

Ancient neurofibromatosis

SIR — Pre-mediaeval descriptions of neurofibromatosis type 1 are unknown. Our extensive review of early artworks from many civilizations has revealed possibly the earliest known model of neurofibromatosis in the form of a statue from Hellenistic times.

Neurofibromatosis type 1 (NF1), or von Recklinghausen neurofibromatosis, is an autosomal dominant condition characterized by multiple tumours including skin neurofibromas and brain gliomas. The earliest convincing medical descriptions occurred in the eighteenth century, preceding von Recklinghausen's classic monograph^{1,2}. Earlier portrayals may occur back to mediaeval times^{2,3}.

The scarcity of pre-Renaissance models of NF1 is surprising from a clinical and genetic standpoint. The skin manifestations make NF1 one of the most externally distinctive inherited diseases, surely of great fascination to early physicians and scholars. NF1 is also one of the most common inherited diseases, with a frequency of 1 in 3,000–4,000, and affects all ethnic types. Rarity in early civilizations is unlikely for several reasons. First, the prevalence of NF1 has remained steady, with the high rate of spontaneous mutation balancing reduced biological fitness⁴. Second, there is no founder effect (unlike cystic fibrosis, for which the initial mutation can be traced back). Finally, there is phylogenetic evidence that the NF1 gene, and therefore the disease itself, is ancient. The NF1 gene is believed to be a tumour-suppressor gene and may be crucial in growth regulation⁵. It contains critical regions that are highly conserved throughout the animal kingdom and in yeasts⁶. We undertook a survey of antique iconographic illustrations, art recordings and ancient medical texts, and have found a statue dating from the Hellenistic era that may represent the first known medical depiction of NF1.

Our statue appears as a photograph in ref. 7 showing a healthy muscular male with multiple skin nodules distributed over the entire visible torso and limbs. The nodules are smooth and sessile, not pedunculated. The limited differential diagnosis includes multiple angioliomas, familial epidermal cysts or lipomas; metastatic carcinoma, skin malignancy, leprosy, syphilis and onchocerciasis. The first three conditions are extremely rare — although lipomas are common, multiple forms as prolific as seen on the statue are exceptional. This person does not appear

to be wasted from malignant disease. Furthermore, the skin lesions neither have the correct appearance for leprosy or syphilis nor typical distribution for onchocerciasis (mainly over bony prominences). Both on appearance and likelihood of disease occurrence, the model is most representative of NF1.

The statue as it appears is labelled as a votive offering⁷. Unfortunately this statue has been lost since the Second World War⁸ so that no modern evaluation could be performed. Votive offerings were grateful gifts to the god Aesculapius from the patient. They typically represented healthy or cured body parts, often as



carved tablets or sculptures. As this statue clearly depicts a pathologic state, a more attractive hypothesis is that it forms part of a known collection of similar statues

illustrating various diseases. These statues were manufactured in Smyrna on the Ionian coast during the Hellenistic period⁹. They were clearly not votive offerings, but instead were part of a repertoire of didactic material dedicated to diagnostic training for the scholars of the local Hippocratic medical school¹⁰. Our statue may have been an early three-dimensional teaching aid!

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Scum summary

SIR — In response to our Scientific Correspondence¹, Lewin speculated² that the main components of tea scum are epidermal waxy lipids removed from the tea leaves by boiling water. This hypothesis does not explain why no scum forms when tea leaf is infused with hot distilled water, distilled water containing calcium chloride or soft water — or why tea scum always forms in temporary hard water, even when instant tea, which contains no insoluble waxy components, is used.

Jones³ and Enzweiler and de Oliveira⁴, on the other hand, believe the brown film on tea is formed by the physical³ adsorption of coloured tannin on calcium carbonate which (we confirm) forms on the surface of hot temporary hard water. Although this hypothesis is nearer the mark, it does not explain why the formation of the dark film is greatly dependent on the oxygen content of the atmosphere above the tea brew^{1,5}; or why the tea scums we have analysed⁶ contain 3–7 wt % calcium and 24–40 wt % carbon whereas the composition expected from CaCO₃ plus an adsorbed layer of tea polyphenolics would be just under 40 wt % Ca and just over 12 wt % C.

It is clear from the above evidence, together with other experimental findings^{5,6}, that tea scum consists mainly of insoluble oxidized tea polyphenolics together with calcium carbonate.

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