

生活環境中的重金屬危害

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毒物科

重金屬在哪裡

- 金屬的比重大大於5，密度大大於4.5g/cm³的金屬，分子量大大於200
- 鉛、汞、鎘、鎳、鉻、砷、銅、鋅等為常見
- 經由食物(蔬菜、海產等)、水、空氣進入人體

可能暴露職業或環境(1)

- 鉛：電池製造業、橡膠業塑膠業、玩具製造業、油漆業、製造鉛的漆加物、顏料及漆料製造業、中藥的紅丹、經常性染髮者。
- 鎳：鎳合金業、焊接業、鎳一鎘電池業、製玻璃瓶業、製錢幣業。
- 金屬汞：牙醫、電鍍業、水銀燈及螢光燈業、半導體光能細胞製造。
- 無機汞：中藥、仙丹、香水與化妝品業。
- 有機汞：殺菌劑、製紙業、殺黴菌劑、殺蟲劑製造、木村防腐劑等。

可能暴露職業或環境(2)

- 鉻：電鍍業、彩色電視影像管製造、玻璃業、水晶、紡織業(色料)、焊接業。
- 鎘：鎘製造業、鉛及鋅的熔鑄業、電鍍業、塑膠穩定劑製造、鎘鎳電池製造業、焊接鍍鎘物質、合金製造業、色料業、電子製造業、寶石製造業。
- 砷：農藥、電子半導體的製造等的相關行業，氫化砷(AsH_3)則易發生在電腦工業及金屬工業、中藥的砒霜等。

廢電池含有鉛、鋅、錳、鎳、鈷、鐵以及對環境為害最大的汞和鎘等重金屬，若不妥善的加以回收一但混進垃圾掩埋場後，這些有毒的重金屬將污染土地和水源，間接的進入人體，無法經由代謝排出體外，經年累月就可能發生重金屬中毒，如嘔吐、腹痛、肌肉疼痛、甚至痴呆等嚴重病況。

表一：全國三一九公頃農地調查計畫受重金屬污染農地面積

地方<縣市>	土地面積<公頃>
彰化縣	184 公頃
新竹市	27.54 公頃
桃園縣	11.46 公頃
屏東縣	6.9 公頃
台中縣	6.34 公頃
高雄縣	6.02 公頃
台南縣	5.33 公頃
台北縣	1.62 公頃
苗栗縣	0.55 公頃
南投縣	0.39 公頃

- 鎘常伴隨低品質之鋅化合物，高鋅添加來源亦出現高鎘含量，故有必要加強染料、塗料色素及製造塑膠穩定劑等工業廢污水及廢棄物
- 鉻、鎳等重金屬與添加皮革粉、皮屑、羊毛粉〈印染過程殘留〉、化工電鍍污泥、一般污泥〈混凝劑、清潔劑殘留〉

重金屬主要的危害機轉及原理

- Affinity to biologic electron-donor ligands, esp. sulfhydryl group

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ligands, esp. sulfhydryl group

Lead

銀灰色 軟金屬

原子序：82

原子量：207.21

熔點：327.4 °C

沸點：1620 °C

密度 19.2 (僅次於金)

鉛：非人體所必需

鉛中毒之歷史

- 外國：西元前 370 年，醫聖
Hippocrates 指出一精煉金
屬

工人有劇烈腹痛(鉛絞痛)

- 中國：元代本草衍義補遺
一中年婦女月內口服鉛丹二
兩，四肢冰冷僵直，食不入口

鉛的毒性

鉛很容易從呼吸道及腸胃道吸收，造成中毒

-- 神經、血液、腎臟及消化系統

神經 - 週邊神經病變(成人):手足痠麻、無力
鉛腦症(小兒):躁動、嗜睡、行為怪異、
昏迷、抽搐、死亡

血液 - 貧血

腎臟 - 間質腎病變、腎臟衰竭、痛風

消化 - 鉛線(lead sulfide)、腹絞痛、食慾不振、
噁心

致癌性-group 2B carcinogen in animals, insufficient in
human carcinogenesis



個案報告

一外勞27歲，男性，在一塑膠原料工廠，分裝硬脂酸鉛，工作時間約半年

症狀：間歇性腹痛二週

明顯貧血

牙齦有“鉛線”

血中鉛濃度高達 180 ug/dL

尿中鉛 186.5 ug/dL



Gingival lead line in adult with lead poisoning

Lead Compounds

Compound	Mol. Formula	Major Use
Lead Arsenate	$\text{Pb}_3(\text{AsO}_4)_2$	Insecticide
Lead azide	$\text{Pb}(\text{N}_3)_2$	Primer cord
Lead carbonate	$2\text{PbCO}_3\text{Pb}(\text{OH})_2$	Paint pigment (basic white lead)
Lead chromate	PbCrO_4	Paint pigment (chrome yellow)
Lead oxide	Pb_3O_4	Paint pigment (red lead)
Lead silicate	PbSiO_3	Porcelain
Lead sulfide	PbS	Lead ore, lead line
Tetraethyl lead	$\text{Pb}(\text{C}_2\text{H}_5)_4$	Gasoline additive

lead





 **RC**
MADE IN INDONESIA
STEARIC-ACID
TRIPLE-PRESSED-QUALITY
N.W. : 600 KGS
L/C NO:
PACKING NO:
TYPE: 301
PRODUCT BY
PT. CIGARANE LAYU CHEMICALS
TEL: 42210 08-1A
JAKARTA — INDONESIA

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Toxicokinetics Of Lead

- Absorption – inhalation & ingestion
inhalation: <math><0.5-1 \mu\text{m}</math>-completed absorbed
GI absorption--  in fasting & diet deficient in iron, calcium & zinc
- Distribution --99% lead bound to RBC, then to labile soft tissue pool & stable bone pool, **adult**:90% in bone, **child**:70% in bone
- Excretion – 65% in urine, 35% in bile

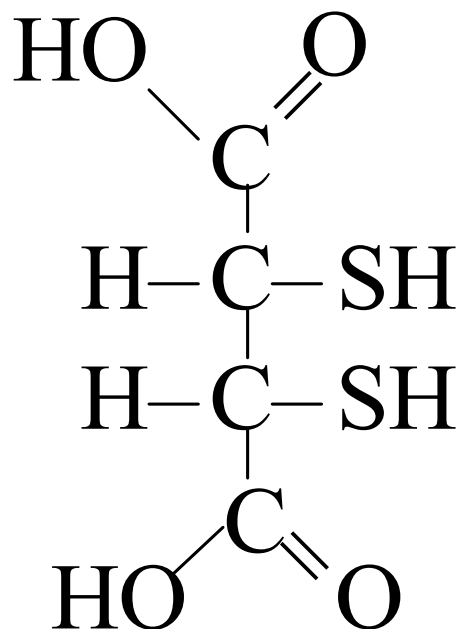
Biological half-life for Lead

- Blood (adult): 25 days
- Blood (children, exposure): 10 months
- Soft tissue: 40 days
- Trabecular bone: 90 days
- Cortical bone: 10-20 years

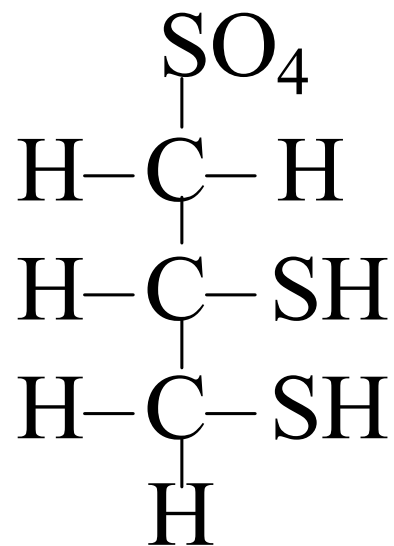
Children	Lead concentration in blood 9ug Pb/dL)	Adults
	150	
		Death
	100	
		Encephalopathy Anemia Decreased longevity
		Encephalopathy Nephropathy Anemia Colic
	50	
		Hemoglobin synthesis ↓
	40	
		Peripheral neuropathies Infertility (men) Nephropathy
		Hemoglobin synthesis ↓
	30	
		Systolic BP (men) ↑ Hearing acuity ↓
		Vitamin D metabolism ↓
		Erthrocyte protoporphyrin (men) ↑
	20	
		Erthrocyte protoporphyrin (women) ↑
		Nerve conduction velocity ↓
		Erthrocyte protoporphyrin ↑
		Vitamin D metabolism ↓ (?)
		Developmental toxicity
	10	
		Hypertension(?)
		IQ ↓
		Hearing ↓
		Growth ↓
		Transplacental transfer

鉛中毒的螯合藥物治療

- BAL (dimercaprol): 50-75 mg/m² im q4h, 3-5d
- **CaNa₂EDTA**: 1000-1500mg/m²/d, iv
- **Succimer**: 350 mg/m² tid for 5d, then bid, 14d; for mild symptoms
- D-penicilline
- **DMPS**



DMSA, Succimer
2,3-dimercaptosuccinic acid



DMPS
2,3-dimercapto-1-
propanesulfonic acid

Indications of Chelating Therapy

- 預防重於治療
- Patients with significant symptoms: encephalopathy, abdominal colic, arthralgias, myalgias
- Evidence of target organ damage: neuropathy/nephropathy
- Asymptomatic with BLL >45 μ g/dL, biochemical toxicity

Mercury Intoxication

- 1940s—Minamata Disease, methylmercury from vinyl chloride plant, 121 victims
- 1971— Iraq, 95,000 tons of seed grain treated with methylmercury as a fungicide was baked into bread

Table 81-2 Nonoccupational exposures to Mercury

Medicinal	Food	Other
Antseptics	Fish	Button batteries
Calomel teething powders	Grains and seed, treated Livestock, fed treated grain	Chemistry sets
Dental amalgam		Home amalgam extraction
Diuretics		Lightbulbs
Laxatives		Self-injection
Sphygmomanomet		Preservatives
Stool fixatives		“Magico-religious” use
Thermometers		
Weighted nasogastric tubes		

鹿林山測站氣態元素汞監測變化

(2007年1月~2008年2月)



圖：環保署提供

資料來源：環保署提供

The Diagnosis of Hg Intoxication

- Dural findings: unexplained neuropsychiatric & renal abnormality
- Confirmed by Hg detection in urine, blood & tissues
- Thin-layer & gas chromatography—distinguish organic or inorganic Hg
- Whole blood < 10 ug/L; urine < 20 ug/L

Table 81-4 Differential characteristics of Mercury

exposure	Elemental	Inorganic	Organic
Primary route of exposure	Inhalation	(Salt)	(Alkyl)
Primary tissue distribution	CNS, kidney	Kidney	CNS, kidney, liver
Clearance	Renal, GI	Renal, GI	Methyl: GI Aryl: renal, GI
Clinical effects CNS	Tremor	Tremor, erethism	Paresthesias, ataxia, tremor, tunnel vision, dysarthria
Pulmonary	+++	—	
Gastrointestinal	+	+++ (caustic)	+
Renal	+	+++ (ATN)	+
Acrodynia	+	++	—
Therapy	BAL, DMSA	BAL, DMSA	DMSA(early)

生物檢體中汞的濃度意義

- 尿液: exposure severity & neuropsychiatric s/s in inorganic Hg poisoning; chelating therapy efficacy monitoring
- 全血: reflect inorganic Hg load; correlate with acute toxicity of methylmercury

砷在環境中的型態

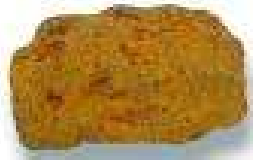
- 無機砷和有機砷。
- 無機砷：五價的砷（V）（如砷酸鹽）和正三價的砷（III）（如亞砷酸鹽）兩大類
- 有機砷則以單甲基砷（methanearsonic acid）和雙甲基砷（cacodylic acid）存在的含量較高。
- 不同型態的砷化合物，在毒性上有很大的差異：砷（III）對生物的毒性最強，砷（V）次之；有機砷較低，但揮發性的有機砷則較毒
- 受砷污染地區的土壤以砷（V）居多，砷（III）次之，有機砷較少。

- 雄黃在中國藥材上的應用，已經有幾千年的歷史。在傳統醫學上，雄黃有廣泛的用途；它可以用於治療皮膚疾病、寄生蟲感染、氣喘、慢性支氣管炎及癲癇等，也可以當成外敷藥用，用於處理毒蛇、毒蠍咬傷的傷口、疹瘡、體癬、包疹、痔瘡、子宮頸糜爛等，甚至有人用在除去新生兒胎毒用途。自古就流傳雄黃酒在端午節有去邪功能並有驅蛇功用，一般民眾也極易在中藥店購買到雄黃自行服用。

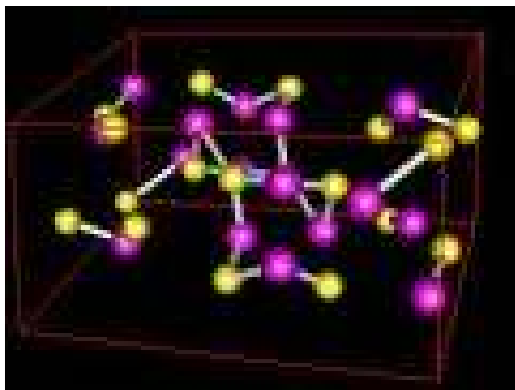
A review of the clinical and toxicological aspects of 'traditional' (herbal) medicines adulterated with heavy metals.

Expert Opin Drug Saf. 2005 Jul;4(4):769-78.

: [Lynch E, Braithwaite R.](#)



- 雄黃，學名：硫化物類礦物雄黃族雄黃，主含二硫化二砷(As_2S_2)。含砷70.0%，主要用於提取砷和製備砷化物。產地：湖南、湖北、貴州、甘肅、雲南、四川。鑑定：形狀-塊狀或粒狀集合物。呈不規則塊狀，深紅色或橙紅色，表面常附有橙黃色細粉。微透明或半透明，晶面有金剛石樣光澤。質脆易砸碎，斷面紅色至深紅色，具樹脂樣光澤。氣味-有特異臭氣，味淡。成分：有效成分：二硫化二砷(As_2S_2 , Arsenic disulphide)，純度要高於90%以上。有毒成分：遇熱分解產物三氧化二砷(Arsenous oxide)。





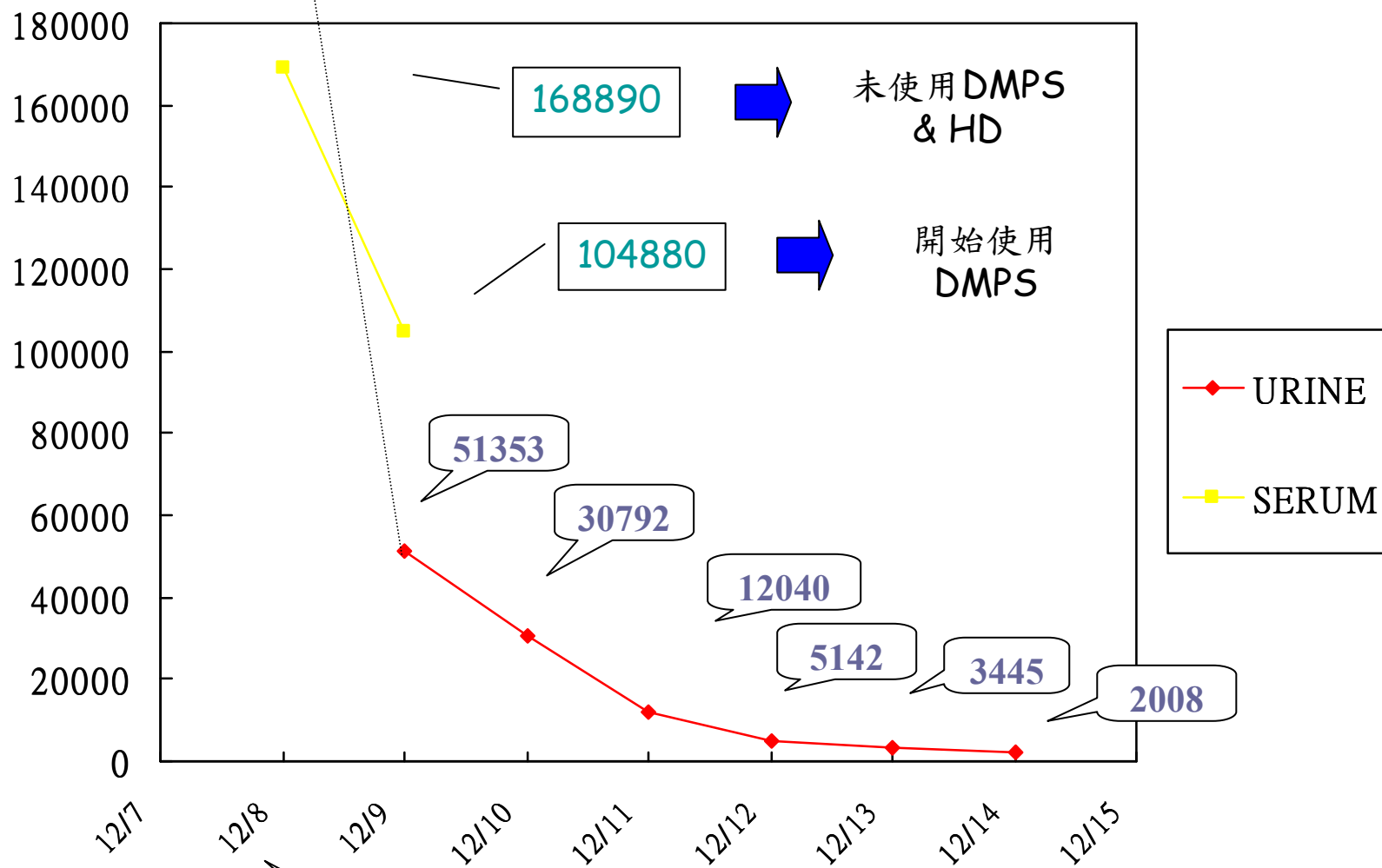
- 一位62歲男性，身體狀況良好，無特別系統性疾病史。民國94年12月7日晚間，他誤喝驅蛇用雄黃酒約30CC，而後將雄黃酒倒入花粉酒中稀釋後又喝了約30CC。隔日開始出現腹痛、腹瀉、頭暈的現象。剛開始時，他被送至區域醫院就診，嚴重腹瀉及低血壓，經初步治療（含活性炭洗胃）後心跳血壓穩定，但腸胃道不適的症狀加劇，並有尿量減少的現象，當天他被轉送至急診室。

- 初到院時生命徵象為體溫 37.1°C 、脈搏105次/分鐘、血壓95/57 mmHg、意識清楚，但外觀衰弱。理學檢查除腹部絞痛外無特殊發現；但入院2小時後，血壓降低至76/24mmHg。實驗室檢查方面：血紅素14.2g/dl，血小板331000/cumm，白血球：17100/cumm，血尿素氮24 mg/dl，creatinine 2.1 mg/dl，鈉142 mmol/L，鉀3.5 mmol/L，血糖232 mg/dl，肝功能方面ALT 19U/L。動脈氣體分析，pH 7.376、 PO_2 108、 PCO_2 31.8、 HCO_3^- 18.8、 O_2Sat 99%。



Serum: As, ug/ml

URINE: As of Crea, ug/g



169647.06 → !?

168890 → 未使用DMPS & HD

104880 → 開始使用DMPS

◆ URINE
■ SERUM

HD
 $(168.89 - 104.88) / 168.89 \times 100\% = 38\%$

DATE

Silver 銀

- Argentum: Ag
- 原子序：47
- 原子量：107.868
- 同位素：107,109
- 物理性質：
 - 白色而有光澤的貴金屬，質較軟，比金硬
 - 導電性和導熱性最高
 - 延展性僅次於金
 - 能與銅、金、鋅、鉛、鎳等金屬形成合金
- 化學性質
 - 氧化態：+1（常見），+2（不常見）
 - 不活潑金屬，一般與氧不起作用
 - 硝酸銀 AgNO_3 是可溶性銀鹽
 - 氯化銀 AgCl 、溴化銀 AgBr 和碘化銀 AgI ，三者不溶於水

Silver

- 應用：
 - 與一種或幾種其他金屬製成合金
 - 銀銅合金可製作貨幣
 - 銀金合金用於珠寶飾物
 - 銀銅鋅合金可用於銀焊
 - 銀鉛合金用於電池
 - 銀鎳合金用於軸承
 - 硝酸銀可用於鍍銀和銀鏡
 - 磷酸銀可用作催化劑
 - 鹵化銀可用於照相
 - 氧化銀可用於玻璃拋光和著色，也可作催化劑和電極板

Silver

– 醫療用途

- Coating artificial heart valve or CVP or foley
- Topically in burn treatment
- 自然療法：
 - Herbal tea
 - Dietary supplement
 - Naturopathic remedy for antibacterial, immune boosting or anti-allergy property

銀的毒性

- Clinical effect
 - Neuro:
 - Peripheral neuropathy
 - Seizure: rare, only 2 case report
 - Animal: (penetrate BBB)
 - Brain stem was first stimulated and then depressed
 - Accumulate in neurons and protoplasmic glia cell of brain and spinal cord
 - Animal experience: IV injection has most significant impact on CNS (Manifested as weakness and rigidity of the legs, loss of voluntary movements) and heart conduction delay
 - » Hill WR, Pillsbury DM. Argyria, The Pharmacology of Silver. 1st edn. The Williams and Wilkins Co. 1939
 - Liver:
 - No human data
 - Animal: hepatic damage
 - Kidney:
 - Only few case and no well documented

銀的臨床毒性

- Clinical effect
 - Hema:
 - Very rare
 - Leukopenia, anemia, hemorrhage
 - Derma:
 - Most side effect and most case
 - Argyria (Discolouration of skin)
 - Pregnancy:
 - No data
 - Carcinogenicity
 - No study was found

Silver product



Case 1

- 41 Y/O F, with past history of HBV, was admitted from 93.5.17 to 93.5.18 with C.C of head full sensation, headache over parietal area and numbness over right face and arm. The MRI showed R/O MS.
- As for symptom persisted, from 94.3.23 to 94.8.23, she took 5-15ml Q4-Q6 silver protein (1.5576g/118ml/bottle). And then S/S got improved.
- So her friend suggested IV 6-15ml+ NS500 Q3D to Q6D
- Total 100 bottle for oral and IV (155.76g)

Case 1

- After IV injection, she started to feel hot intolerance, numbness and hotness over hands and feet, so she went to 聖馬爾定 hospital, there leukopenia, anemia and impaired liver function were noted, no discoloration and then was transferred to 中榮 hema from 94.11.28 to 12.6.
- During the hospitalization, bone marrow biopsy showed MDS, R/O silver induced, MRI showed no change.
- After stop silver, WBC from 1820 to 2300. Hgb from 8.1 to 9.8, then Hema OPD F/U.

Case 1

- Toxi OPD, serum Ag=823.78 μ g/L, whole blood 838.9 μ g/L, so admitted from 95.4.12 to 4.22 for DMPS injection and oral
- DMPS 2amp + NS500 BID for 3 days and then DMPS 1# oral tid for 7 days
- NCV/EMG: normal

Case 1

Date	Urine(L)	Ag(μ g/L)	Ag μ g
4/12	R/O spot	807.67	
4/13	R/O spot	953.55	
4/13	3100	1080.48	3349.488
4/14	4900	1413.7	6927.13
4/15	3000	691.49	2 074.47
4/16	2640	584.29	1542.5256
4/17	3400	544.78	1852.252
4/18	No data	No data	
4/19	3000	485.54	1456.62
4/20	3200	510.11	1632.352
4/21	3500	425.74	1490.09

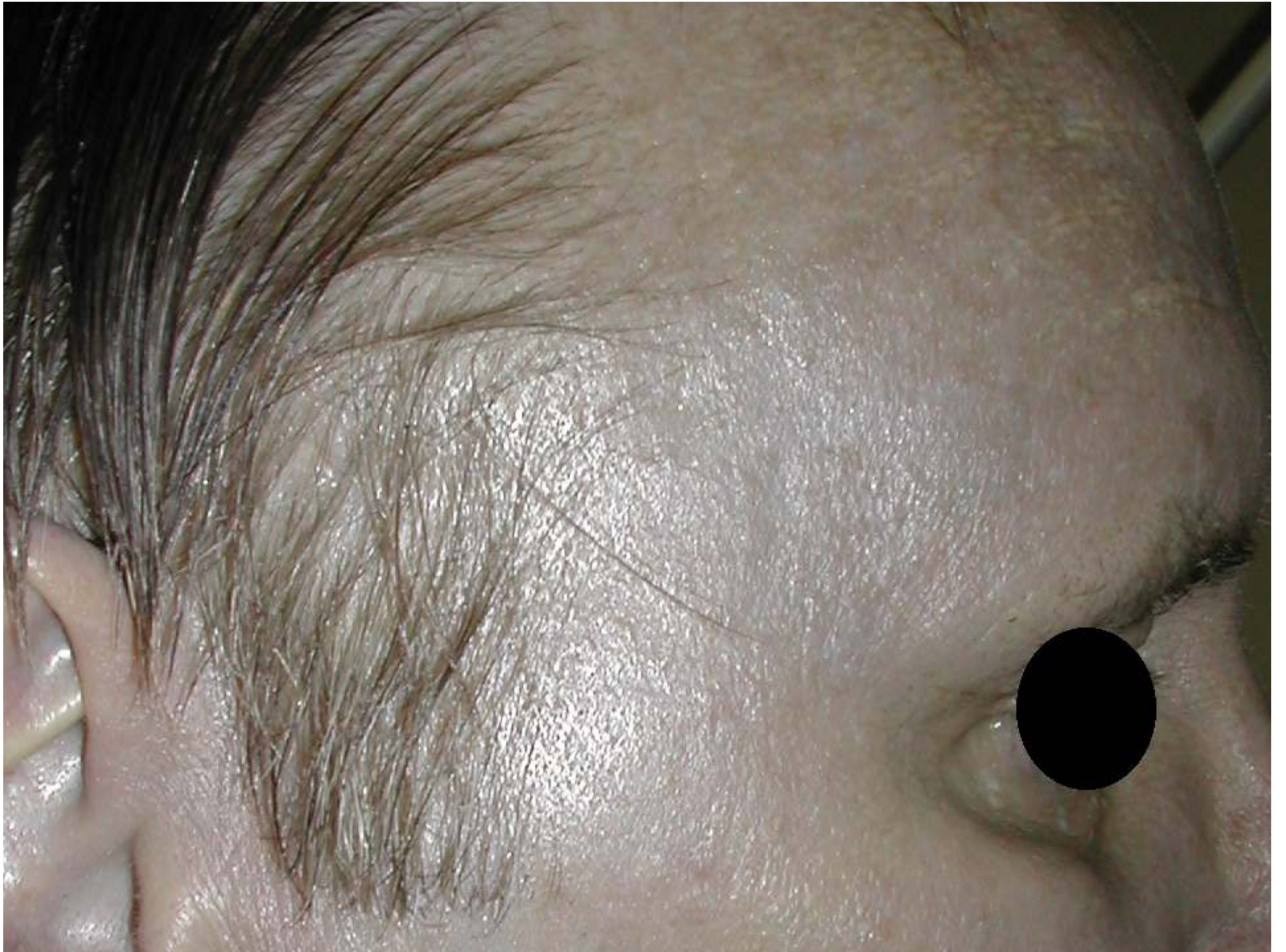
Date	Ag (serum)	Ag (whole blood)
3/21	823.78	838.3
4/12	380.42	
4/28		500.61

DMPS IV: 4/12下午至4/15早上，共六劑

DMPS oral: 4/14早至4/22早，共21劑

排出; 20 324.9276 μ g

排出比例：0.013%





The End

問題/指教