National Cancer Institute

EFFICACY OF PRUSSIAN BLUE ON ^{137}Cs DECORPORATION THERAPY

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PURPOSE

- Compile the available information about the efficacy of Prussian blue treatment;
- Suggest an appropriate Prussian blue dosage for cesium decorporation therapy.

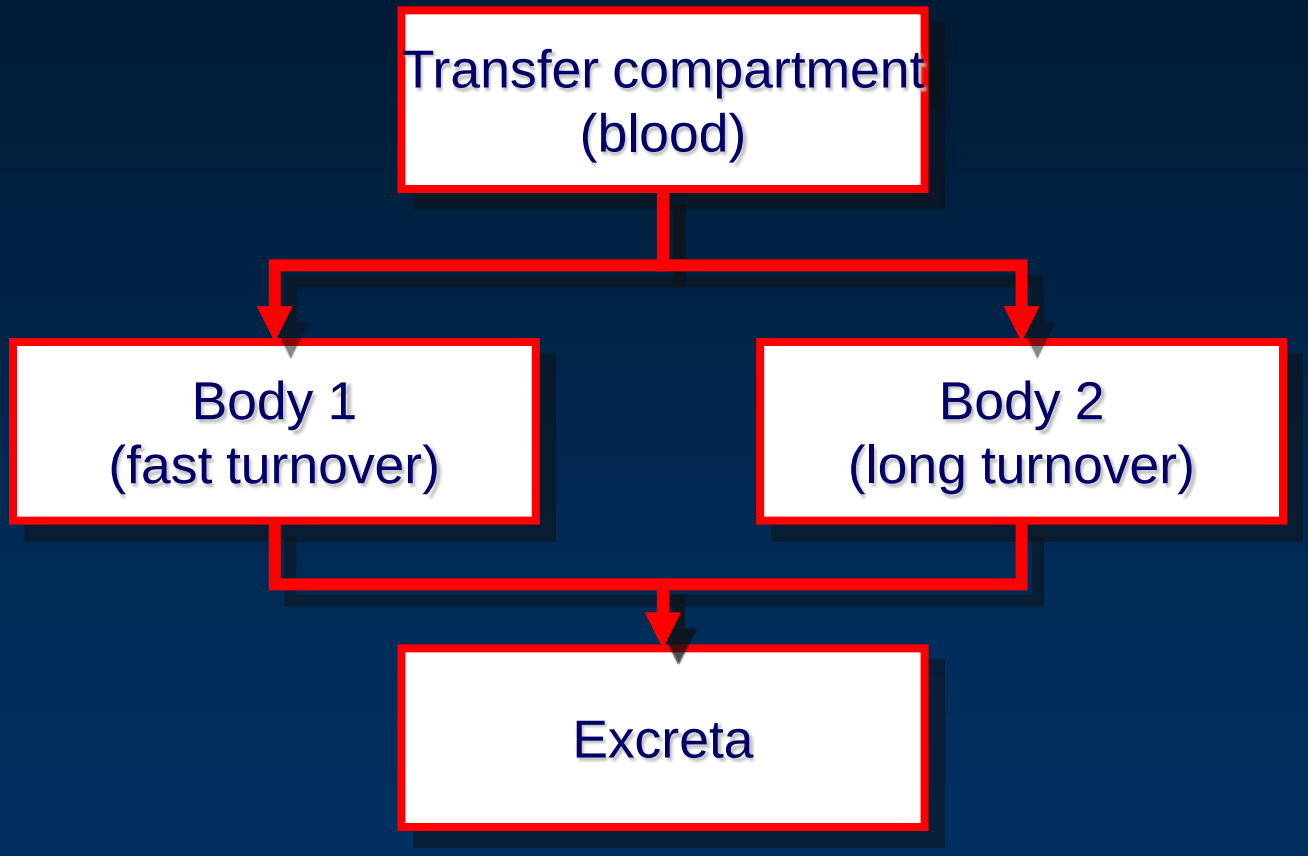
PRUSSIAN BLUE

- Oral administration;
- Relatively non-toxic, well tolerated, and refractory to absorption from the alimentary tract;
- *In vitro* study - cesium binding to PB has a clear pH-dependent profile (maximal at pH 7.5).

SIDE EFFECT OF PB

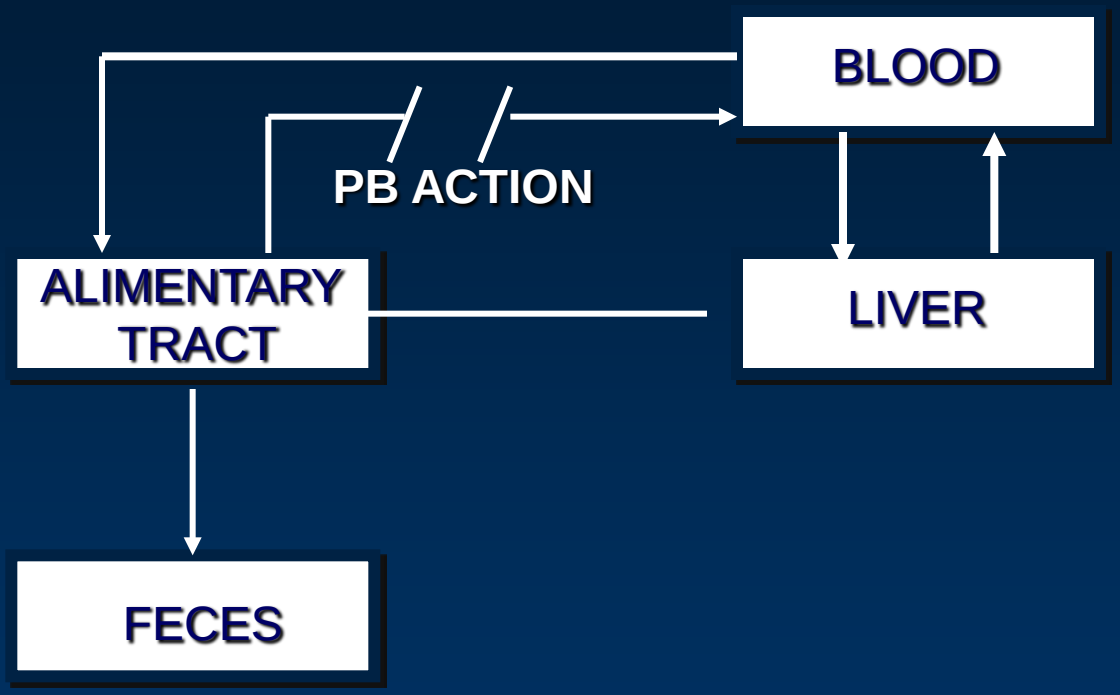
- Goiania data (Farina and Brandao-Mello, 1991):
  - Intestinal constipation was a clinically observed side effect in a total of 10 out of 42 patients treated with PB;
  - It varied from a light degree in seven patients, to moderate in three patients.

PREVIOUS CESIUM BIOKINETIC MODEL



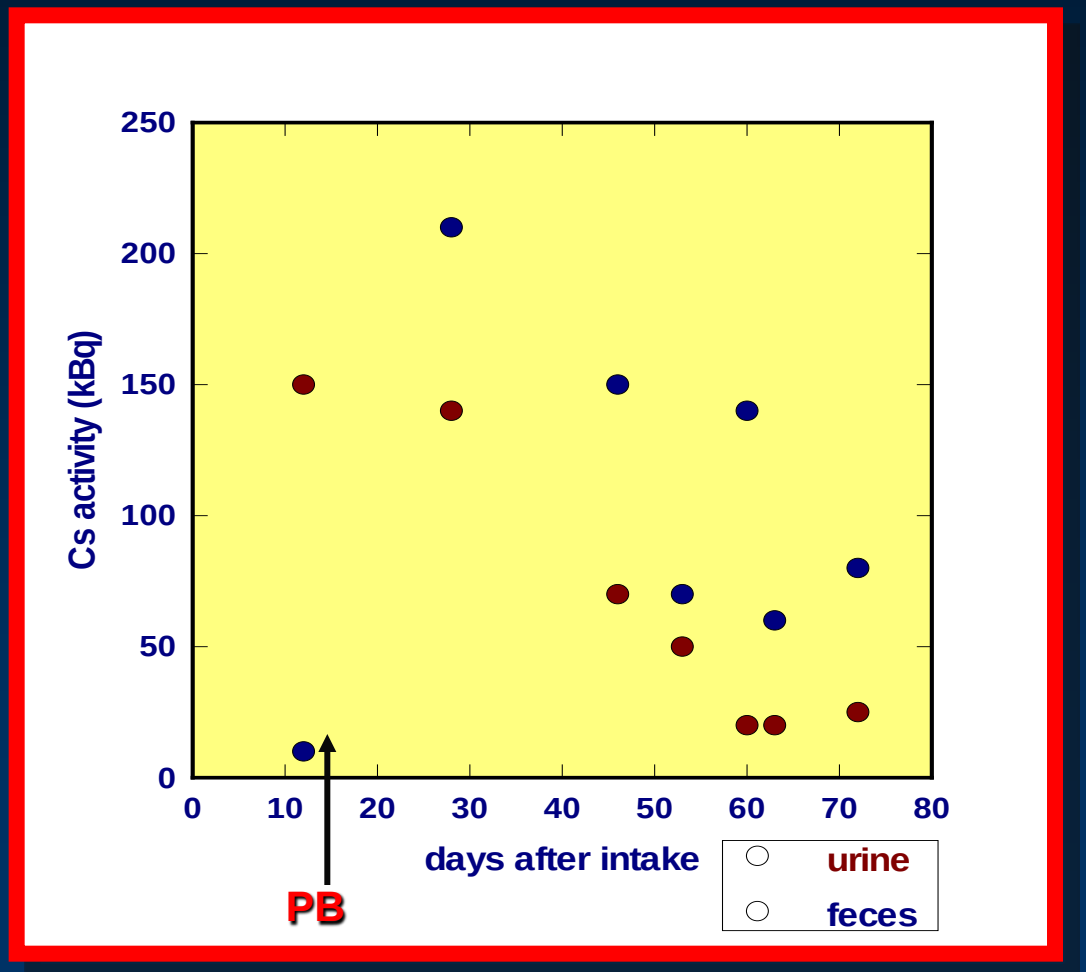
$$R(t) = A_1 e^{-\frac{0.693}{T1}t} + A_2 e^{-\frac{0.693}{T2}t}$$

PRUSSIAN BLUE



PB acts in the lumen of the alimentary tract decreasing or interrupting the enterohepatic circulation and increasing the amount of Cs excreted by feces.

PRUSSIAN BLUE TREATMENT



PRUSSIAN BLUE TREATMENT IN HUMANS ($3\ gd^{-1}$)

Start (dai)	Duration (d)	Biological half-time (T2) (d)		Reduction (%)	Reference
		PB	No PB		
12	5 (2 X)	50	140	64	**Richmond (1967)**
35	100	38	124	69	**Ma Ru-wei (1983)**
35	75	39	54	28	
35	82	25	61	59	
35	100	17	36	53	
35	100	16	36	56	
67	5 (2 X)	70	110	36	**Ye Gen-yao (1981)**
114	6 (3 X)	43	71	40	**Tang et al., (1988)**
114	6 (3 X)	48	54	11	
114	6 (3 X)	29	60	52	
300	-	40	115	65	**Madshus (1966)**
300	-	40	110	64	
-	108	38	124	69	**Ruwei (1985)**
-	93	39	54	27	

PRUSSIAN BLUE TREATMENT IN HUMANS
GOIANIA DATA – ADULTS (10 d.a.i.)

Gender	Biological half-time – T2 (d)				Reduction T2 (%)		
	3gd^{-1} PB	6gd^{-1} PB	10gd^{-1} PB	No PB	3gd^{-1} PB	6gd^{-1} PB	10gd^{-1} PB
F		20	33	58	-	66	43
F	22			53	58	-	-
M	42			66	36	-	-
M		18		98	-	82	-
M		17	17	99	-	83	83
M	21	17		75	72	77	-
M		17	25	85	-	80	70
M		21		80	-	74	-
M	26	63		106	75	40	-
M			27	89	-	-	70
M		18	29	70	-	74	59
M	17	39		80	79	51	
M	21	15		75	72	80	
x $\pm$ s	25 $\pm$ 9	25 $\pm$ 15	26 $\pm$ 6		66 $\pm$ 16	70 $\pm$ 14	65 $\pm$ 15

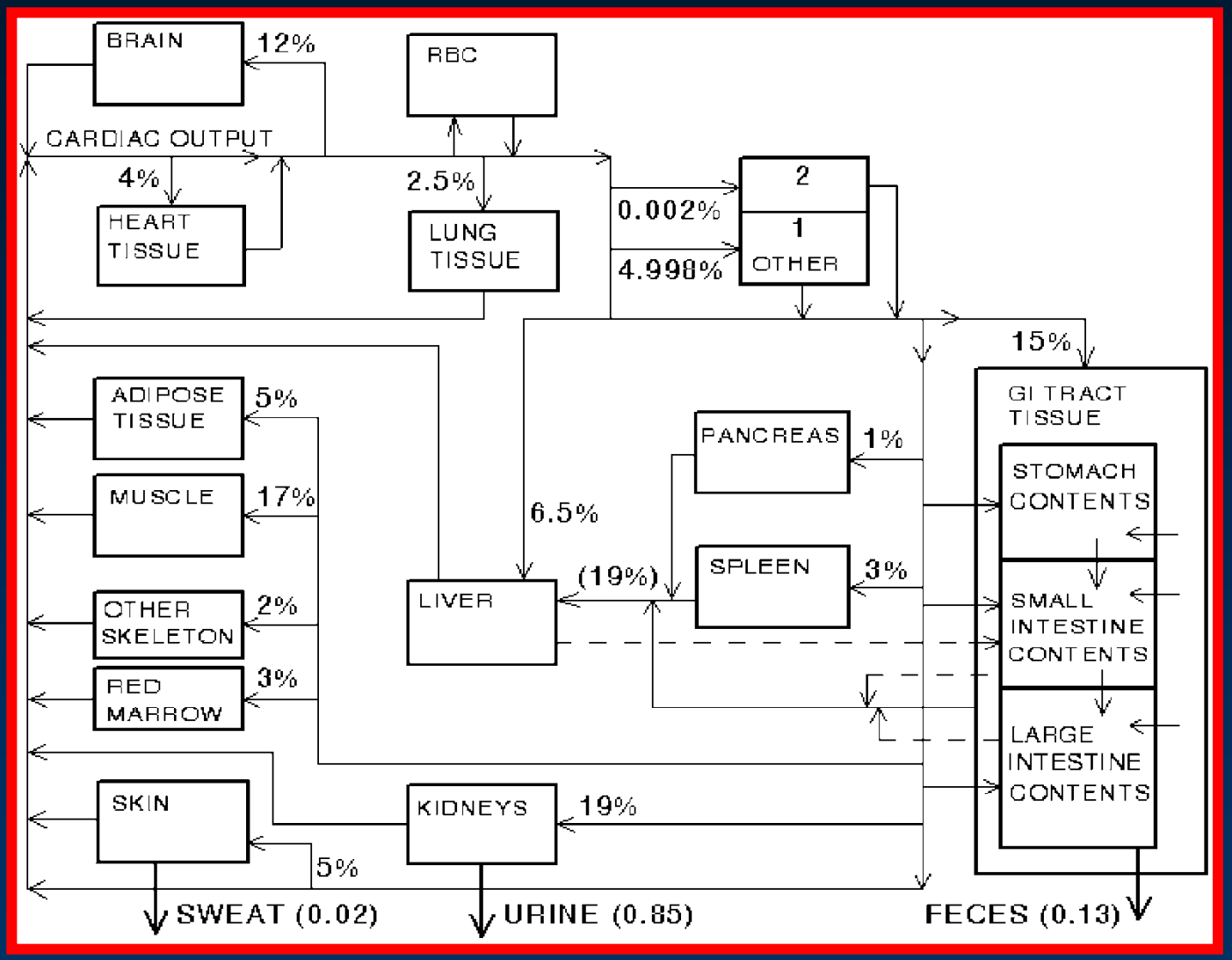
FECES:URINE RATIO
GOIANIA DATA - ADULTS

Gender	Feces:urine ratio			
	No PB	3gd^{-1} PB	6gd^{-1} PB	10gd^{-1} PB
M	0.19	1.13	1.45	
M	0.24	1.15	1.75	
M	0.02	1.58	1.95	
M	0.50		1.44	
M	0.28		2.05	5.76
M	0.17	1.61	2.52	2.84
M			2.50	5.50
M		2.16	1.62	4.62
M		1.44	1.25	
F			2.82	
x	0.23	1.51	1.94	4.68

SIMULATION OF PB EFFECT CESIUM BIOKINETIC MODEL

- Detailed systemic biokinetic model for cesium was used to evaluate the efficacy of PB treatment;
- Enterohepatic circulation was interrupted at a time post uptake of cesium representing a starting time for PB treatment;
- Model simulations were conducted for four different PB starting times after acute uptake of cesium into blood of an adult male or female:
  - 1 hour, 1 d, 10 d and 30 d;
  - In each simulation it was assumed that daily PB administration was maintained to 90 d after injection.

CESIUM BIOKINETIC MODEL

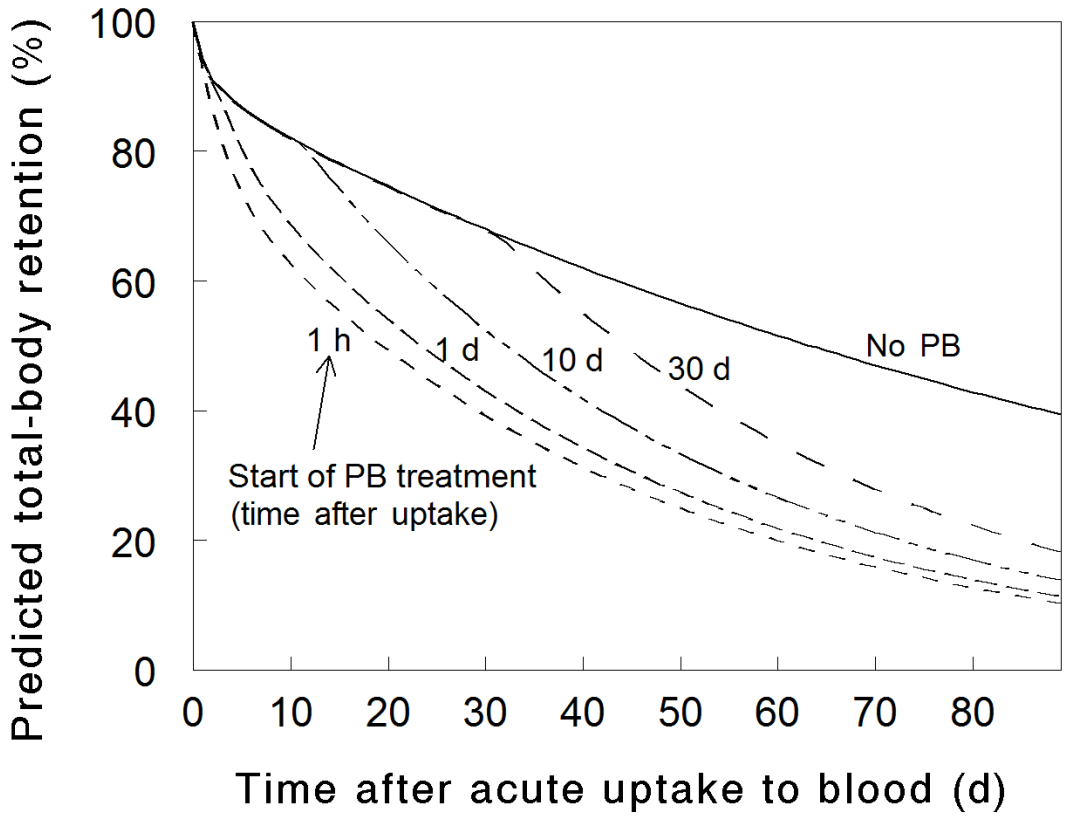


Leggett R.W., Williams, L.R., Melo, D.R., Lipsztein, J.L. A physiologically based biokinetic model for cesium in the human body. The Science of the Total Environment 317: 235–255 (2003)

SIMULATION OF PB EFFECT CESIUM BIOKINETIC MODEL

Start of PB treatment	Long-term T2 after start of PB (d)		Reduction in long-term T2 (%)		Cesium in the body 90 days after uptake (%)	
	Male	Female	Male	Female	Male	Female
No treatment	96	71	-	-	49	39
1h post intake	39	30	59	58	17	10
1d post intake	39	30	59	58	18	11
10 d post intake	39	30	59	58	21	14
30 d post intake	39	30	59	58	26	18

RESULTS OF SIMULATION
PB EFFECT FOR ADULT FEMALE



CONCLUSIONS

- No matter what PB dosage was administered, the reduction of the biological half-time was about the same (average 60 $\pm$ 8% for the adult);
- The secretion of cesium into alimentary tract is a limitation for the efficacy of PB treatment;
- Increases in the PB daily dosage will not further decrease the long term half-time of cesium in the body, 3 gd^{-1}should be considered as the appropriate PB dosage;
- Dosages greater than 3 gd^{-1} may increase constipation; and associated to the increased cesium activity in the lumen of intestine may result in an increasing of colon dose;
- The treatment is more efficient if started in the day that cesium intake has occurred.