BIOSYNTHESIS OF INSULIN DURING STRESS DUE TO BURN TRAUMA

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The sharp increase in the blood level of 11-hydroxycorticosteroids in rats with burns was accompanied by a decrease in insulin biosynthesis, due to inhibition of incorporation of labeled amino acid into the B chain, whereas the intensity of synthesis of the A chain remained similar to that in intact animals. The biosynthesis of total proteins in stress, according to data for the incorporation of labeled amino acids, was considerably depressed in the pancreas, thymus, and testes and slightly depressed in the adrenals; the intensity of this process in the thyroid was unchanged.

Stress, produced by various factors, causes sharp changes in the total hormonal profile of the body [5-8]. The study of the biosynthesis of hormones, as the principal metabolic regulators, is of great interest in this state.

The object of the present investigation was to study insulin biosynthesis in stress due to burn trauma. The biosynthesis of total proteins of some endocrine glands also was studied.

EXPERIMENTAL METHOD

The criterion of the state of stress was the blood concentration of 11-hydroxycorticosteroids (11-HCS), the level of which rises sharply [1] in the initial period after burning. Protein synthesis was estimated from the incorporation of labeled amino acid into protein.

Male albino rats weighing 150-200 g were burned with a flame for 30 sec, the burn covering 20% of the body surface. Immediately before burning, the animals were injected with labeled amino acid: 1-C^{14}-glycine or 1-C^{14}-tyrosine with specific activity 139 and 90 μCi/g, respectively, in a dose of 0.25 μCi/100 g body weight.

TABLE 1. Specific Activity of Insulin and Its A and B Chains in Intact and Burned Rats [pulses/min/mg (M ± m)]

C^{14}-amino acid	Control	Burns	P*
	Insulin		
C^{14}-glycine	2 725±134	1 350±54	<0,01
C^{14}-tyrosine	2 800±147	800±74	<0,01
	A chain		
C^{14}-tyrosine	647±53	603±48	>0,05
	B chain		
	2 550±177	1 252±80	<0,01

*n = 4.

Intact rats receiving injections of radioactive amino acids in the same doses served as the control. The intact and burned rats were sacrificed by decapitation 30-60 min later. The 11-HCS concentration in the blood plasma was determined fluorometrically [4]. Insulin was isolated from the pancreas and liver and separated into A and B chains [3]. Total proteins were extracted from some endocrine glands [2] and their radioactivity was determined.

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TABLE 2. Specific Activity of Total Proteins of Endocrine Glands in Intact and Burned Rats [pulses/min/mg (M ± m)]

Organ	C^{14}-glycine			C^{14}-tyrosine		
	control	expt.	P*	control	expt.	P*
Adrenals	612±31	502±39	>0,05	1 526±91	131±74	>0,05
Pancreas	5 015±312	2 910±251	<0,01	8 336±135	4 720±127	<0,01
Thymus	600±49	302±29	<0,01	—	—	—
Testes	834±75	444±47	<0,01	—	—	—
Thyroid	624±51	629±60	>0,05	1 307±109	1 187±82	>0,05

*n = 4.

TABLE 3. Radioactivity of Protein-Free Filtrates of Organs from Intact and Burned Rats after Injection of C^{14}-glycine [in pulses/min/100 mg (M ± m)]

Organ	Control	Burns	P*
Adrenals	727±67	1 587±115	<0,01
Pancreas	7 025±221	7 321±259	>0,05
Thymus	598±67	633±44	>0,05
Testes	1 555±101	1 468±97	>0,05
Thyroid	932±85	1 580±121	<0,01

*n = 4.

EXPERIMENTAL RESULTS

Burn trauma led to a sharp increase in the blood 11-HCS concentration (23 ± 1.01 μg% in the normal state, 45.9 ± 1.1 μg% 30 min after burning, 46.1 ± 1.7 μg% 60 min after burning; $P < 0.01$).

Incorporation of labeled amino acids into pancreatic insulin was considerably reduced in the burned animals (Table 1). To determine the characteristics of this phenomenon, it was important to investigate the incorporation of labeled amino acids into the A and B chains composing this protein. Incorporation of C^{14}-tyrosine into the A chain was unchanged after burning, but incorporation into the B chain was reduced (Table 1). The changes in insulin biosynthesis were thus due mainly to depression of synthesis of the B chain.

Investigation of the incorporation of labeled amino acids into total proteins of the endocrine glands (Table 2) showed that the specific activity of the proteins of the pancreas, thymus, and testes was much lower in the burned rats than in the control animals, with respect to the incorporation of both C^{14}-glycine and C^{14}-tyrosine. The specific activity in the adrenals and thyroid of the burned rats was similar to that in the intact animals.

To determine whether the changes in permeability associated with burning influenced the radioactivity of the proteins of the organs investigated, the free radioactivity was determined in protein-free filtrates from these organs. As Table 3 shows, the content of free radioactivity was unchanged as a result of burning in the pancreas, thymus, and testes, whereas the specific activity of the proteins of these organs was reduced (Table 2). Meanwhile, the values of the free radioactivity in the adrenals and thyroid rose while the specific activity of the proteins of these glands was unchanged. The differences in specific activities of the total proteins of some endocrine glands discovered in these experiments were thus not the result of changes in permeability to free amino acids, but they evidently reflected changes in the biosynthesis of these tissue proteins.

It follows from these results that stress due to burn trauma inhibits biosynthesis of insulin by sharply depressing the incorporation of labeled amino acid into the B chain.

It is interesting to note that in a study of insulin biosynthesis in stress due to a sharp decrease in body temperature of the animal (down to 28°C) changes in synthesis of the B chain also were observed, whereas the intensity of synthesis of the A chain remained unchanged. However, in that state synthesis of the B chain was increased by comparison with its level in intact animals [3].

Various extremal states (burns, a decrease in the animal's body temperature) thus cause changes in insulin biosynthesis as the result of changes in the intensity of synthesis of the B chain. Synthesis of the A chain is stable in the stress states investigated.

Against the background of an increased blood level of 11-HCS and depressed insulin biosynthesis, the intensity of biosynthesis of the total proteins was reduced in the pancreas, thymus, and testes.

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