LOCAL AND GENERAL CHANGES IN RECOVERY FROM INFLAMMATORY LUNG DISEASES

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Recovery from inflammatory lung diseases is nowadays considered mainly from the clinical point of view.

The object of this investigation was to study local (lung tissue) and general (blood) healing processes in experimental inflammation of the lungs.

EXPERIMENTAL METHOD

Inflammation of the lungs was induced in 38 rabbits by intratracheal introduction of a foreign body (a Kapron thread 0.5 mm in diameter and 6-8 cm long) [1]. The thread was removed after 1 month from 25 rabbits. Investigations were carried out 1 and 6 months after introduction of the thread, and also 2 weeks and 1, 2, and 4 months after its removal. The control group consisted of 10 healthy rabbits.

Lung sections were stained with hematoxylin and eosin and by Van Gieson's method. DNA was revealed by Feulgen's method, RNA by Brachet's method, total protein with mercuric chloride and bromphenol blue, NAD-diaphorase with nitro-BT, and alkaline phosphatase by Gomori's method.

DNA in polymorphonuclear leukocytes (PML) and lymphocytes (Ly) in the blood was demonstrated by Feulgen's method, acid phosphatase (AcP) by Burstone's method, and cationic protein in PML was revealed by bromphenol blue. The content of dyes in the cells was measured microphotometrically by a two-wave method. Permeability of lysosomal membranes (PLM) of the leukocytes was estimated from the fraction (percentage) of cells with diffuse distribution of reaction products for AcP [5]. Chemiluminescence (CL) of blood plasma and erythrocytes, stimulated by hydrogen peroxide (final concentration 0.03 M) was measured on an apparatus for recording very weak luminescence. Numerical results were subjected to statistical analysis by Student's t test. The level of significance (P) of differences between affected and healthy rabbits is indicated in Table 1.

EXPERIMENTAL RESULTS

After 1 month of development of inflammation of the lungs after introduction of the thread was characterized locally by bronchopneumonia with abscess formation, accompanied by marked exudative changes and a predominantly catabolic trend of lung tissue metabolism (a decrease in the content of DNA, RNA, and protein, and in activity of NAD-diaphorase and alkaline phosphatase in the bronchial epithelium, vascular endothelium, and septal cells). General stages at this stage consisted of lowering of the DNA level in the leukocytes, evidence of inhibition of biosynthesis in these cells [2], labilization of lysosomal membranes and activation of acid phosphatase in them, and an increase in the content of CP (a component of the bacterial system [3], in PML. At the 6th month of development of inflammation repair processes were more marked than after 1 month, and they were characterized mainly by substitution (organization of suppurative and necrotic foci in the lung tissue) and by pathological generation (hyper- and metaplasia of the bronchial epithelium, polypi, the formation of false bronchi, diffuse sclerosis of the relatively unchanged lung tissue). This picture was accompanied by a decrease in acid phosphatase activity in the blood leukocytes.

After removal of the thread from the trachea healing began, in the form of three principal interconnected processes.

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TABLE 1. Changes in Structural and Metabolic Parameters of State of Leukocytes and Intensity of Chemiluminescence of Erythrocytes and Blood Plasma of Rabbits during Development of Inflammation of the Lungs and Recovery (M ± m)

Parameter	Test object	Control (n=10)	Experiment				
			one month of inflammation (n=8)	after removal of thread			
				two weeks (n=9)	one month (n=4)	two months (n=8)	four months (n=4)
DNA, relative units	Ly	1,27±0,07	0,74±0,21	2,02±0,46	1,84±0,21	—	1,10±0,21
	P		<0,05		<0,05		
	PML	1,24±0,09	0,77±0,18	—	2,15±0,27	—	1,21±0,24
	P		<0,05		<0,05		
AcP, relative units	PML	1,15±0,18	2,41±0,28	1,70±0,56	—	0,86±0,19	—
	P		<0,05				
CP, relative units	PML	1,07±0,11	1,40±0,06	1,10±0,12	0,93±0,15	1,22±0,07	1,03±0,08
	P		<0,05				
PLM, %	Ly	3,5±0,6	25,5±2,6	20,0±1,3	12,4±1,4	11,8±0,3	9,7±1,3
	P		<0,01	<0,01	,01	<0,01	<0,01
	PML	16,7±1,2	39,2±3,4	31,4±2,7	23,1±1,5	24,1±1,5	18,7±2,5
	P		<0,01	<0,01	<0,05	<0,01	
CL, pulses, sec	Erythrocytes	397±27	1045±72	406±239	—	277±102	—
	P		<0,05				
	Blood plasma	149±12	94±9	132±10	—	—	—
			<0,05				

The first process is observed in the early stages of recovery (2 weeks) and is manifested locally as the absence of recent foci of injury and inflammation in the lungs. This is accompanied by normalization of the CP content in blood PML and of CL of the erythrocytes and blood plasma. These changes are evidence of systemic inhibition of injury and, consequently, of inflammation.

The second process develops immediately after inhibition of inflammation and is characterized locally mainly by weakening of the severity of the exudative changes in the lungs. The density and extent of cellular infiltration of the tissue is reduced. The proportion of PML in the infiltrating tissue decreases. In the final stages of healing (4 months) tissue edema disappears. A general manifestation at this stage is stabilization of lysosomal membranes. Taken as a whole, these findings are evidence of regression of inflammation.

The third process is regeneration of lung tissue. This proceeds parallel with inhibition and regression of inflammation in the form of restitution, substitution, and pathological regeneration. An important role is played by the intracellular form of regeneration, which is basic for the lungs [4].

Substitution and pathological regeneration during healing are characterized by the same local and general manifestations as during progression of inflammation. Restitution includes partial restoration of the bronchial and alveolar epithelium and the vascular endothelium. Intracellular regeneration is activated during inhibition of inflammation, and is manifested as an anabolic trend of cellular metabolism, reflected in above normal values for the DNA, RNA, and protein content, and activity of NAD-diaphorase and alkaline phosphatase in the cells of all the main lung structures. These changes proceed through stages. The initial stage (2 weeks) is characterized by a greater increase in DNA content and NAD-diaphorase activity compared with the other parameters studied. In the final stage (4 months) normalization of metabolism of the lung tissue is observed: The DNA and RNA content in the bronchial epithelium and the RNA content in the septal cells remain a little on the high side. This comparative analysis shows that a general manifestation of restitution and intracellular regeneration is an increase in the DNA content in the blood leukocytes.

Evaluation of local and general changes and of the correlation between them thus gives a general picture of the morphogenesis of healing in inflammation of the lungs, comprising three interdependent processes: inhibition and regression of inflammation and the development of regeneration.

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