servations were made in the present investigation on 2 subjects who developed a mild circulatory collapse immediately after injection of Na^{24} into the synovial space. Continuous recordings of Na^{24} concentration in the knee were made. During the period of faintness and hypotension the Na^{24} absorption was slow. Upon recovery the absorption of Na^{24} was more rapid. Thus the removal of sodium from the knee joint is dependent on both membrane permeability and circulation.

Discussion. The implication of these observed variations in Na^{24} clearance from the joint space of the knee is not clear. The possible difference attributable to the stage of the menstrual cycle at which the experiment is carried out suggest, however, an hormonal control of synovial permeability to Na^{24}. The experimental work done in rabbits by Seifter (3) supports an hormonal explanation for the variations of synovial permeability found in this investigation. When phenolsulphonthalein was injected into the rabbit synovial space, the clearance was accelerated by parenteral administration of desoxycorticosterone but retarded if cortisone was administered.

Paul and coworkers(4), however, have failed to find any effect of cortisone and ACTH on synovial permeability. Utilizing the same methods as described by Seifter, they found no significant alteration of synovial membrane permeability unless cortisone was injected into the joint. The use of Na^{24} may obviate inherent difficulties of previous methods described for the study of electrolyte exchange across the synovial membrane(5) and may serve as a useful technic for the study of the influence of endocrine substances on joint physiology.

Summary. 1. By means of injection of Na^{24} into the knee joint, the clearance of Na^{24} through the synovial membrane has been studied. 2. A significantly more rapid clearance of Na^{24} from the knee joint occurs in women than in men. There is suggestive evidence that the accelerated Na^{24} clearance in women depends upon an hormonal influence associated with the menstrual cycle. 3. Removal of Na^{24} from the joint space is less rapid than it is from subcutaneous or muscle tissue.

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Effects of Liver Fractions and Vitamin B_{12} on Body and Organ Weights of Thyroid-Fed Rats. (19722)

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The recent data of Ershoff(1,2), Betheil *et al.*(3,4), and Emerson and Folkers(5,6) indicate that liver contains an "anti-thyrotoxic factor" which counteracts the growth retardation of young rats when fed a purified diet containing thyroid. According to Ershoff (7-10), this factor is present mainly in the water insoluble fraction of liver (liver residue) and is reported to be distinct from vit. B_{12}.

This communication confirms these reports and includes new data on the effects of thyroid, defatted liver residue, liver concentrate N.F., and vit. B_{12} on some organ weights of immature rats.

TABLE I. Basal Diet Composition.

Components	g/1000 g
Casein*	220
Sucrose	715
Salts IV†	45
Cod liver oil	20

Micronutrients in mg/kilo: Thiamin, 10; riboflavin, 20; pyridoxine, 10; d-Ca pantothenate, 100; nicotinamide, 100; inositol, 50; para amino benzoic acid, 300; choline, 1000; biotin, .5; pteroylglutamic acid, 2; α-tocopherol, 142; 2-methyl 1,4-naphthoquinone, 142.

* Vitamin free casein, Nutritional Biochemicals Corp., Cleveland, Ohio.

† Hegsted *et al.*(11).

Procedure. Male, weanling albino rats weighing 35 to 45 g were kept in suspended, mesh-bottomed cages and weighed weekly. Food and water were given *ad libitum.*

The composition of the basal diet is given in Table I.

Supplements were added as per cent of the basal diet unless otherwise indicated. The following supplements were used:

Thyroid U.S.P. (*Wilson*).

Defatted liver residue (*Wilson*), insoluble fraction from pork liver after removal of water soluble substances. Dried *in vacuo,* extracted with benzol and the solvent removed *in vacuo.*

Liver concentrate N.F. (*Wilson*), water soluble fraction from pork liver.

Vitamin B_{12}, Cobione Merck.

Results. Our results are shown in Table II. In our colony 0.25% thyroid depresses growth sufficiently and allows many of the animals to live for 28 days. Addition of 10% defatted liver residue counteracts the effect of thyroid on growth and permits most of the animals to survive the experimental period. Liver concentrate N.F. or vit. B_{12} is without significant effect. This confirms the published data of Ershoff(10).

Our data indicate that the adrenal and spleen are hypertrophied while the thymus is atrophied as a result of thyroid feeding. The effect on the adrenal has been reported by Ershoff(12), and by Leathem and Howell (13). Our data show that the addition of defatted liver residue tends to restore adrenal weight to normal but does not change the enlarged spleen due to thyroid feeding. Liver concentrate and vit. B_{12} restore the spleen

TABLE II. Effect of Liver Residue, Liver Concentrate and Vitamin B_{12} on Body and Organ Weights of Thyroid Fed Rats.*
(Each experiment continued for 28 days.)

Dietary supplement	Thyroid, %	No. of rats Start	No. of rats End	No. of exp.	Gain in body wt, g (mean ± S.E.)†	Organ wt, mg/100 g body wt (mean ± S.E.)† Adrenal	Thymus	Spleen
None	None	51	50	7	105.3 ± 6	17.23 ± .8	285.1 ± 19.7	545.5 ± 76
None	.25	51	31	7	69.7 ± 1.8	43.86 ± 3.58	211.1 ± 24	775 ± 83.6
Defatted liver residue, 10%	.25	51	44	7	98.1 ± 4	24.29 ± 1.81	272.3 ± 17.7	742.8 ± 79
Liver concentrate N.F., 4%	.25	32	25	4	77 ± 1.68	35.5 ± 2.22	272.5 ± 25	549 ± 30.6
Vitamin B_{12}, 30 μg/kg	.25	22	9	3	74 ± 2.89	42.3 ± 6.5	152 ± 41.6	470 ± 52.5

* In one experiment 12.5 mg of lyxoflavin per kg of diet was without effect on weight loss due to thyroid feeding. We are indebted to Dr. Karl Folkers of Merck and Co. for crystalline lyxoflavin employed.

† Stand. error $= \sqrt{\frac{d^2}{(n)\ (n-1)}}$ where "d" is the deviation from the mean and "n" is the number of experiments.

weight to normal. Neither vit. B_{12} nor liver concentrate has an effect on the enlarged adrenal.

Atrophy of the thymus due to thyroid feeding on a soy bean diet has been previously reported from this laboratory(14). It has also been produced by Leathem and Howell (13). In our experiments the addition of defatted liver residue restores the thymus weight to normal. Liver concentrate has a similar effect on the thymus, whereas vit. B_{12} is without effect.

Discussion. Our data, using a large number of animals, confirm the work of others that liver residue counteracts the growth retardation of young rats when fed a purified casein diet containing thyroid. The effect is not due to vit. B_{12} since the addition of 30 μg of this vitamin or 40 g of liver concentrate N.F. containing 120 μg of cyanocobalamin activity to a kilo of food is without effect. Ten per cent of defatted liver residue which contributes only 20 μg of cyanocobalamin activity per kilo of food is effective.

Liver concentrate is as effective as defatted liver residue in restoring the atrophied thymus to normal. In these experiments vit. B_{12} is ineffective, which is contrary to results obtained in this laboratory using a soy bean diet (14). A difference in basal diet may account for these results.

The effect of liver concentrate on the spleen may be due to its B_{12} content since this vitamin restores spleen size to normal in our experiments.

Experiments are in progress comparing defatted liver residue with other materials as a source of "antithyrotoxic factor." Emerson and Folkers(6) reported antithyrotoxic activity for lyxoflavin on a thyroid-soy bean diet. We have fed 12.5 mg of lyxoflavin per kg of diet and observed no effect on weight loss due to thyroid feeding. This disagreement between laboratories may be due to a difference in basal diets employed.

Summary. Addition of thyroid to a casein-sucrose diet retards growth, causes hypertrophy of adrenal and spleen and atrophy of the thymus. Feeding 10% of defatted liver residue counteracts growth retardation and restores the adrenal and thymus weights to normal. It is without effect on the spleen. Liver concentrate N.F. has very little effect on growth or on the adrenal, but does tend to restore the thymus and spleen to normal. Vit. B_{12} is without effect except in respect to the spleen where its prevents hypertrophy of this organ due to thyroid feeding. Lyxoflavin was found to have no antithyrotoxic effect on our diet.

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