

## PRELIMINARY COMMUNICATIONS

## Insulin and the Lung

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*Summary.* In 6 patients undergoing cardiac catheterization (in whom shunts were excluded) simultaneously sampled central venous and arterial blood specimens were analyzed for insulin, free fatty acids and glucose. Insulin levels were usually (4/6) 15–19% lower in arterial than central venous blood, but once was only 10% lower and once 8% higher. No consistent differences in central venous and arterial blood were noted for either free fatty acids or glucose.

*L'insuline et le poumon*

*Résumé.* On a analysé l'insuline, les acides gras libres et le glucose du sang artériel et veineux central sur 6 patients soumis à un cathétérisme cardiaque (les communications anormales entre la circulation pulmonaire et systémique ont été exclues). Chez 4 des 6 patients les taux d'insuline du sang artériel étaient inférieurs de 15–19% à ceux du sang veineux central; mais chez un des 6 patients il n'était inférieur que de 10% et chez un autre il était

supérieur de 8%. On n'a pas observé de différences importantes dans le sang veineux et artériel central pour les acides gras libres ou pour le glucose.

*Insulin und die Lunge*

*Zusammenfassung.* Bei 6 Patienten, bei denen eine Katheterisierung des Herzens vorgenommen wurde (wobei sich das Vorliegen eines Shunt ausschließen ließ), wurden gleichzeitig zentral-venöse und arterielle Blutproben entnommen. In diesen wurden Insulin, freie Fettsäuren und Glucose bestimmt. Bei 5 Patienten lag der Insulinspiegel im arteriellen Blut um 13% tiefer als im venösen Blut. Dieser Befund läßt einen Insulinverbrauch oder eine Insulinaktivierung in der Lunge vermuten. Im Hinblick auf freie Fettsäuren und Glucose ließen sich im zentral-venösen und im arteriellen Blut keine wesentlichen Differenzen feststellen.

*Key-words:* Serum insulin, free fatty acids, cardiac catheterization, lung.

Although insulin inactivating systems have been isolated in liver, kidney, muscle and other tissues [7, 8, 6, 1, 18] there seems to be little information on the role of the lung in insulin metabolism. We have obtained simultaneous blood samples from the right and left sides of the heart during cardiac catheterization and measured the concentration of insulin, glucose and free fatty acids across the lung.

*Subjects and Methods*

Patients undergoing cardiac catheterization for diagnostic purposes or prior to surgery were studied, but those found to have a shunt in either direction were excluded. All patients fasted overnight and throughout the procedure, which commenced in the morning and was performed under sedation with promazine and pethidine and levallorphan tartrate. Samples of blood were withdrawn simultaneously from the right ventricle or pulmonary artery (RV in Table 2) and the aorta or iliac artery (A in Table 2) for comparison in 6 patients whose age, sex and diagnosis are tabulated (Table 1).

Blood was collected in heparinized tubes and immediately centrifuged. Plasma free fatty acids were extracted according to TROUT, ESTES and FRIEDBERG [16] and measured potentiometrically [14]. The titrant was 0.02 N ethanolic potassium hydroxide and the

Table 1

Case	Age (Years)	Sex	Diagnosis
1	58	M	Congenital aortic stenosis, severe
2	47	M	Rheumatic aortic incompetence, severe, with mild stenosis
3	59	F	Rheumatic aortic stenosis, severe, with mild incompetence and moderate mitral stenosis
4	52	M	Congenital aortic stenosis, mild
5	60	F	Rheumatic mitral stenosis, moderate, with mild incompetence and mild aortic incompetence
6	9	M	Congenital aortic stenosis, moderate

result was calculated from a standard curve of palmitic acid. Plasma glucose was measured on the Autoanalyzer by the ferrieyanide reduction method. Insulin was assayed by a modification [17] of the double antibody precipitation technique [9]. All the samples were measured in the same assay and each specimen was set up in duplicate or triplicate at a number of dilutions (e.g. 1 in 10, 2 in 10, 5 in 10). There was excellent agreement between the results obtained with varying concentrations of plasma.

### Results and Discussion

The results are given in Table 2. The cardiac disease may have influenced the results, but in the small number of cases studied no relationship between insulin levels and left atrial, left ventricular end-diastolic or pulmonary artery pressures could be found. The rather high values for glucose are attributed to the stress of the cardiac catheterization. None of the patients were known diabetics.

The mean value of all estimations for insulin on each blood sample is tabulated. The "clearance" of

surface of the capillary; there coenzyme A derivatives undergo oxidation to carbon dioxide or esterification to triglycerides and phospholipids. Glucose is also taken up and converted to L- $\alpha$ -glycerophosphate. On the other hand, NASR and HEINEMANN [11] have shown that lung tissue may release newly synthesized free fatty acids into the perfusate.

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Table 2

Case	Insulin ( $\mu$ U/ml)			F. F. A. ( $\mu$ Eq/L)		Glucose (mg %)	
	RV	A	$\frac{RV - A}{RV}$	RV	A	RV	A
1	15.5	13.0	0.16	464	590	130	131
2	40.0	34.0	0.15	730	448	125	112
3	31.0	25.0	0.19	512	419	114	128
4	13.0	14.0	—	467	460	124	125
5	8.4	7.6	0.10	349	553	75	64
6	30.0	25.0	0.17	397	695	108	100

insulin [13] by the lungs in a single trans-pulmonary passage is shown by the ratio (right ventricular-arterial difference/right ventricular insulin concentration) [(RV-A)/RV].

Four of the 6 arterial plasma insulin levels were 15–19% lower than the corresponding central venous plasma concentrations, 1 was only 10% lower and 1 was 8% higher. Although the percentage fall in insulin across the lung is, therefore, lower than the 40% extracted by the liver [13], and the 30% by the kidneys [12, 15], it is none the less significant in terms of overall insulin homeostasis.

The only similar observation is that of JONSSON [5], who found that only 25% of intravenously injected insulin could be recovered in arterial blood after 1 passage through the heart and lungs in 2 young acidotic diabetic patients. Although insulinase has not been specifically identified in lung tissue, certain proteolytic enzymes are found in high concentrations in this organ [2]. In contrast to these results is the observation that insulin-like activity as measured by the rat epididymal fat pad is enhanced by oxygenation of blood, either *in vivo* by the lungs or by bubbling through oxygen *in vitro* [19].

No trends emerged indicating a change in either free fatty acid or glucose concentration in plasma after passage through the lungs. Previous studies have shown rapid incorporation of plasma palmitate-1- $C^{14}$  into phospholipid and neutral fat in the lungs of dogs [10], and it is likely that circulating free fatty acids represent an important source of ester fatty acid for synthesis of pulmonary lipids [4]. FELTS [3] has suggested that free fatty acids enter the alveolar cells directly from plasma and from hydrolysis of plasma triglycerides by lipoprotein lipase at the endothelial

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