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Biological monitoring of inorganic mercury – can the kidney burden be estimated?

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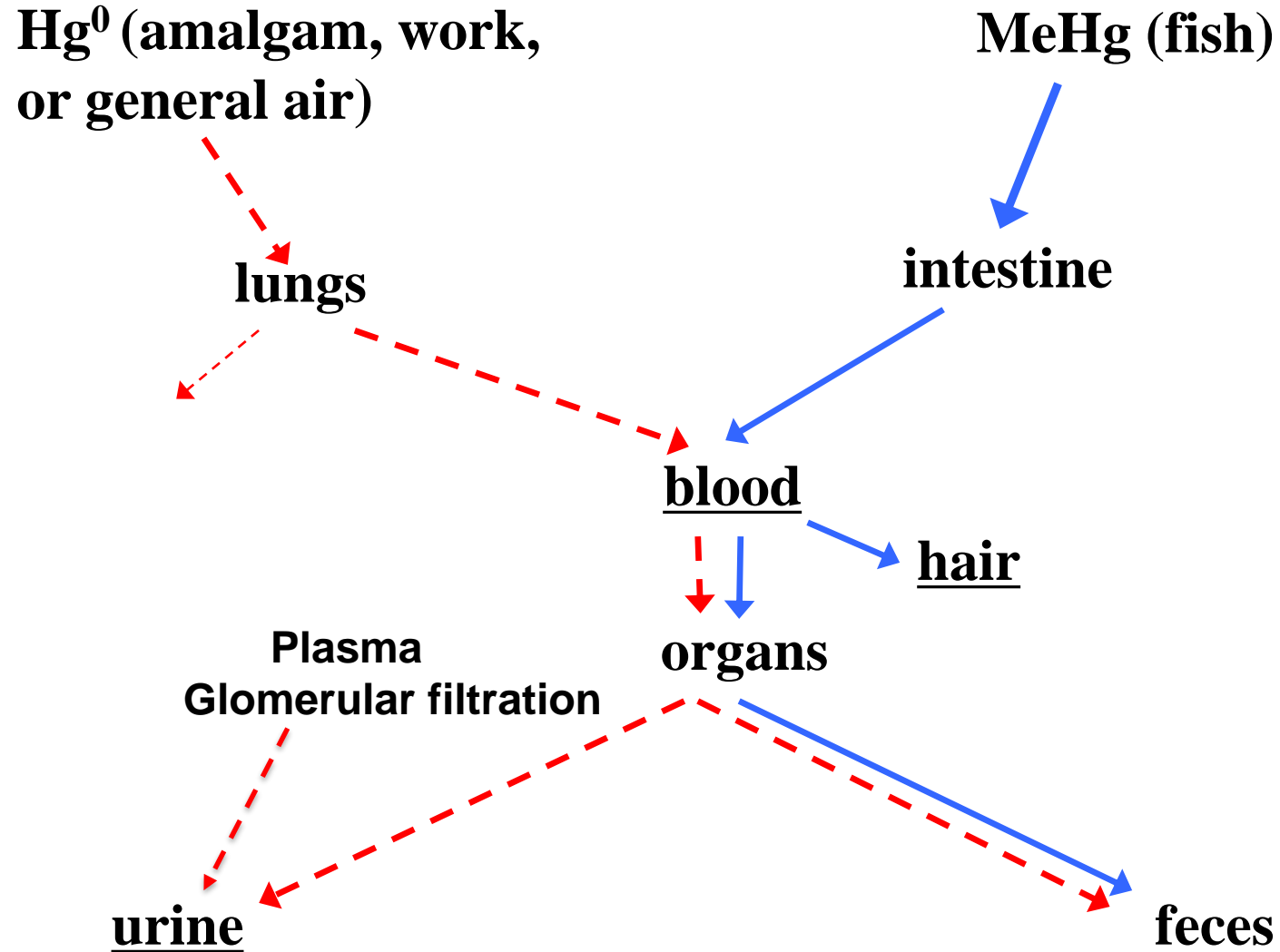
Background



- The general population is exposed to mercury (Hg) from amalgam fillings (inorganic Hg) and by fish consumption (organic, methyl mercury, MeHg). Mercury accumulates in many organs but the longest retention times are in the kidneys, brain and testicles.
- U-Hg and B-Hg are widely used as measures of long-term Hg exposure or body burden.
- No previous study of the relationships between Hg in kidney, blood and urine for living subjects with valid analytical methods



Biomonitoring of Mercury



Research questions

1. Relationship between Hg in kidney and urine and blood
 1. Relationship between U-Hg, P-Hg, B-Hg and K-Hg
 2. Biological half-time of Hg in the kidney
2. Can kidney-Hg be estimated from U-Hg?



1. Study design

- 109 living kidney donors
- Questionnaire
(work history, amalgam, diet...)
- Biological samples
 - 24h urine (UHg/24h)
 - Overnight urine (UON)
 - Blood (whole blood and plasma)
 - Kidney cortex biopsy
- Samples analyzed for:
 - U-Hg / B-Hg / K-Hg (CVAFS)

	All	Men	Women
Subjects	109	49	60
Age: median (range)	51 (24-70)	52 (32-70)	50 (24-64)
Amalgam surfaces, median (range)	19 (1-58)	20 (1-58)	17 (1-53)
Fish meals, N			
< 1/month	14	9	5
>1/month - <1/week	42	25	17
1/week	33	17	16
>1/week	20	9	11
Overnight U-Hg (µg/gC): Mean (Range)	1.7 (LOD-11)	1.4 (0.2-8)	1.9 (LOD-11)
K-Hg (µg/g) Mean/median range	0.33/0.21 (LOD-2.4)	0.23/0.18 (LOD-1.2)	0.40/0.25 (LOD-2.4)

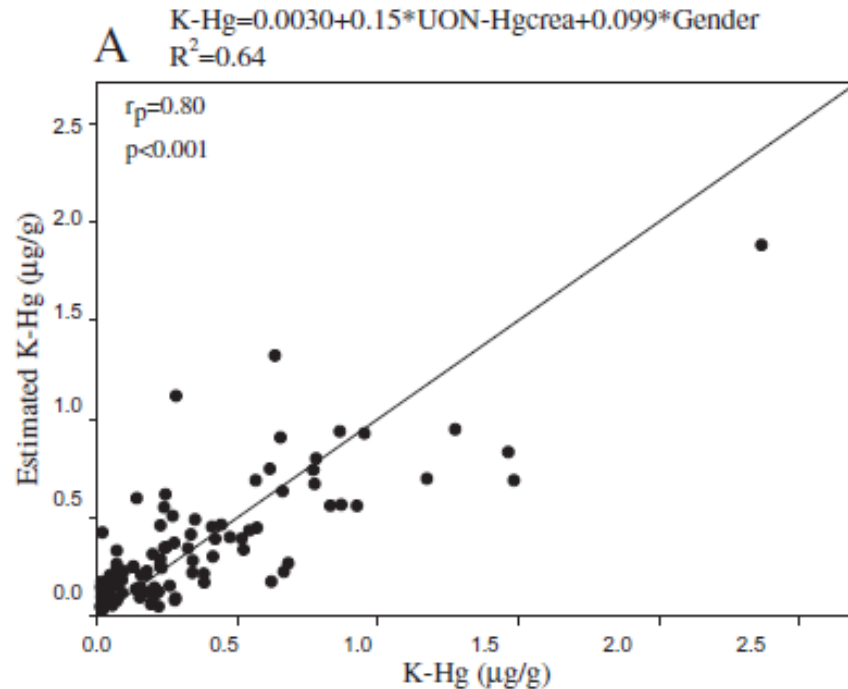
Associations with K-Hg (Pearson correlation coefficients)



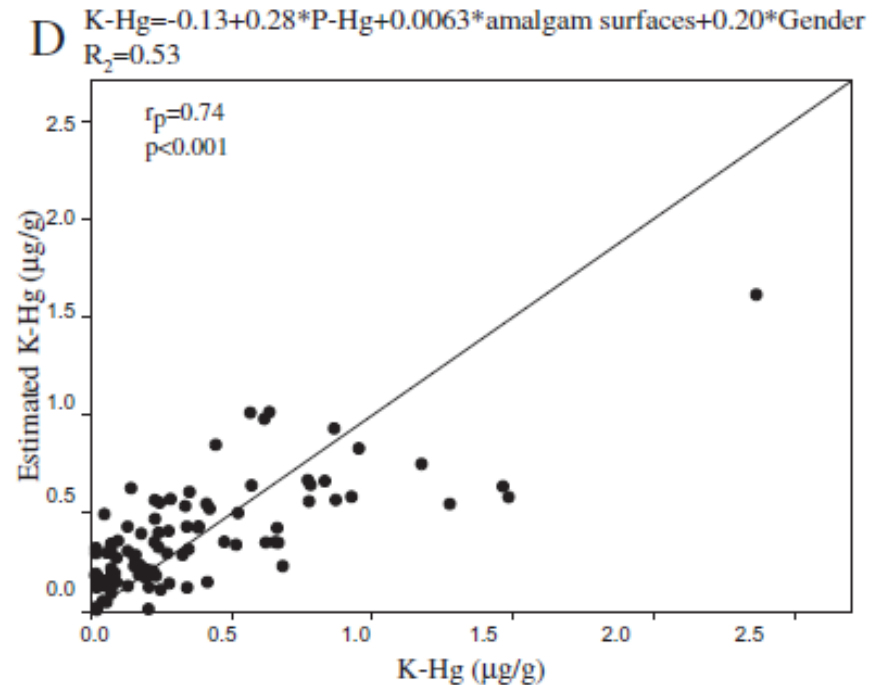
Variable	N	Concentration/rate		K-Hg ($\mu\text{g/g}$)		Correlation
		Mean	Range	Mean	Range	r_p (p-value)
U24-Hg ($\mu\text{g/L}$)	88	1.1	<LOD ^a -6.2	0.33	<LOD ^a -2.4	0.72 (<0.001)
UON-Hg ($\mu\text{g/L}$)	106	2.3	<LOD ^a -13	0.33	<LOD ^a -2.4	0.53 (<0.001)
U24-HgCrea ($\mu\text{g/gC}$) ^b	86	1.5	<LOD ^a -12	0.34	<LOD ^a -2.4	0.83 (<0.001)
UON-HgCrea ($\mu\text{g/gC}$) ^b	106	1.7	<LOD ^a -11	0.33	<LOD ^a -2.4	0.79 (<0.001)
U24-HgSG ($\mu\text{g/L, SG}$) ^c	74	1.1	<LOD ^a -5.8	0.32	<LOD ^a -2.4	0.84 (<0.001)
UON-HgSG ($\mu\text{g/L, SG}$) ^c	87	1.8	<LOD ^a -10	0.36	<LOD ^a -2.4	0.74 (<0.001)
U24-Hg/h ($\mu\text{g/h}$) ^d	88	0.077	<LOD ^a -0.45	0.33	<LOD ^a -2.4	0.76 (<0.001)
UON-Hg/h ($\mu\text{g/h}$) ^d	106	0.088	<LOD ^a -0.59	0.33	<LOD ^a -2.4	0.73 (<0.001)
U-Hg/24h (μg) ^e	88	1.9	<LOD ^a -11	0.33	<LOD ^a -2.4	0.76 (<0.001)
B-Hg ($\mu\text{g/L}$)	109	2.0	0.30-12	0.33	<LOD ^a -2.4	0.29 (0.002)
P-Hg ($\mu\text{g/L}$)	109	0.77	<LOD ^a -4.6	0.33	<LOD ^a -2.4	0.65 (<0.001)
U-Alb/24h (mg) ^f	87	7.1	<LOD ^a -21	0.33	<LOD ^a -2.4	0.08 (0.5)
GFR (mL/min/1.73 m^2)	108	101	77-140	0.32	<LOD ^a -2.4	0.05 (0.6)

Regression models for estimation of K-Hg

Hg in overnight urine + gender



Hg in plasma + amalgam + gender



Associations between Hg-biomarkers: urine, blood and plasma

Pearson correlation between Hg biomarkers.

Biomarker	UON-HgCrea ^a	UON-HgSG ^b	UON-Hg/h ^c
	r_p (N)	r_p (N)	r_p (N)
U-Hg/24h ^d	0.84 ^{***} (120)	0.87 ^{***} (101)	0.88 ^{***} (120)
B-Hg	0.46 ^{***} (146)	0.47 ^{***} (119)	0.42 ^{***} (146)
P-Hg	0.72 ^{***} (124)	0.76 ^{***} (102)	0.72 ^{***} (126)

^a Overnight urinary mercury concentration adjusted for creatinine. U-Crea <0.3 g/L or >3.0 g/L are excluded.

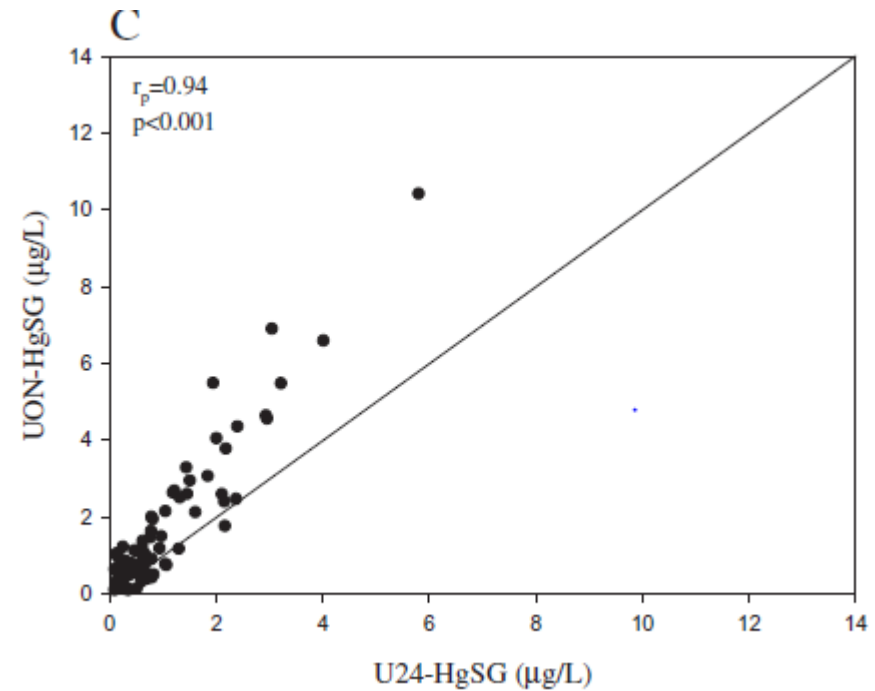
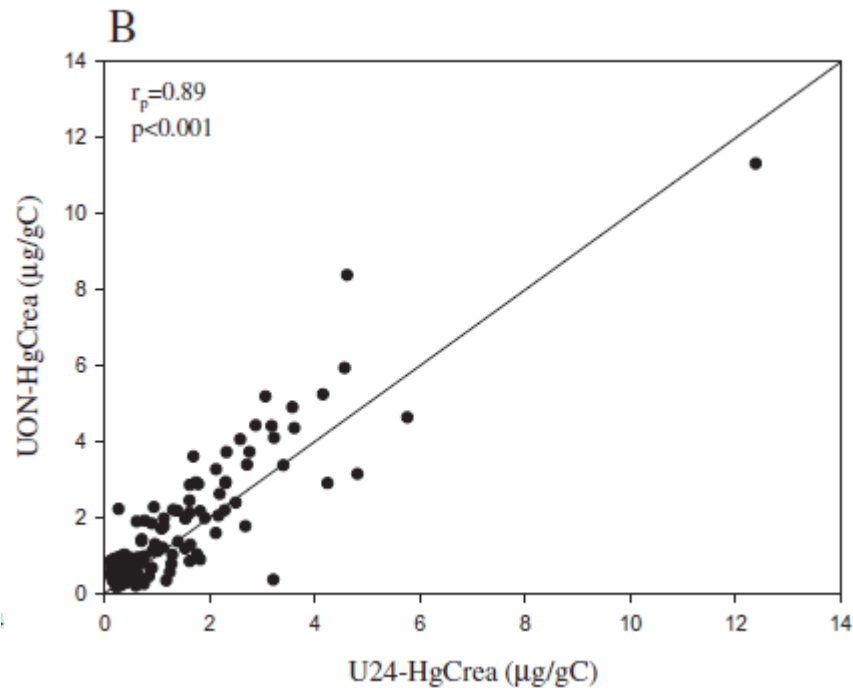
^b Overnight urinary mercury concentration adjusted for specific gravity. SG <1.010 or >1.030 are excluded.

^c Overnight urinary mercury excretion rate.

^d 24 h urinary mercury excretion.

*** p < 0.001.

Hg in overnight spot urine (UON) higher than 24 Hour urine



Determinants for Hg excretion in urine

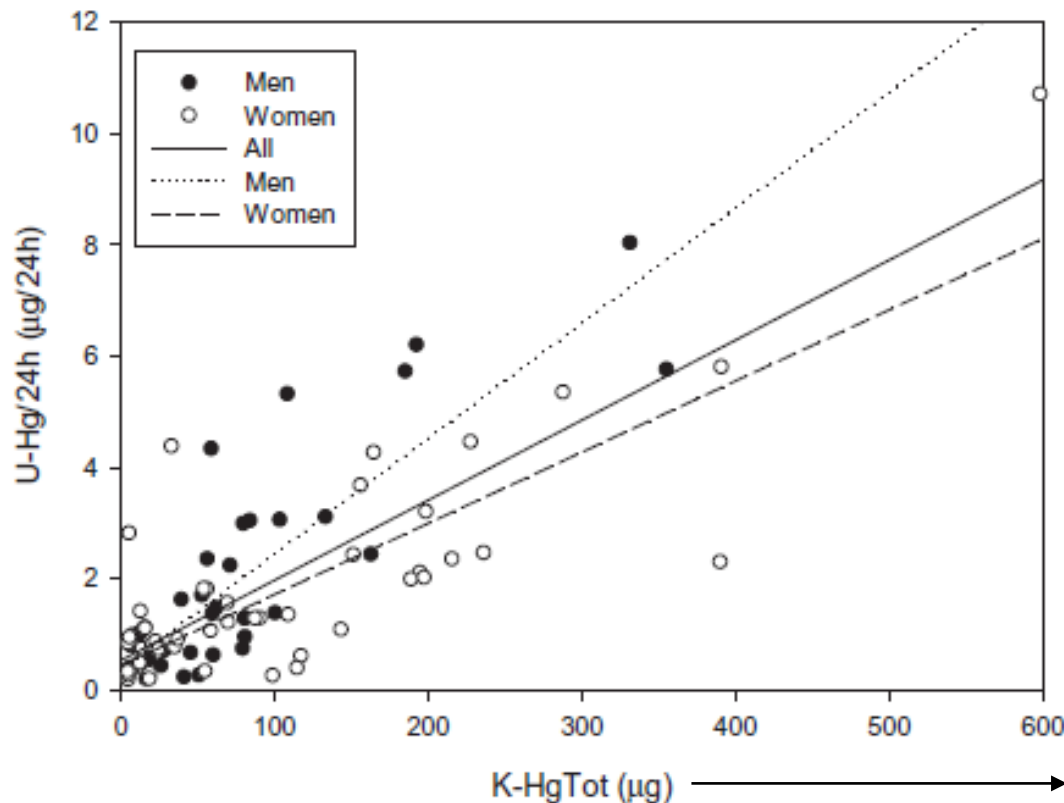
Table 3
Effects of kidney Hg, plasma Hg, and urinary albumin on 24 h urinary Hg excretion.

Model ^a	Dependent variable ^b	Independent variables ^c	Estimates (p-value)	R ²	Correlation ^d (p-value)
All (N = 86)	U-Hg/24h	Intercept	-0.79 (0.07)	0.72	0.86 (<0.001)
		K-Hg _{tot}	0.0086 (<0.001)		
		P-Hg	1.0 (<0.001)		
		log(U-Alb/24h)	0.59 (0.01)		
Men (N = 39)	U-Hg/24h	Intercept	-1.2 (0.05)	0.76	0.88 (<0.001)
		K-Hg _{tot}	0.020 (<0.001)		
		log(U-Alb/24h)	0.84 (0.008)		
Women (N = 47)	U-Hg/24h	Intercept	0.15 (0.5)	0.75	0.87 (<0.001)
		K-Hg _{tot}	0.0074 (<0.001)		
		P-Hg	1.2 (<0.001)		

^a Models derived by using backwards elimination from the full model $U\text{-Hg}/24h = \text{intercept} + K\text{-Hg}_{\text{tot}} + P\text{-Hg} + \log(U\text{-Alb}/24h) + \text{age} + \text{gender} + \text{UF} + \text{GFR}$ for all individuals and $U\text{-Hg}/24h = \text{intercept} + K\text{-Hg}_{\text{tot}} + P\text{-Hg} + \log(U\text{-Alb}/24h)$ for men and women.

The fraction excreted in urine per 24h was 1.7%

2.3% for men and 1.5% for women (sign. difference)



Half time (T_{1/2} including PHg):
Total: 74 days
Men: 37 days
Women: 92 days

Total Hg in the kidneys was estimated from the Hg concentration and kidney weight.

Fig. 1. Association between urinary mercury excreted in 24 h and total amount of mercury in kidney, including regression lines (assuming straight line with intercept) for all individuals and separate lines for men and women.

Conclusions

- Strong associations between Kidney-Hg and Hg in urine and plasma
- Hg in Overnight (ON) urine samples higher than in 24 h samples
- Kidney-Hg can be estimated using Hg in ON-urine and gender
- Kidney-Hg ($\mu\text{g/g}$)/U-24-Hg (μg)= 0.22
- Estimates of the biological half time of Hg in kidney were 37 days for men and 92 days for women