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SELECTION OF ANTIBIOTICS IN ACUTE PYELONEPHRITIS BASED ON RENAL INTERSTITIAL (LYMPH) CONCENTRATIONS

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Previous communications by our group[1,2,3] have characterized the distribution of six antibacterial agents. Determining the concentration of each antimicrobial in renal lymph was the unique aspect of these studies. Corresponding biological fluid samples were obtained from plasma and urine in order to allow conventional comparisons to be made. All of these experiments were performed in mongrel dogs.

The purpose of these experiments is to report the distribution of cycloserine (Seromycin) and oxytetracycline (Terramycin) in renal lymph, urine and plasma. In addition, new data are reported on the lymphatic distribution of nitrofurantoin; we compare concentrations of this antiseptic in renal hilar lymph and cisterna chyli lymph.

Read at annual meeting of Western Section of American Urological Association, Inc., Honolulu, Hawaii, June 18-24, 1967.

These studies were supported by grants from the United States Public Health Service HE 09834-03 and National Aeronautics and Space Administration NsG 237-62.

METHODS AND PROCEDURES

Mongrel dogs were anesthetized and the lymphatics were cannulated. We have previously detailed our techniques. Cisterna chyli lymph was collected via a polyethylene cannula carefully inserted into a major channel.

Cycloserine, 50 mg/Kg, was infused intravenously as a bolus after obtaining baseline lymph, plasma and urine. Cycloserine was analyzed by the method of Jones[4].

Oxytetracycline, 48 mg/Kg, was also infused intravenously as a bolus. The analysis of oxytetracycline was carried out using a fluorescent technique[5]. A slight modification was necessary for oxytetracycline.

Nitrofurantoin, 7 mg/Kg, was administered by gastric tube. We have previously detailed the chemical and biological assay methods for this antibacterial.

RESULTS

Two separate experiments characterizing the distribution of cycloserine in renal lymph, plasma and urine are illustrated in Figures 1 and 2. Renal lymph levels exceed the corresponding plasma concentrations in almost all instances. Similar patterns were seen in a total of five animals.

The distribution of oxytetracycline in renal lymph, plasma and urine is listed in tabular form (Table I). Renal lymph levels of oxytetracycline exceed the corresponding plasma in the early post-injection periods. The lymph levels then decline to

lesser concentrations which are equal to or less than the corresponding plasma levels. Urinary levels range from several hundred micrograms to levels of 40-50 micrograms several hours later.

Nitrofurantoin was assayed in renal hilar lymph and cisterna chyli lymph (fig. 3 and 4). Hilar lymph concentrations are higher than corresponding cisterna chyli lymph concentrations. The renal lymph concentrations however, are several times higher than the plasma levels several hours after administration of the drug.

DISCUSSION

Cycloserine, a second choice selection in the treatment of renal tuberculosis would appear to be effective on the basis of it's interstitial concentrations. After obtaining baseline lymph, plasma and urine, cycloserine (50 mg/Kg) was infused intravenously as a bolus. Our data suggests that cycloserine may well be the most effective agent in treating renal tuberculosis.

Selected proteus and aerobactor infections causing interstitial pyelonephritis may also respond to cycloserine providing tube dilution sensitivity studies are performed.

Oxytetracycline, an antibiotic with effective urinary concentrations when given as prescribed, appears to passively diffuse into renal lymph. Renal lymph levels exceed the relatively low corresponding plasma levels several hours after injection and may account for it's effectiveness in selected cases. Still

underway in our laboratory are studies to evaluate the effects of protein binding on the family of tetracyclines. While still conjectural, it is possible that drugs which exist in higher free concentrations, while unbound to protein, may more easily diffuse into the renal interstitium.

Nitrofurantoin, the first antiseptic we demonstrated to concentrate in renal lymph, was administered in several animals. Hilar lymph levels exceed the cisterna chyli levels in dogs. Hilar levels up to 6 mcg/ml were obtained. Plasma levels are quite reduced.

We believe that these studies which plot the distribution of antibiotics in various body compartments or tissue spaces are important. Clinical applications might be made based on the needs of selected tissue compartments. In pyelonpehritis renal lymph concentrations are highly important. Antibiotic selection should be based on the drug's distribution in renal lymph. For urinary stasis with subsequent infection, an antimicrobial which has high urinary concentrations would be the agent of choice. When considering treatment for pyelonephritis, high blood levels, while important for any antibiotic, should not remain the primary requisite.

TABLE I

OXYTETRACYCLINE IN RENAL LYMPH

DOG #	TIME in HOURS	LYMPH mcg/ml	PLASMA mcg/ml	URINE mcg/ml
1251	0	0	0	0
	1	15.4	12.4	85
	2	10.6	11.6	130
	3	5.8	7.8	50
	4	3.8	5.8	50
	5	3.5	5.6	
1430	0	0	0	0
	1	32.9	12.7	440
	2	9.1	9.4	90
	3	8.1	15.4	105
	4	8.5	14.9	140
	5	6.8	8.6	100
1458	0	0	0	0
	1	19.0	10.4	145
	2	9.4	11.6	425
	3	7.1	6.1	110
	4	5.6	6.3	60
	5	5.3	5.6	40
			4.6	

LEGEND

Figure 1. Distribution of cycloserine in renal lymph, plasma and urine.

Figure 2. Second experiment. Distribution of cycloserine in renal lymph, plasma and urine.

Figure 3. Distribution of nitrofurantoin in hilar lymph, cisterna chyli lymph and plasma.

Figure 4. Second experiment. Distribution of nitrofurantoin in hilar lymph, cisterna chyli lymph and plasma.

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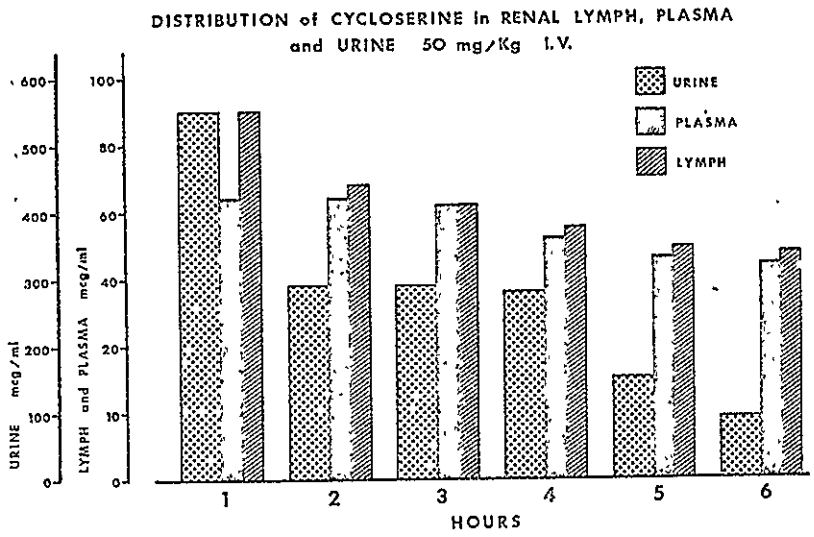
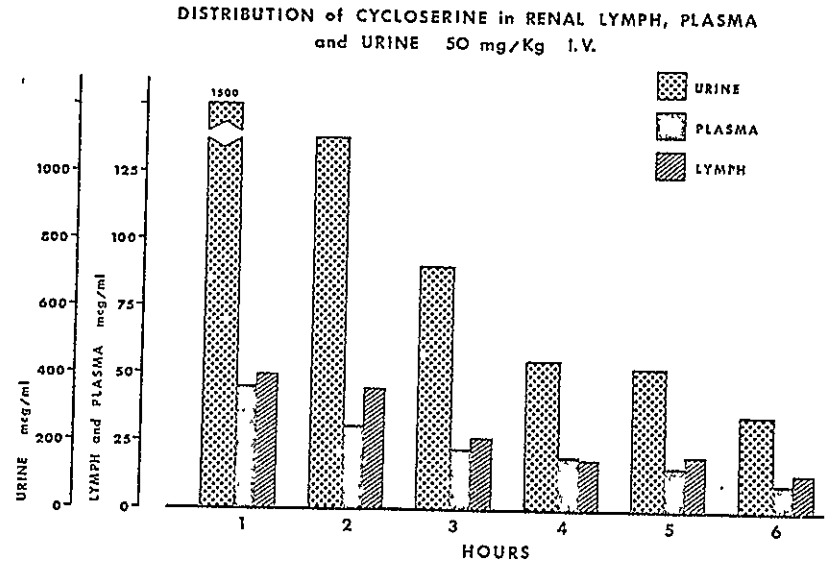


Figure 1



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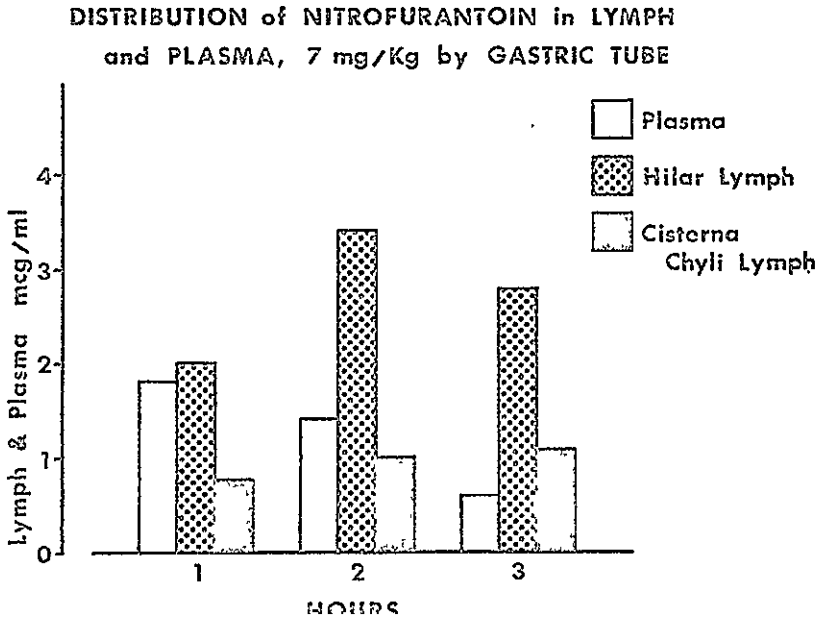

Figure 3

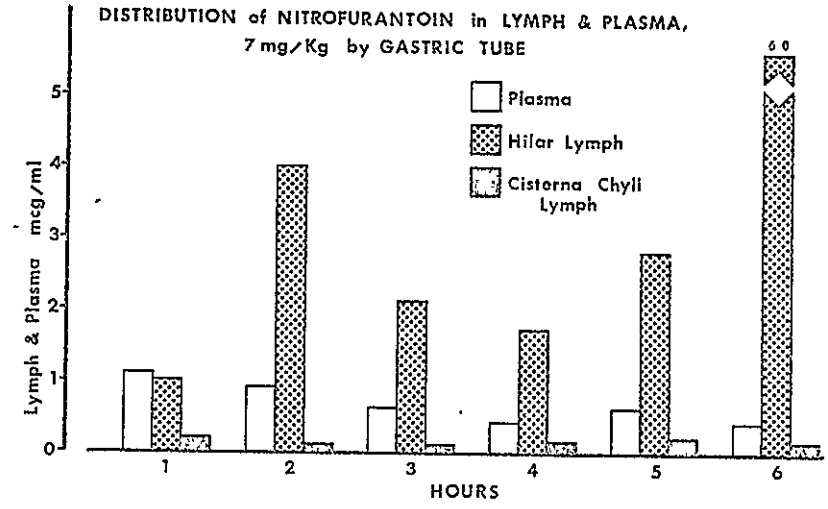

Figure 4