# EXTRACORPOREAL BIOLOGICAL PERFUSION OF THE ISOLATED DOG THYROID GLAND

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According to some authorities [1, 5-7] biological perfusion methods, in which the perfused organ is connected to a living intermediate recipient or to an isolated heart-lung preparation, are the best methods of supplying an organ with oxygen and oxidation substrates and of removing carbon dioxide and other metabolic products.

The method of thyroid gland perfusion, in which the organ continues to function under physiological conditions, can be used to study the effects of various factors (transplantation, cryoconservation, antithyroid agents, stimulating drugs) on individual parameters of thyroid function. Methods of perfusion of the surviving thyroid gland with buffered salt solutions [8-11] and also with blood, using a pulsating valve pump [14], developed previously cannot be regarded as adequate for these purposes.

In this paper we describe a model of extracorporeal biological perfusion of the isolated thyroid gland which we have developed. The basis for development of the model was the principle of the scheme of perfusion of the testis [2, 3]. Considering the anatomical features of the dog thyroid gland, i.e., the total isolation of its two lobes, only the right lobe was perfused whereas the left remained *in situ* and served as the control.

## EXPERIMENTAL METHOD

Experiments were carried out on dogs of both sexes weighing 20-35 kg. The animals were anesthetized with 0.005% fentanyl solution and 0.25% droperidol solution (2 ml of each, intramuscularly), followed by intravenous injection of 2.5% hexobarbital solution in a total dose of 5-7 mg/kg. The right lobe of the thyroid gland was mobilized on its vascular pedicle, consisting of a segment of the common carotid artery with the thyroid artery branching from it, through a longitudinal incision in the neck. The extra-thyroid branches of the thyroid artery were ligated and divided. Heparin was injected intravenously into the dogs in a dose of 250 U/kg body weight. The right lobe of the gland together with the segment of the common carotid artery was removed and transferred to a thermostatically controlled chamber whose temperature was kept constant at 37°C. The segment of the common carotid artery was connected by means of polyethylene tubes to the central end of the divided right femoral artery, and its peripheral end was connected to the peripheral end of the divided left femoral artery (Fig. 1). The veins of the gland were divided. Venous blood drained away freely into the chamber through perforations in the support beneath the gland, and it was collected in a special receiver and returned to the dog's blood stream. Blood from the left lobe of the thyroid gland (control) was collected from the dissected thyroid vein, which was divided and placed in a test tube. The dog's systolic arterial pressure was maintained throughout the experiment at 90-120 mm Hg. In the course of perfusion for 6 h the volume of plasma expanders (the Soviet dextran equivalent polyglucin, 0.9% NaCl) was 0.5 liter and the hematocrit index never fell below 40. The duration of ischemia of the extracorporeally perfused lobe of the gland did not exceed 10 min. Throughout perfusion a careful watch was maintained on the dog's hemodynamics. The perfused lobe of the gland was weighed before and after perfusion. Thyroid function was assessed by measurement of several parameters. The thyroxine and triiodothyronine levels (by radioimmunoassay using kits from Amersham International, England) and concentrations of glucose (orthotoluidine test) and lactic acid (enzyme assay) were determined in afferent and efferent thyroid blood. At the end of perfusion the thyroxine and triiodothyronine levels [12] and the glycogen (anthrone method) and lactic acid concentrations in the gland tissue were determined.

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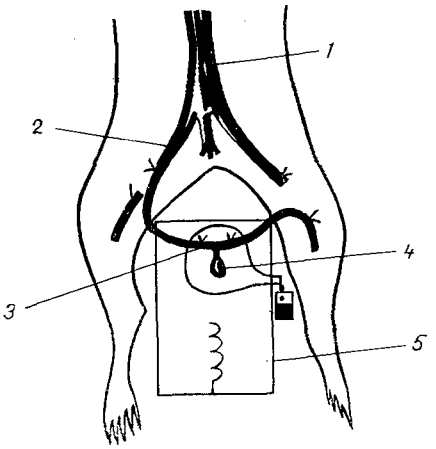


Fig. 1. Extracorporeal biological perfusion of the isolated dog thyroid gland: 1) aorta; 2) femoral artery; 3) segment of common carotid artery; 4) lobe of thyroid gland; 5) thermostatically controlled chamber.

## EXPERIMENTAL RESULTS

During perfusion the gland preserved its usual color and was externally indistinguishable from the control gland, perfused *in situ*. The blood flow in the lobe was resumed immediately after connection to the cannulas, as was confirmed by pulsation of the thyroid artery and also by the appearance of blood from the divided veins. The minute volume of the thyroid blood flow in the intact lobe was 2.2 ± 0.2 ml/min. In the experimental lobe of the gland the minute volume of the blood flow fluctuated very slightly and significantly exceeded the control values, namely 4.0 ± 1.3 ml/min ($P < 0.0001$). The weight of the lobe of the gland was 1.8 ± 0.05 g before perfusion and 2.05 ± 0.05 g ($P < 0.0001$) at the end of perfusion.

The mean levels of thyroid hormones in samples of plasma collected throughout the period of perfusion are given in Table 1. Secretion of thyroid hormones in the perfused lobe of the thyroid bland was preserved and exceeded the level of secretion in the lobe perfused *in situ*. Concentrations of thyroxine and triiodothyronine in the tissue of the control and experimental lobes of the thyroid gland, however, were virtually indistinguishable.

The results of determination of the glucose concentration in outflowing thyroid blood showed that glucose consumption in the control and experimental lobes of the gland was at the same level (Table 1). Investigation of the lactic acid concentration in the blood revealed no significant difference in the value of this parameter in thyroid arterial and venous blood in the control and experiment. Glycogen and lactic acid levels in gland tissue taken for analysis after the end of perfusion also were closely similar in the control and experiment.

The results are evidence of the absence of biochemical disturbances in the thyroid gland when perfused by the suggested method. The hypothesis that during free drainage of venous blood from the gland elution of the hormones from the perfusion lobe could take place was not confirmed, in our opinion, for hormone concentrations in extracts of the experimental and control lobes of the thyroid gland, determined at the end of 6 h of perfusion, were equal. In the opinion of Shumakov et al. [6], the method of predrainage of blood from perfused organs

TABLE 1. Parameters of Thyroid Function of Dogs during Perfusion with Blood *in Situ* (Control) and in Thermostatically Controlled Chamber (experiment)

| Sample tested | n | Parameter | | | | |
|---|---|---|---|---|---|---|
| | | glucose, mg% | lactic acid, mg% | glycogen, g% | thyroxine, nmoles/liter | triiodothyronine, nmoles/liter |
| Blood plasma | | | | | | |
| carotid artery | 4 | 37,4±2,91 | 41,7±3,11 | — | 28,3±5,1 | 0,37±0,01 |
| thyroid vein | | | | | | |
| control | 4 | 34,9±4,15 | 42,3±4,17 | — | 39,25±1,96 | 0,70±1,01 |
| | | | | | $P<0,05$ | $P<0,03$ |
| experiment | 4 | 34,5±4,83 | 41,6±5,83 | — | 43,7±0,73 | 1,23±0,16 |
| | | | | | $P<0,05$ | $P<0,01$ |
| Thyroid tissue | | | | | ng/mg | |
| control | 4 | — | 13,6±1,23 | 0,0087±0,00021 | 62,65±2,66 | 2,94±0,014 |
| experiment | 4 | — | 10,9±0,92 | 0,0075±0,00009 | 62,72±3,78 | 2,73±0,021 |

Note. Thyroxine and triiodothyronine in blood plasma expressed in nanomoles/liter, in thyroid tissue, in nanograms/mg. P calculated compared with values of arterial blood.

has several advantages: Blood perfusing the organ prevents it from cooling or drying and reduces the risk of its mechanical injury by the chamber walls. Moreover, during perfusion of the thyroid gland in dogs, which has a vein of small diameter, and often friable in character, this method of venous drainage considerably facilitates the experimental technique. Heparinization of the blood and artificial hemodilution, which we used, reduce the viscosity of the blood and improve its rheologic properties and the blood flow in the microcirculatory system [4, 13]. The factor of a reduction of viscosity of the blood together with denervation, delymphatization, operative trauma, and ischemia, is evidently the cause of the increased blood flow in the experimental lobe.

The model of extracorporeal biological perfusion of a lobe of the dog's thyroid gland described above thus provides physiological conditions for function of the organ. This model can be used to study several problems connected with thyroid transplantation, for it reproduces the conditions of its transplantation in the early stages. It can also be used as a bench model with which to study the effect of various factors on the isolated thyroid gland.

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