neuronal sites[12]. Provided that nerve endings in the pulmonary trunk, ductus, and aorta are similar in their storage and uptake abilities, both the endogenous CA content and the uptake ratio would reflect the density of nerves in these vessels.

The significance of the relatively high concentrations of dopamine in the ductus of fetal lamb, as compared with the human ductus where no measurable dopamine was found[4], is unknown.

Contrary to the visual estimate of our earlier observation[3], the quantitative estimate of CA content and NA uptake revealed both to be consistently higher at the pulmonary end of the ductus than at the aortic end. The presence of this gradient along the ductus does not, however, necessarily imply a specific role of adrenergic innervation in function of the ductus alone, since this is only part of a larger gradient extending from within the pulmonary trunk through to, and including the aorta. Since KENNEDY[13] stressed the importance of a rise in arterial Po_2 as a major determinant of closure, this hypothesis has been substantiated by many studies on the ductus of the human[14,15] and of animals[16–18]. However, the possible interrelations between effects of oxygen and those of innervation were not clarified, e.g., whether the response to raised Po_2 was diminished after denervation.

A number of experiments have favored the involvement of a nervous mechanism in the closure of the ductus. The autonomic innervation of the fetal heart and blood vessels is readily responsive to stimuli[19–23].

Taken together, these several pieces of evidence suggest that adrenergic innervation of the ductus may play a role in closure of the ductus auxiliary to that played by arterial Po_2. The possible role of the previously demonstrated cholinergic innervation[5] must also be investigated[24].

Zusammenfassung. Die Verteilung von Noradrenalin und Dopamin im Ductus arteriosus des Lammes wurde studiert und mit ^{14}C-Norepinephrin die Fähigkeit, exogenes Noradrenalin aufzunehmen, geprüft.

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Cardiac Output in Thyroid Disease

Concomitant cardiovascular disorder in thyroid disease is a well known fact since the early description of MOEBIUS in 1896[1]. Thyroid hormone possesses a positive chronotropic and inotropic action. Heart rate, maximum velocity of fiber shortening, rate of tension development and cardiac output are therefore increased. In hypothyroidism these parameters are all reduced[2,3]. Decreased peripheral vascular resistance is another important factor in thyroid-induced high output state. The effects of thyroid hormone seem to be independent of the norepinephrine stores of the heart[2,4].

Increased oxygen consumption alone does not explain the elevated cardiac output in hyperthyroidism, and the augmentation of cardiac output, when compared to oxygen consumption, is in excess of that observed during exercise[5]. Nevertheless some relationship between cardiac output and oxygen consumption seems to exist. The purpose of this study was to investigate the correlation between basic metabolic rate (BMR) and cardiac output.

Material and methods. 24 patients with clinical evidence for thyroid disease and 6 normal controls were investigated. Thyroid function studies including BMR (according to method of Harris) and tracer studies with I^{131}[6] were done in all and protein-bound iodine determinations (PBI) were done in 22 protein. Within 5 days right heart catheterization with microcatheters was performed by previously described methods[7] and right atrial-, right ventricular- and pulmonary artery pressures were measured. Cardiac output was calculated according to the Fick prin-

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Influence of thyroid state on cardiac output and oxygen consumption

	Hypothyroid (BMR $<-2\%$) $N = 3$			Euthyroid (BMR -2% to $+12\%$) $N = 6$			Hyperthyroid (BMR $>+12\%$) $N = 15$		
Cardiac output (l/min/m^2)	1.2	2.2	3.1	3.0	3.8	4.7	3.3	5.6	8.5
O_2 consumption ($\dot{V}O_2$/m^2)	74	83	92	117	131	139	128	170	244
BMR (%)	-32	-24	-19	-2	$+6$	$+10$	$+16$	$+37$	$+67$
PBI (γ%)	0.9	1.5	2.0	4.5	6.6	8.3	7.5	12.1	24.1

Lowest and highest scores are to the left and right of the mean value.

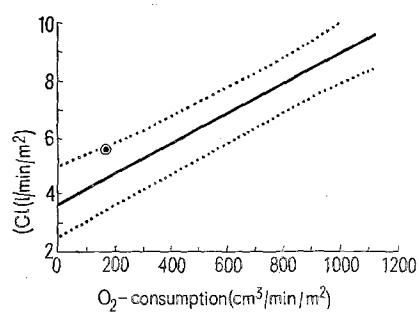

Fig. 1. Cardiac output to be unproportionally increased compared to O_2 consumption in 15 patients with hyperthyroidism. The mean cardiac index (CI) being 5.6 l/min/m^2 with a mean O_2-consumption of 170 cm^3/min/m^2. Solid and dotted lines represent regression line and 95% confidence limits for normal exercising males (DONALD et al.[9]).

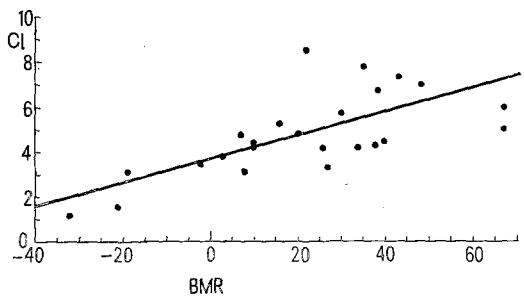

Fig. 2. Correlation between basic metabolic rate (BMR) and cardiac output per m^2 (CI) in 18 patients with thyroid dysfunction and 6 normal controls ($r = 0.671$; $p < 0.001$).

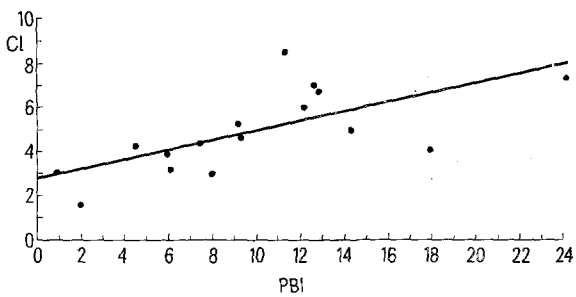

Fig. 3. Correlation between protein-bound iodine (PBI) and cardiac output per m^2 (CI) in 11 patients with thyroid dysfunction and 5 normal controls ($r = 0.667$; $p < 0.01$).

ciple. None of the patients had an elevated pulmonary artery mean pressure; none of the patients was taking cardiac glycosides, diuretics or thyroid hormone. 6 patients with thyroid hyperfunction had elevated right atrial pressure (>5 mm Hg), elevated right ventricular enddiastolic pressure (> 5mm Hg) or increased diastolic pulmonary artery pressure (>13 mm Hg) and were excluded from the study because of the possibility of altered cardiac output due to right or left heart failure[8]. Thus the results of 18 patients with thyroid disease and of 6 normal controls are presented. The thyroid dysfunction in the 18 patients with hypo- or hyperthyroidism was confirmed by the I^{131} tracer studies.

Results. As shown in the Table the thyroid state influences oxygen consumption, but in hyperthyroidism cardiac output is unproportionally increased compared to oxygen demand (Figure 1). Nevertheless, in our patients quite a good correlation ($r = 0.671$; $p < 0.001$) was found between BMR and cardiac index as well as PBI and cardiac index ($r = 0.667$; $p < 0.01$) (Figures 2 and 3), documenting the value of measuring BMR to assess hemodynamic changes in thyroid dysfunction. These data support previous reports[2,3,5] that cardiac response in thyroid hyperfunction is mainly secondary to positive inotropic, positive chronotropic and vasodilatory effects of thyroid hormone.

Zusammenfassung. Bei Patienten mit Schilddrüsenfunktionsstörung besteht eine gute Korrelation zwischen Grundumsatz und PBI einerseits und Herzminutenvolumen andererseits. Die Grundumsatzbestimmung gibt demzufolge nicht nur Aufschluss über den Schweregrad der Schilddrüsenfunktionsstörung, sondern auch über das Ausmass der hämodynamischen Veränderung.

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