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# Clinical copper metabolism parameters in patients with retinitis pigmentosa and other tapeto-retinal degenerations

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SUMMARY Reports have appeared of abnormal copper metabolism in retinitis pigmentosa, and of a family with vitelliform retinal degeneration in which other members suffered from hepatolenticular degeneration. In the present study 15 patients with retinitis pigmentosa, 4 with various other retinal degenerations, and 1 with a family disposition to retinitis pigmentosa were examined. The copper concentration in serum and the coeruloplasmin concentration in plasma were found to be within normal limits. In 9 of the patients with retinitis pigmentosa the urinary excretion of copper per 24 hours was determined and was found to be normal. The results of the present study lend no support to the hypothesis of abnormal copper metabolism in retinitis pigmentosa.

In view of their findings in patients with retinitis pigmentosa of normal serum copper concentration, reduced plasma coeruloplasmin concentration, and increased urinary excretion of copper Gahlot *et al.* (1976) suggested that retinitis pigmentosa might be caused by a disorder of copper metabolism. We found it worthwhile to perform a similar study, as we were already engaged in metabolic studies of pigmentary retinopathies (Ehlers and Schønheyder, 1977), and because Brink (1974) had reported a family with vitelliform retinal degeneration in which several other members suffered from Wilson's hepatolenticular degeneration, well known as a disorder of copper metabolism.

## Material and methods

Twenty patients were included in this study (Table 1). In accordance with the case history and the results of ophthalmoscopy, perimetry, dark adaptation, and electroretinography the patients were classified in 2 groups. The first group (Table 1A) comprised 15 patients with retinitis pigmentosa. The second group (Table 1B) comprised 4 patients with various other retinal degenerations, and 1 patient (No. 18) who had a family disposition to retinitis pigmentosa but showed no evidence of retinal degeneration.

The copper concentration in serum and the coeruloplasmin concentration in plasma was deter-

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Table 1 *Material*

| | *Patient no.* | *Age in years* | *Sex* | *Diagnosis* |
|---|---|---|---|---|
| *A.* | 1 | 10 | female | Retinitis pigmentosa |
| | 2 | 12 | male | Retinitis pigmentosa |
| | 3 | 14 | male | Retinitis pigmentosa |
| | 4 | 15 | male | Retinitis pigmentosa |
| | 5 | 17 | female | Retinitis pigmentosa |
| | 6 | 17 | male | Retinitis pigmentosa |
| | 7 | 22 | male | Retinitis pigmentosa |
| | 8 | 27 | male | Retinitis pigmentosa |
| | 9 | 37 | female | Retinitis pigmentosa |
| | 10 | 51 | male | Retinitis pigmentosa |
| | 11 | 52 | male | Retinitis pigmentosa |
| | 12 | 57 | male | Retinitis pigmentosa |
| | 13 | 57 | female | Retinitis pigmentosa |
| | 14 | 61 | female | Retinitis pigmentosa |
| | 15 | 62 | male | Retinitis pigmentosa |
| *B.* | 16 | 14 | female | Tapetoretinal degeneration, uncertain type |
| | 17 | 15 | male | Stargardt degeneration |
| | 18 | 20 | female | Myopia |
| | 19 | 35 | female | Flecked retina syndrome |
| | 20 | 50 | female | Fundus albipunctatus |

Table 2 *Results*

| *Patient no.* | *Copper concentration in serum (μg/100 ml)* | *Coeruloplasmin concentration in plasma (g/l)* | *Copper urinary excretion (μg/24 h)* |
|---|---|---|---|
| *A.* 1 | 100 | 0·29 | — |
| 2 | 134 | 0·41 | 25 |
| 3 | 106 | 0·30 | 43 |
| 4 | 126 | 0·44 | — |
| 5 | 96 | 0·28 | — |
| 6 | 130 | 0·35 | 51 |
| 7 | * | 0·24 | 47 |
| 8 | 109 | 0·32 | — |
| 9 | 116 | 0·32 | — |
| 10 | 110 | 0·31 | 68 |
| 11 | 108 | 0·37 | 38 |
| 12 | 131 | 0·34 | 47 |
| 13 | 128 | 0·35 | 13 |
| 14 | 158 | 0·57 | 60 |
| 15 | 132 | 0·41 | — |
| *B.* 16 | 122 | 0·40 | — |
| 17 | 100 | 0·27 | — |
| 18 | 101 | 0·31 | — |
| 19 | 125 | 0·32 | — |
| 20 | 106 | 0·32 | — |
| Normal ranges (±2 SD) | Male 74 to 146<br>Female 83 to 159 | 0·18 to 0·42 | 9 to 80 |

*Sample lost in preparation

mined in all the patients by the methods described below. The urinary excretion of copper per 24 hours was determined in 9 of the patients with retinitis pigmentosa.

Copper concentration in serum was determined photometrically by the method of Jensen *et al.* (1964). By double determinations performed at intervals of one week the values could be reproduced with a standard deviation of 3·4 μg/100 ml, corresponding to about 3%. Urinary excretion of copper was determined by atomic absorption. The standard deviation was 9 μg/1. Coeruloplasmin concentration in plasma was determined by radial immunodiffusion by Manzini's method with a standard deviation of about 2·5%.

## Results

The findings are shown in Table 2. The concentration of copper was found to be within normal limits in all the patients examined, the average value being 117·8 (SEM 3·65) μg/100 ml. For coeruloplasmin all values except 2 were within the normal range. Patients 4 and 14 had raised concentrations. The average value was 0·346 (SEM 0·0164) g/l. The urinary excretion of copper per 24 hours was found to be within normal limits in all the 9 cases examined, the mean being 43·6 (SEM 5·60) μg/24 hours. It will be seen from the bottom two rows of Table 2 that even an age variation in the normal ranges of about 10–12%, as given by some authors, will not alter the findings of normal parameters.

## Discussion

The disorders of copper metabolism reported by Gahlot *et al.* (1976) in patients with retinitis pigmentosa, namely, reduced coeruloplasmin concentration and increased urinary copper excretion, were not found in the present study. Therefore the hypothesis that retinitis pigmentosa might be caused by an inborn error of copper metabolism is not supported.

Of course it is not possible from a limited study like the present to draw definite conclusions; moreover, the diagnosis of retinitis pigmentosa applies to conditions differing with regard to heredity, age of onset, severity, rate of progression, and coincidence with other diseases. Such differences were also evident among the cases classified as retinitis pigmentosa in the present series. It should also be realised that blood levels and urinary excretion are probably not a very sensitive way of investigating copper metabolism. Therefore the observations available so far do not exclude the possibility that some cases of pigmentary retinopathy, or perhaps certain stages in the degeneration, may be related to copper toxicity or to a disorder of copper metabolism.

### References

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