

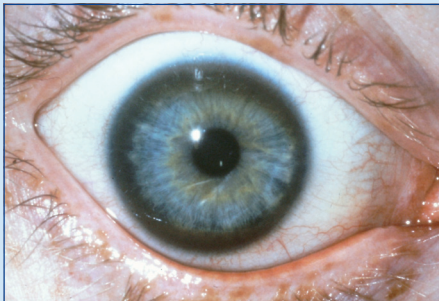
# The Kayser–Fleischer ring

## Introduction

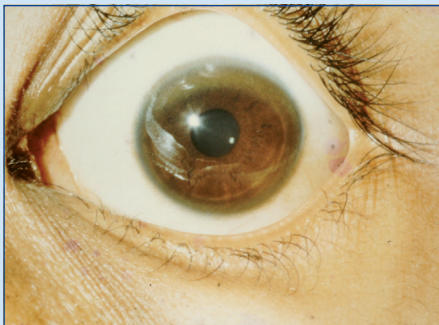
The Kayser–Fleischer ring is a deposit of copper, as a granular copper proteinate, in Descemet’s membrane of the cornea. The copper nature of the pigmented ring was established by Gerlach and Rohrschneider in 1949. In appearance the ring circles the periphery of the iris. Viewed in patients with a blue iris the ring always appears brown (*Figure 1*), when viewed over a brown iris it may sometimes appear grey (*Figures 2 and 3*), and when viewed under infrared light the ring appears green. On occasions it may be accompanied by a sunflower cataract.

The rings were described first by Kayser in 1902 and a year later by Fleischer in patients with a diagnosis of pseudosclerosis. For many years the rings were believed

**Figure 1. A very obvious complete brown ring seen over a blue iris.**



**Figure 2. Ring seen over a brown iris: the pigment is most obvious in the segment from 12 to 6 o’clock.**



to be diagnostic of Wilson disease (hepatolenticular degeneration), but it is now known that they can be present in patients with primary biliary cirrhosis or other forms of long-standing liver disease with biliary retention (Fleming et al, 1975, 1977).

The copper deposit does not always form a complete ring. Copper deposition is seen first at 12 o’clock, then at 6 o’clock (*Figure 4*). These arcs then spread laterally, eventually joining up to form a complete ring. The copper deposition extends from the margin centrally to varying depths, depending on the duration of the illness, seldom exceeding 5 mm. The deposits are heaviest peripherally fading centrally. In patients treated with chelating (decoppering) agents the rings fade, first being broken laterally then fading to small top and bottom crescents before finally disappearing completely (*Figure 5*) (Walshe, 2011). As the copper is removed the deep surface of the cornea appears to be scarred or pitted much like beaten metal. This is a valuable sign that treatment is effective.

Cairns and Walshe (1970) postulated that the deposition of copper first in the

**Figure 3. The ring appearing grey seen over a brown iris.**



**Figure 4. A broken ring seen as top and bottom crescents.**



superior and inferior crescents was a result of the vertical flow of the copper-bearing aqueous in the anterior chamber of the eye leaving these areas irrigated more freely with metal-bearing fluid.

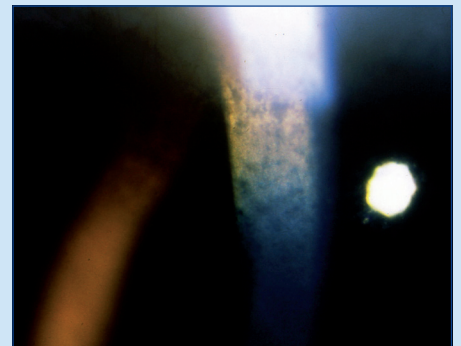
In the view of Scheinberg et al (1986) and Scheinberg and Sternlieb (1984) copper deposition is always present in the cornea of patients with neurological Wilson disease, but it may or may not be present in patients with the presymptomatic and hepatic forms of the disease. Occasional reports of patients with neurological disease not having such rings may be a result of misdiagnosis (about one third of patients referred to the author’s Wilson disease clinic were incorrectly diagnosed), may be the result of obscuring of the ring by an arcus or the result of failure to see a faint ring over a brown iris by an inexperienced observer. When doubt exists the eye should always be examined with a slit lamp and gonioscope (*Figure 6*).

Exceptionally rarely false Kayser–Fleischer rings have been reported –

**Figure 5. The eye of a well-treated patient showing no sign of residual pigment.**



**Figure 6. Slit lamp and gonioscope picture of copper pigment in granular form deposited in Descemet’s membrane.**



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Cairns and Walshe (1970) described one such patient in some detail. In this case the pigment was homogeneous, not granular and was not deposited in Descemet's membrane; it required a slit lamp examination to establish the differences. The false rings are probably composed of melanin.

## Examination of the eye

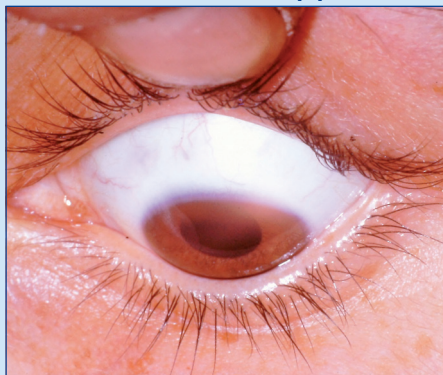
The eye should be examined for the presence of Kayser–Fleischer pigment in all children and young adults with a neurological or hepatic presentation. It is difficult to give an upper age limit cut off as it is now becoming clear that Wilson disease is occasionally found in patients well into middle age or, very rarely, even older. This may well be a question of awareness as the diagnosis of Wilson disease has, hitherto, not been sought in this age group.

It must be remembered that Wilson disease is genetically determined by a mutation on a P type ATPase – it is autosomal recessive and is coded on chromosome 13q14. If the iris is blue and the ring complete identification is simple (*Figure 1*). If the iris is brown the task can be more difficult; in such cases the eye should be viewed from above with a good beam of light. The brown pigment can then be seen over the black of the pupil (*Figure 7*) and this can be confirmed by slit lamp examination.

## Differential diagnosis

The differential diagnosis between a true and a false Kayser–Fleischer ring depends upon slit lamp and gonioscopic examination by an experienced observer but the latter are so rare that this is unlikely to present a problem. Chemical examination

**Figure 7. Oblique view of the ring, seen as a faint brown fuzz over the black of the pupil.**



of the blood to assess the concentrations of copper and caeruloplasmin, which are always depressed in Wilson disease, should settle this difficulty. The finding of the Kayser–Fleischer ring is a valuable early aid to diagnosis but it is not always present in the presymptomatic and hepatic stages of the disease. The diagnosis must always be conformed by finding the abnormalities of copper handling typical of the disease.

As Wilson disease is one of the very few chronic, fatal diseases of the brain and of the liver that is amenable to treatment it is essential to determine whether the patient's signs and symptoms are caused by Wilson disease, by primary biliary cirrhosis or by some other form of chronic liver disease with prolonged cholestasis. Unlike Wilson disease, biochemistry should give a clear diagnosis in all other forms of chronic liver disease, as reported elsewhere (Walshe, 1984), the caeruloplasmin and serum copper are markedly elevated (*Table 1*). Urine copper and hepatic copper concentrations are of much less diagnostic value in this

situation as there can be much overlap between the two diseases. **BJHM**

*Conflict of interest: none.*

- Cairns JE, Walshe JM (1970) The Kayser Fleischer ring. *Trans Ophthalm Soc UK* **90**: 187–90
- Fleischer B (1903) Zwei weitere falkle von grunliche verfarbung der kornea. *Klin Mbl Augenheilk* **41**: 489–91
- Fleming CR, Dickson ER, Hollenhorst RW, Goldstein NP, McCall JT, Baggenstoss AH (1975) Pigmented corneal rings in a patient with primary biliary cirrhosis. *Gastroenterology* **69**: 220–5
- Fleming CR, Dickson ER, Wahner HW et al (1977) Pigmented corneal rings in non Wilsonian liver disease. *Ann Intern Med* **86**: 285–8
- Gerlach W, Rohrschneider W (1949) Besteht das Pigmet des Kayser-Fleischeren Hornhautringes aus Sliber? *Klin Wochenschr* **13**: 38–9
- Kayser B (1902) Über einen Fall von angeborener grünlicher Verfärbung des Cornea. *Klin Monatsbl Augenheilk* **40**: 22–5
- Scheinberg IH, Sternlieb I (1984) *Wilson's Disease*. WB Saunders Company, Philadelphia
- Scheinberg IH, Sternlieb I, Walshe JM (1986) Wilson's Disease and Kayser Fleischer Rings. *Ann Neurol* **19**(6): 613–14
- Walshe JM (1984) Copper: Its role in the pathogenesis of liver disease. *Semin Liver Dis* **4**: 252–63
- Walshe JM (2011) The Eye in Wilson Disease. *Q J Med* **104**: 451–3

**Table 1. Caeruloplasmin and serum copper values in healthy individuals and patients with Wilson disease**

|                              | Healthy individuals | Wilson disease |
|------------------------------|---------------------|----------------|
| Serum copper (ug/dl)         | 90–120              | 0–90           |
| Serum caeruloplasmin (mg/dl) | 25–45               | 0–25           |
| 'Free' serum copper (ug/dl)  | <10                 | >10            |

## KEY POINTS

- Always remember to examine the eyes in patients with obscure neurological or hepatic disease, particularly children and young adults.
- Patients with neurological Wilson disease always have Kayser–Fleischer rings.
- The pigment does not necessarily form a complete ring but may be present as top and bottom crescents.
- The rings are brown when viewed over a blue iris, they may appear brown or grey over a brown iris.
- The rings cannot necessarily be seen in the presymptomatic and hepatic forms of Wilson disease.
- Wilson disease is fatal if not treated, it is essential to make the diagnosis.
- Missing the diagnosis can lead to expensive litigation.
- When looking for Kayser–Fleischer rings it is best to have a hand lens and a pocket torch with a good beam of light.