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EXCHANGEABLE COPPER - A NEW DIAGNOSTIC INDICATOR FOR WILSON'S DISEASE

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Introduction. Wilson's disease (WD) biochemical markers continue to evolve. Classical tests have their own limits (tab.1), and they are often insufficient to diagnose or exclude WD. The "free" copper was proposed as a diagnostic test, but it was showed a large overlapping of this parameter between non-WD subjects and WD patients. New biomarkers are being investigated.

Tab. 1 The limits of classical tests

	False negative	False positive
Serum ceruloplasmin	- In marked inflammation - 15-36% of children with WD *Overestimation* by immunologic assay - Pregnancy, oral contraceptives pill, Copper intoxication, Zinc deficiency, Cancer, Alzheimer's disease	- Protein-wasting states, acquired copper deficiency, severely impaired hepatic synthetic function, rare genetic disorders, neurological diseases, healthy heterozygotes WD, individually winter season
24-hour urinary copper	- Incorrect urine collection - Children without liver disease - Asymptomatic sibiling	- Hepatocelluar necrosis, other types of liver disease, copper contamination of the collection device, healthy heterozygotes

Purpose. The paper aims to analyze the bibliographic data on the new tools for diagnostic in WD, like exchangeable copper (CuEXC).

Material and methods. An advanced search was performed in the PubMed, and ScienceDirect databases, using the search English terms: *"Wilson's disease"*, *"diagnostic test"*, *"exchangeable copper"* and *"relative exchangeable copper"*.

Results. CuEXC is a new validated method for the direct determination of labile copper that can be correlated with the toxic fraction of copper and used to monitor treatment in Wilson patients. The relative exchangeable copper (REC) - the ratio of CuEXC/total serum copper – is the best biomarker for the diagnosis of WD showing 100% sensitivity and 100% specificity. Studies confirm that a REC value >18.5% appears to be a highly discriminatory tool to differentiate WD between controls, presymptomatic patients, heterozygotes, and patients with non-Wilsonian liver disease, in cirrhosis and cholestasis, both in adults and in children. Family screening in asymptomatic subjects observed that REC determination significantly differentiated subjects non-WD from WD patients with a cutoff of 15%.

Conclusions. CuEXC proved a helpful contribution in starting quickly the treatment without waiting for genetic testing results. Being a tool with high sensitivity and specificity, the determination of REC can be useful, reliable, rapid, and easy to set up to confirm or exclude WD in both adults and children, in carriers or asymptomatic patients.

Keywords. Wilson's disease, diagnostic test, exchangeable copper.