymine derivatives.

Di-hydro-thymine-4-carboxylic acid when injected intramuscularly into splenectomized rabbits in dosages of 100 mgm./kgm. does not cause a reticulocytic response, whereas 2-thio-5-methyl-uracil (in 100 mgm./kgm. dosage) and 2-amino-5-methyl-uracil (100 mgm./kgm.) do (see graph).

The 2-thio-5-methyl-uracil compound (thio-thymine) is particularly interesting in that it contains the —NH.CS.NH— grouping which Astwood[4] has suggested is the common radical in many anti-thyroid compounds. We have found that when this compound is given by mouth to 21-day old female rats (Wistar) in a dosage of 40 mgm./100 gm. daily for ten days and the rats then sacrificed, the thyroids of these rats are grossly enlarged and hyperæmic. Histological examination of the glands revealed colloid loss, increased vascularity, and hyperplasia of the acinar epithelium. A dosage of 20 mgm./100 gm. daily by mouth for ten days did not cause any very marked thyroid changes.

Hence thio-thymine has both anti-thyroid properties and hæmopoietic activity. Moreover, the daily injection of 100 mgm./kgm. intramuscularly for ten days to splenectomized rabbits does not affect the white blood-cell counts of these animals. Again, the intramuscular injection of 20 mgm./kgm. daily (higher dosages caused death of some rabbits from pulmonary œdema) into normal rabbits for ten



●, Thymine, 100 mgm./kgm. intramuscularly
○, Thio-thymine, 200 mgm./kgm. intramuscularly
×, Di-hydro-thymine-4-carboxylic acid, 100 mgm./kgm. intramuscularly
□, Amino-thymine, 100 carboxylic acid, 100 mgm./kgm. intramuscularly

days produced, if anything, a polymorphonuclear leucocytosis (see table). Thio-thymine would seem, therefore, to be free from the depressant action on the bone marrow which has been noted in the use of thiourea[5] and thiouracil[6].

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Treatment of Myasthenia gravis with Di-isopropylfluorophosphonate

A number of papers have appeared recently dealing with di-isopropylfluorophosphonate, which was prepared by McCombie and Saunders[1] in 1941 and found by Adrian, Feldberg and Kilby[2] to cause a prolonged inhibition of cholinesterase. One of us (J. H. G.) tested its effect on myasthenia gravis in 1943, but had to abandon the work owing to lack of clinical material. This work was continued by the other, and the object of this letter is to report the results.

The drug was injected intramuscularly. In the earlier experiments it was freshly dissolved in water; later, the more stable solution in arachis oil was used. Serum cholinesterase was estimated manometrically using acetylcholine as substrate, and the strength of the muscles controlling the hand was measured with a dynamometer. Neostigmine (prostigmine) had its usual dramatic effects on all these patients. General weakness, ptosis, diplopia and dysphagia disappeared

Type of animal	Dosage of thio-thymine (mgm./kgm.)	White blood cell count in thousands on days										
		1	2	3	4	5	8	9	10	11	12	15
Normal rabbit	20	8·4	6·6	10·6	16·8	16·0	15·5	17·8	19·8	19·8	15·2	21·4
Splenectomized rabbit	100	10·8	12·0	9·6	8·1	7·7	11·3	12·9	13·0	12·7	8·7	10·3

The above figures are the average counts from three rabbits. Injections were given daily from day 3 to day 14.