The effect of polysaccharide-protein complex isolated from *Candida albicans* on regional blood flow in rats

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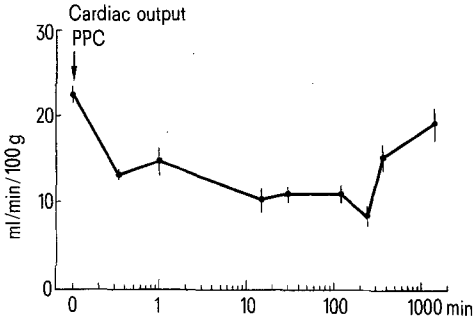
Summary. After i.v. administration to rats of polysaccharide-protein complex, isolated from *Candida albicans,* a decrease of cardiac output was observed from 20 sec to 240 min postinjection, followed by a recovery at 360 min. Concomitantly the regional blood flow was maintained in heart and lungs, moderately decreased in intestine, liver and adrenals and markedly reduced in skin, muscle, spleen and kidney.

Shock and fever may accompany acute disseminated candidiasis. Mechanisms leading to their manifestation have not been completely understood. Some extracts or morphological components of *C. albicans* exert biological activities similar to those of bacterial endotoxins[1]. Marked hemodynamic[2], reticuloendothelial activity changes[3] and mast cell degranulation[4] were observed after administration of polysaccharide-protein complex (PPC) isolated from *C. albicans*[5]. The effect of this substance on cardiac output (CO) and its fractional distribution was investigated in the present work.

Material and methods. Male 180–230 g Wistar albino rats anesthetized with urethane, 150 mg/100 g, were used. CO was estimated by the dye dilution technique using Evans blue as indicator[6]. Fractional distribution of CO was determined by Sapirstein's ^{86}Rb method[7]. From CO and ^{86}Rb fractional distribution the tissue blood flow was calculated in control rats and at different times after i.v. administration of 100 mg PPC from *C. albicans* per kg b.wt. PPC was kindly supplied by D. Šikl, Institute of Chemistry, Slovak Academy of Sciences, Bratislava.

Results and discussion. CO decreased significantly within 1 min after administration of PPC (figure). The reduced state persisted during a period of 240 min and at that time it reached also the lowest value. Recovery of CO was registered 360 min postinjection. Changes of the tissue blood flow, expressed as percentage of control values, are shown in the table. Kidney and heart received the greatest fraction of CO in control animals. The response of blood flow to PPC administration was different in various organs. A marked increase of blood flow was observed in heart and lungs 15 and 30 min after PPC, followed by a decrease after 2 h. The distribution of CO to the other organs decreased from the first min. In intestine, liver and spleen, the initial decrease of blood flow was followed by a recovery. In contrast, blood flow in skin, muscle and kidney remained low throughout the experiment. In these organs also, the greatest reduction of blood flow was seen.

As we previously described, i.v. administration of PPC in rats induced rapid fall in systemic blood pressure followed by a significant decrease in heart rate[2,8] indicating a development of shock-like state. Early hemodynamic changes may be a result of released histamine and serotonin from rat mast cells and thrombocytes observed in vitro[4,9]. Changes of CO and its fractional distribution are important for understanding the mechanisms acting in the pathophysiology of shock[10]. The results presented confirm serious



Cardiac output changes following i.v. administration of 100 mg polysaccharide-protein complex from *Candida albicans* per kg at 20 sec, 1 min, 15 min, 30 min, 120 min, 240 min, 360 min and 1440 min postinjection. Each value is mean from 6 experiments±SEM.

Tissue blood flow at different times after i.v. administration of 100 mg polysaccharide-protein complex from *Candida albicans* per kg in rats

Tissue	Control blood flow ($ml \cdot min^{-1} \cdot g^{-1}$)	Blood flow after administration of PPC (percent of control)						
	(42)	1 min (6)	15 min (6)	30 min (6)	120 min (6)	240 min (6)	360 min (6)	1440 min (6)
Heart	1.68	61.53*	144.98*	171.58*	69.77*	48.85*	71.86*	83.63*
	0.10	4.53	18.39	27.45	7.02	5.31	3.78	5.16
Lungs	0.79	61.90*	163.54*	160.20*	77.71*	80.92*	87.14	82.72
	0.06	5.92	32.72	33.70	10.32	12.43	14.54	13.65
Adrenals	1.42	79.70	43.74*	61.41*	79.48	58.91*	93.38	71.89*
	0.22	26.00	12.47	15.93	17.57	11.14	18.09	7.68
Intestine	0.89	71.91	37.25*	39.80*	54.87*	24.54*	84.72	86.02
	0.12	6.85	8.01	6.12	8.54	4.72	12.35	16.32
Liver	0.29	49.62*	30.72*	57.31*	88.60	45.79*	111.34	86.39
	0.04	4.33	9.08	15.29	15.12	9.16	17.87	12.57
Kidney	3.98	39.47*	17.55*	38.95*	39.54*	18.81*	60.99*	70.08*
	0.47	7.43	5.29	9.12	2.55	3.39	12.11	11.96
Muscle	0.14	48.49*	27.16*	37.25*	40.18*	19.00*	69.25*	55.14*
	0.02	5.59	11.42	7.58	7.39	2.63	12.93	9.43
Spleen	0.24	42.21*	7.73*	31.09*	50.10*	19.93*	40.56*	89.00
	0.04	3.09	3.79	17.78	12.20	8.00	12.22	35.00
Skin	0.16	12.53*	11.54*	23.60*	33.18*	26.96*	58.86*	41.53*
	0.02	1.23	4.60	7.47	7.11	7.28	19.62	9.32

All values are means ± SEM. * Significantly different from controls ($p < 0.05$); number of animals in parentheses.

alteration of hemodynamics caused by PPC. CO is distributed so as to maintain coronary blood flow at the expense of splanchnic, skin, muscle and kidney blood flow. Changes of CO and the pattern of its distribution following PPC administration resemble those after endotoxin[11,12]. However, the onset of reaction to PPC is very rapid in comparison with endotoxin. Also there is a more pronounced increase of blood flow values in heart and lungs compared to endotoxic shock. Some dissimilarities, regarding changes of CO distribution, observed in various forms of shock[13] indicate that there may be different mechanisms responsible for the redistribution of blood flow.

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A duration-dependent negative potential in the cichlid electroretinogram

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Summary. A negative potential can be evoked in the local electroretinogram of the cichlid fish *Cichlasoma octofasciatum* by light stimuli of duration longer than 70 msec. This response superficially resembles the proximal negative response, but differs in some waveform components and dependence upon stimulus configuration and duration.

The corneal vertebrate electroretinogram (ERG) represents the activity of several cell types, each component potential change consisting of the summed activity of classes of cells acting in synchrony[1]. Traditionally, the primary components of the vertebrate ERG are a negative a-wave, rapid positive b-wave, slow positive c-wave and a d-wave (off-response) of varying polarity. The a- and b-components appear common to all vertebrate ERG's; however, rod-dominated retinas have conspicuous c-waves and negative d-waves, while cone-dominated retinas have reduced c-waves and positive d-waves[5]. 2 additional components have been subsequently described: a proximal a-wave contribution[4] and a proximal negative response[2]. The latter response (PNR) may dominate the form of the electroretinogram by obscuring or competing with the b-wave component in certain stimulus configurations and intensities. However, in the analysis of the response of the vertebrate retina to light stimuli, the effect of stimulus duration on the form of the ERG has received a lesser degree of attention than the other stimulus variables of wavelength, intensity and configuration.

Electroretinograms recorded from the cornea of the cichlid fish *Cichlasoma octofasciatum* (the Jack Dempsey) show a significant dependence upon stimulus duration. Stimuli longer than approximately 70 msec generate a substantial negative potential whose appearance succeeds the initiation of the b-wave by about 80 msec. Shorter stimuli generate an ERG which assumes the classical waveform (figure 1). This 'cichlid negative response' can be generated from light- and dark-adapted retinas and by a variety of light intensities.

ERG's were recorded with agar, 1.0 M NaCl wick electrodes extruded from 10-cm Pasteur pipettes. Electrodes were apposed to the cornea and trunk of the cichlid, which

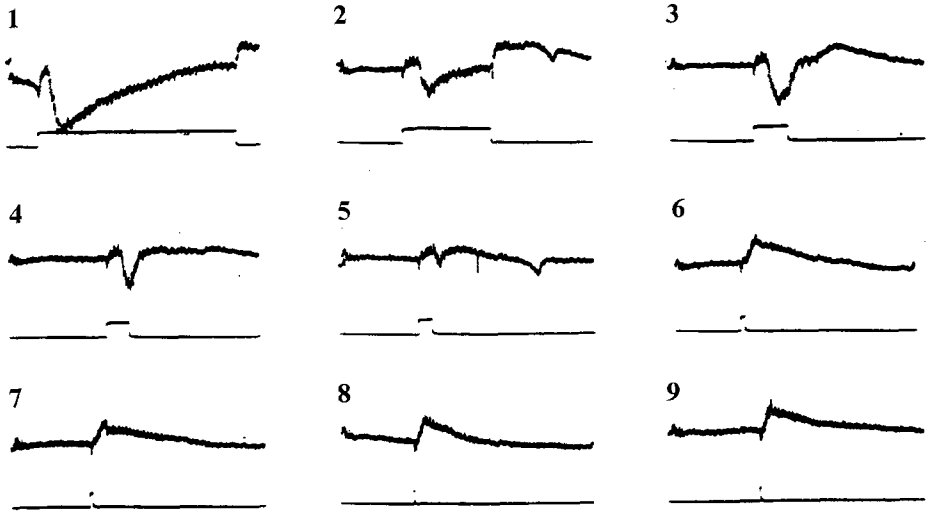

Fig. 1. A stimulus duration series from a light-adapted *C. octofasciatum*. Sweep speed is 2 sec, amplification is 50 μV cm^{-1}, bottom trace is stimulus duration. Durations are 1560, 690, 310, 180, 70, 40, 20, 10 and 5 msec, respectively.