Tissue cyanide concentrations and cytochrome oxidase activities in experimental cyanide poisoning

B. BALLANTYNE, S. P. BOARDMAN, J. BRIGHT, D. J. COFFEE, T. D. WEBBER and P. WILLIAMS (introduced by F. W. BESWICK)

Ministry of Defence, Medical Division, Chemical Defence Establishment, Porton Down, Wiltshire

Autopsy features are not specific in acute cyanide poisoning (Ballantyne, 1970), but the radical is easily detected in various animal tissues shortly after death (Ballantyne, Bright, Swanston & Williams, 1971a). However, since difficulties may arise with analyses in human postmortem material (Finck, 1969), it was considered that estimations of tissue cytochrome oxidase activity might facilitate diagnosis.

Cyanide was measured in blood and various tissues from control and cyanide-killed rabbits (Ballantyne, Bright, Swanston & Williams, 1971b). Tissue cytochrome oxidase activity was measured quantitatively (Pearl, Cascarano & Zweifach, 1962) and demonstrated histochemically (Burstone, 1960) using N-phenyl-*p*-phenylenediamine as substrate. All analyses were performed on tissues perfused with saline.

Animals given hydrogen cyanide had greater concentrations of cyanide in blood and certain tissues than did those killed with potassium cyanide (Table 1). This was reflected in lower tissue cytochrome oxidase activities in those killed with hydrogen cyanide (Table 2). However, there were no differences in the histochemistry of tissues from controls or from those killed with cyanide.

TABLE 1. *Concentrations of cyanide, expressed as mean* ± S.E., *in blood and various saline perfused tissues from female rabbits killed by intramuscular HCN or KCN at a dosage of* 8 *mg CN/kg (six animals in each group)*

	Cyanide concentration*		
Tissue	Killed with HCN	Killed with KCN	*P*†
Liver	20·9± 6·3	6·3± 3·5	<0·05
Kidney	7·6± 5·7	0	<0·15
Myocardium	53·1±15·6	35·0± 6·2	<0·2
Brain	211·9±56·7	37·9±15·2	<0·01
Spinal cord	36·6±12·0	13·9± 5·1	<0·1
Blood	930±137	530±74	<0·025
Serum	202±34	163±30	<0·025

* Concentrations expressed as μg cyanide/100 g wet tissue and 100 ml blood or serum; cyanide radical not detected in blood or tissues from controls. † Significance of difference between animals killed with HCN and those killed with KCN.

TABLE 2. *Cytochrome oxidase activities in saline perfused tissues from control rabbits and those killed with HCN or KCN at a dosage of* 8 *mg cyanide/kg (six animals in each group)*

	Cytochrome oxidase activities (ΔOD/min)/g±S.E.					
	HCN group			KCN group		
Tissue	Controls	HCN	*P**	Controls	KCN	*P**
Liver	0·78±0·18	0·22±0·11	<0·0125	0·82±0·27	0·94±0·23	<0·4
Kidney	2·13±0·32	1·42±0·41	<0·05	2·76±0·69	2·59±0·10	<0·3
Myocardium	4·43±0·40	0·78±0·17	<0·0005	2·97±0·33	1·57±0·31	<0·01
Brain	1·82±0·14	0·47±0·07	<0·0005	1·45±0·17	1·30±0·16	<0·3
Spinal cord	0·95±0·10	0·43±0·07	<0·0025	0·59±0·07	0·41±0·09	<0·1

* Significance of difference in activities between controls and cyanide injected rabbits.

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New dialysis technique for the continuous measurement of the concentration of vasoactive hormones

J. G. COLLIER (introduced by J. R. VANE)

Department of Pharmacology, Institute of Basic Medical Sciences, Royal College of Surgeons of England, Lincoln's Inn Fields, London WC2A 3PN

A method has been developed to measure the plasma concentration of vasoactive hormones in the blood of man. So far experiments have been confined to the dog. Heparinized blood is pumped at 50 ml/min through the central channel (volume 75 ml) of a miniature Kiil dialysis machine, and is then returned intravenously to the animal. Krebs solution is passed at 5 ml/min in a counter-current direction through the outer channel (volume 20 ml) of the machine and is then allowed to cascade over a bank of isolated tissues (Vane, 1964, 1969). The two channels are separated by a dialysis membrane made of reconstituted cellulose (Cuprophan 150 P/M).

To estimate the passage of vasoactive hormones from blood to Krebs the substance under study was infused at a known concentration for 12–24 min into the blood as it entered the machine. The concentration of the substance diffusing into the Krebs solution was then estimated by biological assay. The degree of dialysis was then calculated as a percentage of the initial concentration in blood. For instance, for noradrenaline (three expts.) the concentration in the Krebs was 42% that in the blood, for oxytocin (four expts.) it was 35%, for adenosine 50% (two expts.), for 5-hydroxytryptamine 20% (one expt.), for prostaglandin E_2 43% (eighteen expts.) and for prostaglandin $F_{2\alpha}$ 35% (four expts.). Maximum dialysis was usually achieved by the 10th min of infusion. When the concentration of substance in blood was altered there was a proportional change in tissue response. Bradykinin (directly infused or produced by an infusion of kallikrein) and angiotensin were bound to the dialysis membrane and the method was therefore unsuitable for their detection, although it can be used as a method of their elimination.

The system has also been used to investigate the binding of drugs to plasma proteins. For this dialysis with Krebs solution on both sides of the membrane was compared with dialysis from blood to Krebs solution. By this method it was not possible to detect binding of PGE_2, $PGF_{2\alpha}$, or oxytocin.

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