Acta Dermatovener (Stockholm) 57: 413–419, 1977

SILVER-BLUE NAILS[1]

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Abstract. The case is reported of a man with uniformly silver-blue discolouration of all fingernails, with deeper colouring over the lunulae. The nail bed changes resulted from the uncontrolled ingestion of a silver-containing granular powder. The total silver intake was over 15 g. The only other sign of argyrosis was a barely perceptible greyish discolouration over the cheeks and in the sclerae. Biopsies were taken from the nail bed and the cheek. Electron microscopy revealed metallic deposits in elastic fibres and basement membranes. The silver deposition was much heavier in the nail bed than in facial skin. Long-wave ultraviolet light (UVA) and lack of melanin protection seem to be responsible for this phenomenon. Argyrosis and the differential diagnosis of nail discolourations are reviewed.

Key words: Argyrosis; Silver-blue nails; Electron microscopy; Nail bed biopsy

Nail discolourations are found in a variety of diseases (Table I). The following case report presents the rather typical, but nowadays rarely encountered, clinical picture of silver-blue nails.

CLINICAL REPORT

A 70-year-old male patient was referred by his family physician for a dermatological consultation because of the "cyanotic" appearance of all his fingernails. Complete medical work-up had disclosed a mild, but well compensated cardiovascular failure which could not explain the cyanosis-like nail bed discolouration.

The patient was in good physical condition. A careful drug-history revealed that he had been taking digitoxin 0.1 mg (Digimerck®; Merck, Darmstadt) tablets for more than 5 years, and no other medications.

Dermatological findings

All fingernails had a uniform slate blue discolouration, with deeper colouring over the lunulae (Fig. 1). The shape of the nails was normal. Diascopy did not alter the blueish tinge of the nail beds. All toenails had normal shape and colour (Fig. 2). A drug-induced discolouration was suspected, but an intensive drug-history search revealed nothing of significance. The patient was instructed to check his medicine files at home and then to report back for further studies. The same afternoon the patient called back and asked if the discolouration of his nails could possibly be due to the granular powder that he had been taking for more than 3 years, for relief from a variety of gastrointestinal problems such as gastritis, diarrhoea, and constipation. The label on each jar instructed that the medication should not be used for more than 2 months. He had carefully saved over 120 of these jars to store nails and screws in his hobbyroom.

Silver was a major component of this medication and thus the apparent cause of the silver-blue discolouration of his nails. The composition of the medicine per gram (Adsorgan®; von Heyden, Munich) was: argent. chlorat. colloid. 4.2 mg; acid silic. 588 mg; argent. colloid. 0.8 mg; carbo medicin. 80 mg; dimethyl-polysiloxan 250/300 c St. 24.0 mg; succ. liquir. 140 mg. Each jar contains 25 g, and thus at least 15 g of silver had been ingested by the patient.

The patient was carefully checked for further signs of argyrosis. A very faint greyish discolouration was seen in the light-exposed parts of both sclerae, and in the skin of the periocular and maxillary regions, which could easily be overlooked due to the darker hue of the patient's complexion. All mucous membranes and the remainder of the body were normal in colour, as was the examination with Wood's light.

BIOPSIES AND TECHNICAL PROCEDURES

Two biopsies were obtained under local anaesthesia, one from the right maxillary area and one from the nail plate of the left fifth digit. A 2 mm punch was driven through the nail plate immediately distal to the lunula. Healing was uneventful and no scar was visible 6 months later at a follow-up visit. The samples of facial skin, nail plate and nail bed were processed for electron microscopy. The tissue was cut into small slices, fixed in 1% phosphate-buffered osmic acid, dehydrated, and embedded in Epon. Semithin sections were stained with azure II-methylene blue for light microscopy. For electron microscopy, thin sections were cut with a diamond knife from selected

[1] Presented in part at the "VIII. Fortbildungswoche für praktische Dermatologie und Venerologie" in Munich, July 26–30, 1976.

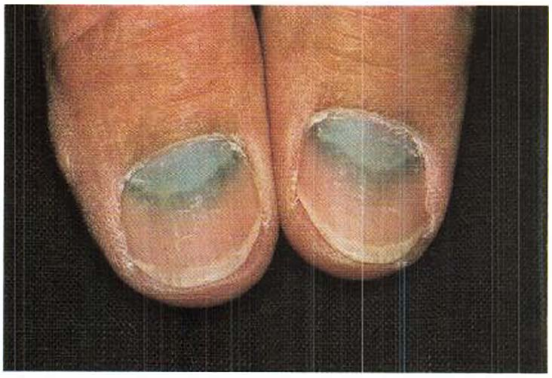


Fig. 1. Silver-blue nails. Blue discolouration of all fingernails. This figure shows both thumbs.

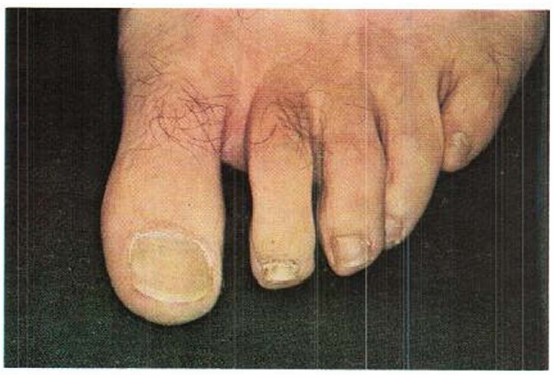


Fig. 2. Absence of discolouration of the light-protected toenails in the same patient.

blocks and stained with uranyl acetate and lead citrate. For comparison, unstained sections were used.

LIGHT AND ELECTRON MICROSCOPIC FINDINGS

Light microscopy

The semithin sections showed a very fine particulate material around the sweat glands and hair follicles in the facial tissue and in the dermis of the nail bed tissue. Dark-field illumination disclosed bright deposits of granular material at these sites.

Electron microscopy

The biopsy from facial skin revealed small, electron-dense particles within the dense layer of the epidermal basement membrane. No such granules were seen within or between epidermal cells. The rather high melanin content of melanocytes and basal keratinocytes was remarkable. A few granules were seen in the basement membrane of vessels and in elastic fibres. The dense particles were regularly found within the conspicuous, dense basement membranes of eccrine sweat glands (Fig. 3).

The punch biopsy from the nail did not reveal any electron-dense material within the nail plate itself. In the dermal tissues of the nail bed, however, excessive dense metal deposits were found. Some material was localized within macrophages, which contained aggregations of individual granules in

Table I. *Differential diagnosis of darkly pigmented nails*

Disease/agent	Comment	Reference
Nevi and pigmented tumours		
Subungual melanoma	Melanin	23
Diffuse melanosis in malignant melanoma	Melanin	17
Nevus cell nevi	Melanin	8
Systemic diseases and pigmentation		
Wilson's disease	Copper	5
Ochronosis	Homogentisinic acid	12
Morbus Addison	Melanin	20
Hemochromatosis	Hemosiderin & melanin	10
Drug-induced pigmentations		
Antimalarials	Melanin?	
Atabrine	Antimalarials	3
Amodiaquine hydrochloride	in chronic	21
Chloroquine	discoid lupus	29
Gold (chrysiasis)	erythematosus	1
Mercury (hydragyrosis)	Gold? Melanin?	9, 22, 34
Phenolphthalein (fixed drug eruption)	Mercury	33
	Melanin?	
Physically induced pigmentation		
X-rays (postirradiation melanonychia)		28
Mechanical trauma (haematoma)		
Microbial infections and pigmentation		
Pseudomonas paronychia	Bacterial pigment	4, 11, 20
Cyanosis		
Cardiovascular failure	Hb	
Methaemoglobin (DDS)	HbOH	
Exogenous discolourations		
e.g. film developers		20

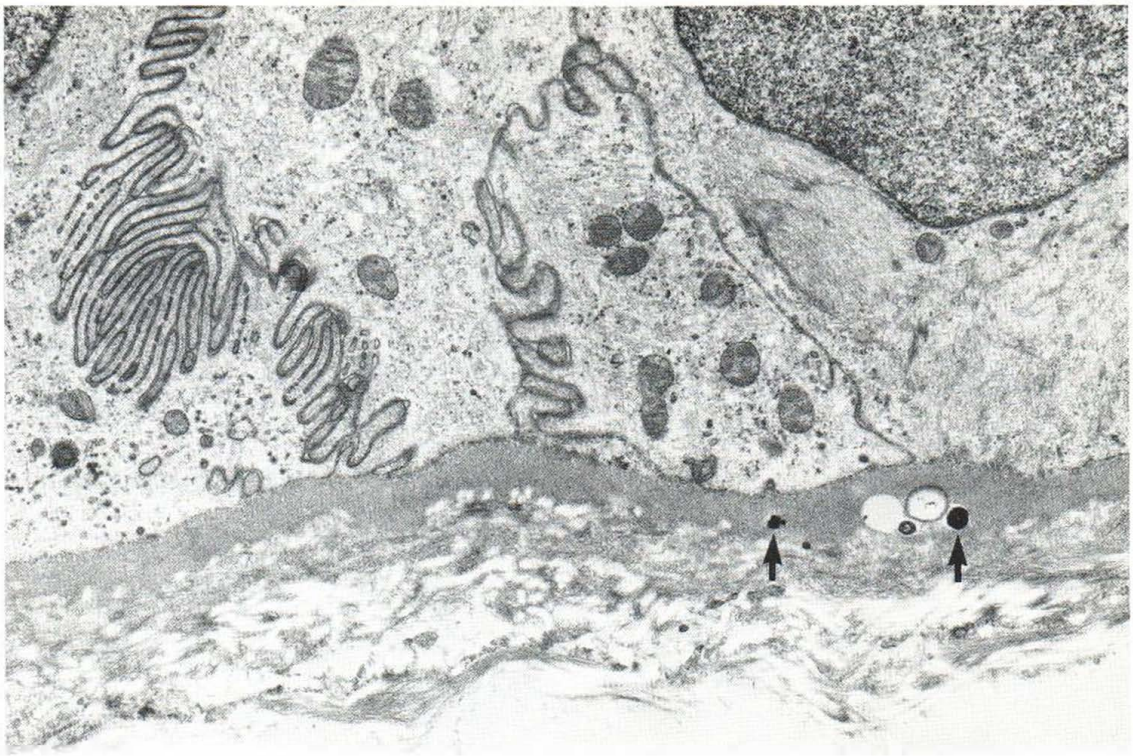
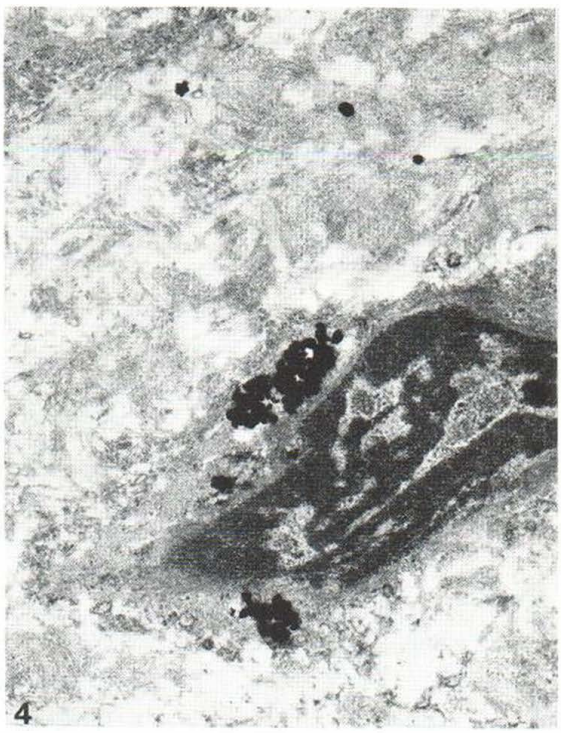
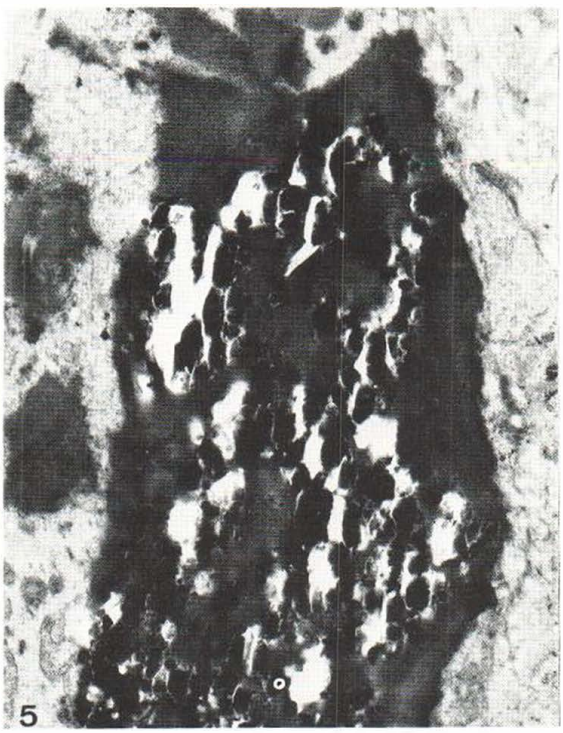


Fig. 3. Argyrosis. Biopsy from facial skin, electron microscopy. Only a few dense granules (arrows) are found, in the basement membrane of an eccrine sweat gland. 15 000 : 1.





Figs. 4 and 5. Silver-blue nails. Nail bed biopsy, electron microscopy. *Fig. 4* shows aggregates of silver granules within a macrophage and a few isolated coarse granules in an elastic fibre. 22 000 : 1. *Fig. 5* demonstrates a large, irregular clump of extracellular electron-dense material. 17 000 : 1.

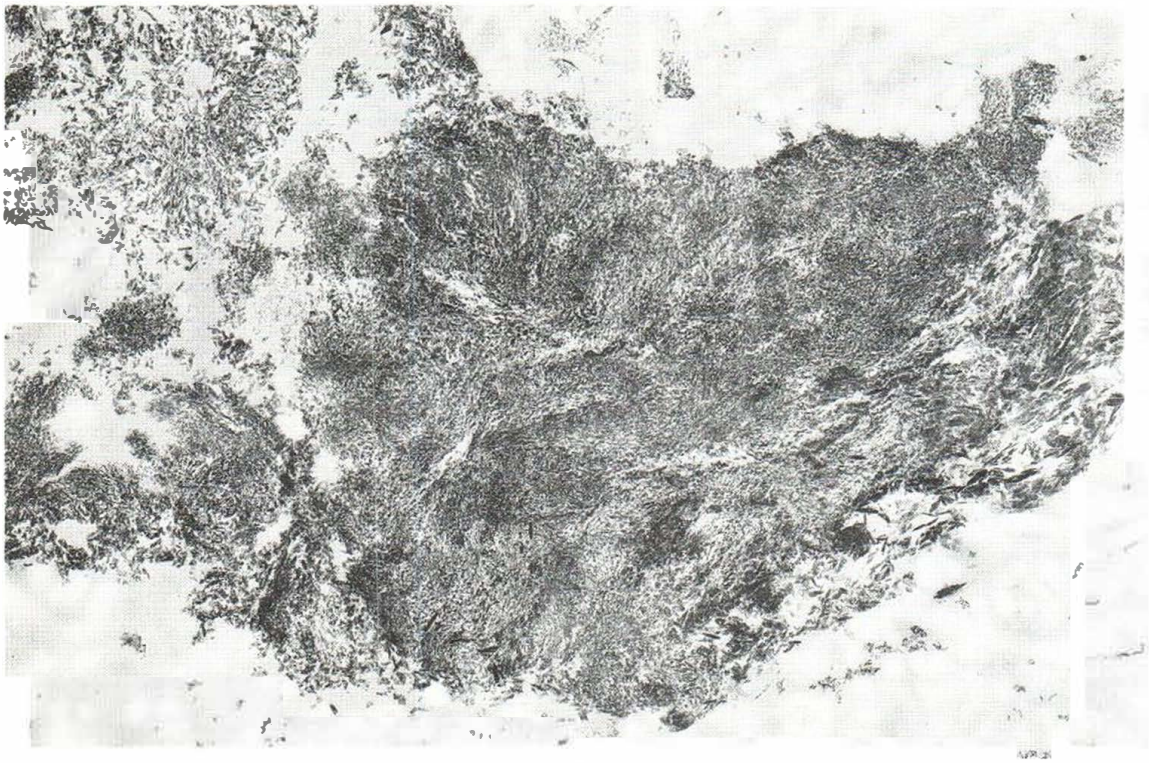


Fig. 6. Electron microscopy of nail bed biopsy material from silver-blue nail. Fine crystalline plates and spicules are seen within an elastic fibre. Unstained section. 40 000 : 1.

phagolysosomes (Fig. 4). Most of the material was found in the extracellular space, where it appeared in three different morphological forms: single coarse granules (Fig. 4), large accumulations of irregular clumps (Fig. 5), or crystalline plates and spicules (Fig. 6). The density of the material was the same in control sections not subjected to heavy metal staining (Fig. 6).

DISCUSSION

The rather dramatic blue discolouration of the nail beds ("silver-blue nails") in this patient prompted us to report the case and to review the literature on argyrosis.

The first medical writing on argyrosis dates back to Angelus Sala in 1647 (15). Argyrosis can be either local or universal.

Local argyrosis may be due to mechanical impregnation of small silver particles, e.g. in workers in the silver industry; or following dental work (silver-amalgam tattooing); or due to silver sutures, e.g. in abdominal surgery (personal communication, H. Neubert, M.D., Munich); or due to prolonged topical application of silver nitrate containing topical remedies such as eyedrops. Rarer sources of silver are topical treatment with silver nitrate or silver protein in burn patients, nasal drops, bladder irrigations, or wound dressings.

Universal or systemic argyrosis was common when silver-salvarsan or Kollargol®[1] (15) injections were still *en vogue*. Other exotic sources were inhalation of silver dust in industrial operations, and in the manufacture of silver nitrate. Silver was widely used in the 18th century for tabes dorsalis, and epilepsy. Not uncommonly this resulted in universal argyrosis with greyish discolouration of the skin, larynx, intestinal tract, peritoneum, kidneys, testicles, and liver; but this discolouration was virtually absent in bone, cartilage, epidermis with adnexa, and the CNS except for the plexus choroidalis.

Silver intoxication in modern times results from industrial hazards, such as silver mining or the mak-

[1] Out of trade

Table II. *Studies of argyria*

Author(s) Ref. & Year		Clinical description	Nail involvement mentioned	Biopsy	Electron microscopy	Comment
Arzt & Zieler, 1935	2	+	+	+	0	
Bearn & McKusick, 1958	5					
Birmingham, 1971	6	+	0	0	0	
Buckley, 1963	7	+	0	+	+	Electron microprobe X-ray analysis
Burke, 1971	8	+	0	0	0	
Gans & Steigleder, 1957	13	+	0	+	0	
Harker & Hunter, 1935	14	+	+	+	0	Autopsy
Hochleitner, 1959	15	+	0	0	0	
Hönigsmann, Konrad & Wolff, 1973	16	+	0	+	+	Emission spectroscopy
Koplon, 1966	18	+	+	+	0	
Korting & Denk, 1974	20	+	+	0	0	
Nasemann, Rogge & Schaeg, 1974	22	+	0	+	+	
Pihl, 1968	24	0	0	+	+	No studies in human skin, various animals used
Present report		+	+	+	+	Nail bed biopsy
Samman, 1972	25	+	+	0	0	
Schreck, 1960	26	+	0	0	0	
Siemund & Stolp, 1968	27	+	0	+	0	
Tzank & Sidi, 1949	30	+	0	0	0	
Weyhbrecht, 1953	31	+	+	+	0	
Whelton & Pope, 1968	32	+	+	+	0	Emission spectroscopy
Zaias & Baden, 1971	35	+	+	0	0	

ing of silver ware, jewellery, metal alloys, metallic films on glass and china, electroplating solutions, from photographic processing, and, of course, from medicine. A common source is antacids, as in our case.

The amount of silver needed to produce systemic argyrosis is estimated to range from 20 to 30 g but may occur with much lower amounts, such as 2–4 g (15). A recent case report mentions 4–5 g (27). In our patient at least 15 g were ingested.

Argyrosis was suspected in several of the reported cases on the basis of clinical evidence and medical history. The diagnosis was established by a positive history of silver exposure, and then by biopsy material which was studied by light- and dark-field microscopy (Table II), by emission spectroscopy (16, 32), or by electron microprobe X-ray analysis (7). Transmission electron microscopy, however, has been used by others (7, 16, 22) previously to demonstrate the metal (silver) particles.

In the present report, light-, dark-field and electron microscopy were successfully applied to demonstrate particulate deposits compatible with inorganic silver in facial and nail bed tissue. The ease with which a small nail plate biopsy sample can be taken for diagnostic purposes, with scarless healing, is demonstrated in our case.

As stated by many other authors (Table II), silver is histologically deposited mainly around elastic fibres. In our case, the silver was deposited mainly around the basement membranes of sweat ducts, hair follicles, and blood vessels. The elastophilia of silver is well known (24). Our light and electron microscopic findings are in agreement with this concept. Further proof that the deposited granular or crystalline material is silver can be obtained by bleaching the histological sections with 1–5% KCN solution. Apart from silver, other causes of nail bed and nail plate discolourations should be excluded (Table I). Universal nail changes should be distinguished from isolated involvement of one finger or toe nail. When all nails—or all the finger nails, at least—are involved, the closest resemblance to argyrosis is seen in Wilson's disease (5), ochronosis (12), hydrargyrosis (9, 22, 34), and in patients who take antimalarial drugs (3, 21, 29). A good differential diagnosis for the involvement of a single nail or occasionally two or three nails is nevus cell nevi (8) or melanoma (17, 23).

Treatment of argyrosis, which is of cosmetic concern and causes the patient no medical disability is practically impossible. The silver deposits are permanent. We have compared colour photographs of the nails in our patient taken 6 months after the initial visit, and have not detected any difference in the silver-blue discolouration. In the old literature, iontophoresis with iodide (20 gtt/day) was recommended, with the idea that the iodide ion could change the silver to a colourless silver iodine; this theory apparently had no clinical success. Chelating complexes and BAL have also been suggested.

It is still not known why light promotes the deposition of silver in the skin, or which wave lengths are responsible. It is noteworthy in our case that the light-protected toenails were normal in colour. In contrast, the sun-exposed nail beds and especially the lunulae contained much more silver deposit than facial skin. This may be explained by the regional variation in melanocyte distribution. The facial skin of our patient was well-tanned (skin type IV). Nail beds and lunulae are not pigmented. The nail plate provides sufficient protection against sun tanning UVB. Long-wave UVA can penetrate through the nail plate (personal data) as demonstrated in phototoxic onycholysis. Thus, from this clinical case, one can assume that UVA is responsible for the precipitation of metallic silver in light-exposed skin of argyrosis patients.

ACKNOWLEDGEMENTS

Miss Elfriede Januschke provided careful technical assistence.

The Deutsche Forschungsgemeinschaft kindly supported this work.

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Received August 9, 1976

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