The first case reported by Gross was a 5-year-old boy[3] and, in discussing his experience with 60 cases recently, whose ages ranged from 5 to 30 years, he stated that operation should be avoided before 6 to 8 years of age.[2] Gross indicated that the risks in babies and very young children are high[3] because collateral channels are not well developed and because the aorta is too small for the anastomosis to be accomplished with facility. He stated further than "an aortic lumen may be established at the anastomosis which is satisfactory for a child of a few years of age, but it will probably be insufficient in size when the person grows to maturity."

The experiments reported in this paper appear to have some bearing on the latter two points. There may be some doubt as to the necessity of delaying operation until a child is 6 to 8 years old to assure that the aorta will be large enough to suture without excessive risk. The dogs in this experiment were under 5 lb in weight and less than 8 weeks old at the time of operation, and yet the technical aspects of the anastomoses were accomplished without mishap. The 4 fatalities in the postoperative period were unrelated to the operative procedures.

On the other hand, it would appear that the diameter of the lumen at the site of anastomosis in these dogs did not keep pace in growth with the rest of the aorta. This would support the view that surgical intervention for coarctation should be deferred until the lumen of the aorta is large enough in diameter to insure adequate size as the individual grows to maturity. To be sure, a single continuous suture was used for the anastomosis which might have some bearing on the formation of the constriction.

Summary. Seven young dogs between the ages of three and eight weeks were subjected to end-to-end anastomosis of the thoracic aorta. Three of these dogs survived and have been studied approximately one year after operation to determine the status of the site of anastomosis.

Narrowing of the aortic lumen at the suture line was demonstrated in each animal by angiocardiographic methods and also in one at thoracotomy.

[3] Gross, R. E., *Surgery*, 1945, **13**, 673.

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17276. Isolation of an Anti-thyroid Compound from Rape Seed (*Brassica Napus*).

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In a study of the toxic reactions produced in rats by phenylthiourea and α-naphthylthiourea (ANTU), it was found that rats which had been pretreated with anti-thyroid compounds or fed on certain goitrogenic diets developed a marked resistance to these toxic compounds.[1] This effect has been used as an assay method in the extraction of a goitrogenic compound from rape seed.

Materials and methods. Adult Sprague-Dawley rats of either sex were used in assaying the rape seed fractions. Crude fractions were tested by mixing them with the normal diet of fox chow and feeding for 4 days, following which the rats were injected intraperitoneally with 30 mg/kg of phenylthiourea. More refined fractions were dissolved in water and given in a single subcutaneous injection, followed 24 hours later by 20 mg/kg of phenylthiourea intraperitoneally. Survival of the rats for more than 48 hours after the toxic dose was used as the criterion of activity in the extracts.

The normal LD 50 of phenylthiourea for

[1] Carroll, K. K., and Noble, R. L., *Fed. Proc.*, 1949, **8**, 22.

adult rats was found to be 3 mg/kg but this increased to more than 30 mg/kg in rats which had been fed for 4 days on a diet of fox chow to which 4% of ground rape seed had been added.

Experimental. The following is a detailed account of the extraction of 4 kg of a typical batch of rape seed (variety—Dwarf Essex).

The seed was first ground in a coffee mill and then stirred with 3 volumes of ether. The ether-soluble oil was inactive. The insoluble material (3 kg) was filtered and washed with ether, dried, and then allowed to stand over night in 5 volumes of water. This suspension was filtered with suction through coarse paper and the extraction was repeated with 4 volumes of water. The combined aqueous solution contained most of the active component.

This solution was extracted continuously with ether for 14 days. The ether-soluble fraction consisted of 28 g of yellow oil which was highly active. This oil was shaken with 10 volumes of water which dissolved 75% of the total. The remaining material appeared to be less soluble in water. The yellow solution was filtered and the filtrate (300 cc) treated with 200 cc of 10% silver nitrate solution. The sticky white precipitate was separated by centrifugation, washed twice with water, once each with alcohol, acetone and ether, centrifuging after each washing. The insoluble silver salt appeared to be unstable, turning yellow and eventually black if allowed to remain in contact with the silver nitrate solution. Its stickiness disappeared during the water wash, and the resulting brittle lumps were broken up with a spatula. The dried product was a light-gray amorphous solid insoluble in the common solvents. In this state it could be kept at room temperature for some weeks without appreciable deterioration. Analysis of one sample of this crude material gave the following results.

Calculated for				
C_5H_6ONSAg:	C–25.4	H–2.56	N–5.94	Ag–45.7
Found	C–22.5	H–2.40	N–6.21	Ag–47.5

The solid (18 g) was suspended in 3% sodium carbonate solution and decomposed with hydrogen sulfide. The precipitate of silver sulfide was separated by centrifugation, washed once with water and the combined aqueous solution was extracted with ether. The ether solution was dried with sodium sulfate and the ether removed *in vacuo,* leaving 5.5 g of a colorless oil which crystallized with difficulty. It could be distilled ($B.P._{0.25}$-160-185°C bath temperature) or purified by crystallization from benzene-ligroin 3:1 (8 cc per g). The recrystallized material melted at 50-51°C and gave the following analysis.

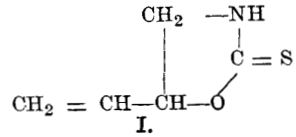
Calculated for				
C_5H_7ONS:	C–46.5	H–5.47	N–10.8	S–24.8
Found:	C–45.4	H–5.13	N–11.0	S–25.2

The compound gave a blue color with Grote's reagent,[2] which changed to green after 20 minutes and gradually faded.

Its anti-thyroid activity was tested by feeding it to immature rats (0.5% in powdered fox chow) for a period of 11 days. The resultant thyroid hyperplasia was slightly less than that produced when thiourea was fed at a 0.5% level for the same period of time.

Discussion. A variety of mustard oils have previously been isolated[3-5] from plants of the Cruciferae family to which *Brassica Napus* belongs, in some cases by the formation and decomposition of a silver salt.[5] However, thiourea derivatives have also been found to form insoluble silver salts,[6] and the properties of the present compound more closely resemble those of thioureas than of mustard oils.

Using the technic of inhibition of uptake of radioiodine by the thyroid as a method of assay, Astwood, Greer and Ettlinger[7] have isolated what appears to be the same compound from rape seed, and have shown that it has the structure I.



I.

[2] Williams, R. H., Jandorf, B. J., and Kay, G. A., *J. Lab. and Clin. Med.*, 1944, **29**, 329.

[3] Gadamer, J., *Ber. Deut. Chem. Ges.*, 1897, **30**, 2322.

[4] Schneider, W., *Chem. Abst.*, 1910, **4**, 3064.

[5] Schmid, H., and Karrer, P., *Helv. Chim. Acta*, 1948, **31**, 1017.

[6] Gadamer, J., *Arch. Pharm.*, 1895, **233**, 646.

[7] Astwood, E. B., Greer, M. A., and Ettlinger, M. G., *Science*, 1949, **109**, 631.

Their experiments indicated that the anti-thyroid activity of this compound in humans is comparable to that of 6-n-propylthiouracil.

Summary. A new method for the detection of compounds which have anti-thyroid activity is described. This method has been used to isolate a crystalline anti-thyroid compound from rape seed having the empirical formula C_5H_7ONS.

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17277. Effect of Amino Acids and Sodium Bicarbonate on the Level of Glutamine in Blood. V.

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In a previous publication[1] we reported on the depressing effect of glucose and insulin administration on the level of glutamine and amino acids in the blood plasma and some of the possible mechanisms involved in producing this effect were discussed. In a subsequent publication[2] it was shown that this was not due to a mere diffusion of amino acids and glutamine into the tissues as had been suggested by Hamilton.[3]

In this paper we wish to report the effect of the intravenous administration of some amino acids, sodium bicarbonate and physiological saline solution on the level of glutamine in the blood plasma of rabbits.

Procedure and methods. Male rabbits, 18 hours post absorptive, were used for these experiments. Six animals were used for each substance which was tested. The amino acids and sodium bicarbonate were made up as a 10 percent solution in distilled water and 10 ml or the equivalent of 1 g of substance per 3 kg of body weight was administered intravenously. The saline solution was administered in quantities of 10 ml. Since the rabbits were very similar in weight (Table I) the volumes varied by only one or two ml. The rabbits were bled from the marginal vein of the ear just before injection and 30 and 60 minutes after injection. About 12 ml of blood were drawn at each bleeding into tubes containing sodium oxalate to prevent coagulation. The blood was immediately centrifuged for about 10 minutes and the plasma was used for the determination of total amino acids and glutamine. The amino acids were determined colorimetrically by Russell's modification of Frame's method[4] and the glutamine by our method as described in a previous publication.[5] The determinations were carried out in duplicate or triplicate and statistical analysis of the data showed that the variations between duplicate determinations were negligible.

Observations. It will be seen from Table I that the initial level of glutamine in the post-absorptive state bore no relation to the level of the total amino acids during this period.

dl-Alanine. Following the intravenous administration of dl-alanine there was a marked rise in the level of glutamine in the first 30 minutes. This amounted to an average increment of 3.3 mg per 100 ml of blood plasma. Although the level tended to decrease in the following 30 minutes it still was above the initial level by an average of 2.0 mg. Statistical analysis by Fisher's "t"[6] method for a

1 Harris, M. M., Roth, R. T., and Harris, R. S., *J. Clin. Invest.*, 1943, **22**, 577.

2 Harris, M. M., and Harris, R. S., PROC. SOC. EXP. BIOL. AND MED., 1947, **64**, 471.

3 Hamilton, P. B., *J. Biol. Chem.*, 1945, **158**, 397.

4 Russell, J. A., *J. Biol. Chem.*, 1944, **156**, 467.

5 Harris, M. M., Roth, R. T., and Harris, R. S., *J. Clin. Invest.*, 1943, **22**, 569.

6 Mainland, D., Treatment of Clinical and Laboratory Data, p. 147, Oliver and Boyd, London, 1938.