Urinary coproporphyrin isomer distribution was studied in 13 patients suffering from the Dubin-Johnson syndrome and several control groups. In patients with the Dubin-Johnson syndrome the isomer distribution was quite the reverse to that of normal persons. The urinary isomer distribution was in the normal range in patients with Gilbert's syndrome, hemolytic jaundice, and fatty liver. In many patients with different acute and chronic liver diseases, a clear deviation from the normal urinary isomer distribution was seen. There was, however, no overlapping with the Dubin-Johnson syndrome. Even the fecal coproporphyrin isomer distribution deviated significantly from the normal in favor of Isomer I.

It has been known since the end of the last century that an increased porphyrin excretion is a common finding in liver diseases (1). The increase of porphyrin excretion was later shown to be mainly due to coproporphyrin (2). A clear deviation from the normal distribution of urinary coproporphyrin Isomers I and III in many cases of liver cirrhosis, obstructive jaundice, and chlorpromazine jaundice has also been noted (3).

The purpose of this preliminary report is to demonstrate the value of urinary coproporphyrin isomer analysis when the syndrome described by Dubin and Johnson (4) is to be differentiated from other liver diseases and diseases which may cause intermittent jaundice.

Material and Methods

The material consisted of 13 patients suffering from the Dubin-Johnson syndrome. The controls were as follows: 30 healthy persons, 10 patients with Gilbert's syndrome, 3 with hemolytic anemia, 7 with viral hepatitis, 10 with obstructive jaundice, 15 with hepatic cirrhosis, 3 with fatty liver, 7 with cardiac jaundice, and 6 with jaundice due to...
metastatic growths in the liver. The diagnoses of the different diseases were based on the usual clinical criteria. The diagnoses were, however, confirmed by needle biopsy and/or laparoscopy in every patient suffering from the Dubin-Johnson syndrome, Gilbert's syndrome, fatty liver, and hepatic cirrhosis, except in 2 cases of hepatic cirrhosis.

The urinary coproporphyrin excretion and isomer distribution were determined as described in detail by Koskelo and Toivonen (5). Fecal coproporphyrin was determined according to Rimington (6). The isomer distribution of purified fecal coproporphyrin was determined by thin-layer chromatography in the same way as the isomers from the urine.

**Results and Comment**

The total urinary coproporphyrin excretion in healthy subjects averaged 67 μg./24 hr. (S.D. ± 23), and varied in patients with Dubin-Johnson syndrome from 27 to 278 μg./24 hr. It was clearly elevated in 4 out of 13 cases. The total excretion was normal in all patients suffering from Gilbert's syndrome, cardiac jaundice, and fatty liver, but was variable in all other groups studied, being above the upper limit of normal in the majority of cases. The analysis of the total urinary coproporphyrin excretion alone seems to be of no value in the differential diagnosis of the diseases studied.

The Isomer I excretion in healthy persons averaged 13.7 μg./24 hr. (S.D. ± 3.9), and that of Isomer III, 53.5 μg. (S.D. ± 20.2). The mean Isomer III excretion expressed as a percentage of the total was 78.2 (S.D. ± 5.8).

The isomer distribution in 13 cases of Dubin-Johnson syndrome was quite the reverse. The Isomer I excretion varied from 25 to 259 μg./24 hr. and that of Isomer III, from 2 to 27 μg. The Isomer III content was below 17% of the total in every case, the mean being 9%. In patients suffering from Gilbert's syndrome and hemolytic diseases the isomer distribution did not significantly differ from that of normal persons. In some—usually the most severe—cases of viral hepatitis, obstructive jaundice, hepatic cirrhosis, metastatic liver diseases, and cardiac jaundice a clear decrease of the proportional excretion of Isomer III was seen. There was, however, no overlapping with the Dubin-Johnson syndrome. The results are shown in Fig. 1.

The fecal coproporphyrin content in 16 control subjects varied from 2.5 to 13.2 μg./g. dry weight, the mean being 7.9 (S.D. ± 4.2). The mean Isomer III content was 32.8% (S.D. ± 11.3) of the total, and the range from 14 to 52%. The total coproporphyrin content in 6 patients with the Dubin-Johnson syndrome varied from 1.8 to 38.0 and
the mean was 9.7 \( \mu g/gm \) dry weight. The Isomer III content ranged from 11 to 32\%, the mean being 18.7\% of the total. A comparison of the mean values reveals a significantly lower fecal Isomer III content in patients with Dubin-Johnson syndrome \( (p > 0.001) \).

![Graph showing urinary coproporphyrin Isomer III content in Dubin-Johnson syndrome and other states.](image)

**Fig. 1.** Urinary coproporphyrin Isomer III content in Dubin-Johnson syndrome and other states.

It seems evident that, by urinary coproporphyrin isomer analysis, the Dubin-Johnson syndrome can easily be differentiated from other diseases that have to be taken into consideration when this syndrome is suspected. We are not able to explain the mechanism which affects the urinary coproporphyrin isomer distribution. Further studies are needed to clarify it.

**References**

4. Dubin, I. N., and Johnson, F. B., Chronic idiopathic jaundice with unidentified pigment in
