Summary

Lynch syndrome (LS), formerly known as hereditary nonpolyposis colorectal cancer (HNPCC) is a familial cancer syndrome with an autosomal dominant inheritance pattern. Its genetic basis is most commonly a germline mutation in one of the mismatch repair (MMR) genes, that are responsible for correction of errors ocurring during DNA replication. Dysfunction of this repairing system leads to the formation and progression of tumors, especially colorectal cancer (CRC). According to the literature LS represents 3-5 % of all CRC.

Additional extracolonic tumors associated with LS include endometrium, ovary, stomach, small bowel, pancreas, hepatobiliary tract, upper uroepithelial tract, brain and cutaneous sebaceous tumors. Early age of onset is a typical feature of LS-associated tumors, in comparison with general population. Malignancy is often the first manifestation, therefore the LS diagnosis is important not only for the individual patient and his next management, but also for his family members. An exception is represented by the formation of cutaneous sebaceous tumors prior to internal malignancy in one of LS phenotypic variant, called Muir-Torre syndrome.

Properly selected screening methods can prevent the formation of malignant tumors by early detection of their premalignant lesions, or at least early stage of malignant tumors. Molecular genetic confirmation of germline mutations is required for the diagnosis of LS. Due to financial and technical demands of this examination it is necessary to select appropriate patients using other auxiliary examination methods. These methods focus on identifying so-called microsatellite instability (MSI) emerging due to MMR system dysfunction. MSI detection is provided either indirectly by immunohistochemical detection of the most important MMR proteins (MLH1, PMS2, MSH2 a MSH6) or directly by genetic analysis of MSI. Application of these methods can be targeted by evaluation of histomorphologic features of MSI-associated tumor. Molecular genetic analysis of *BRAF* V600E mutation and *MLH1* promoter hypermethylation is further performed to exclude somatic (epi)mutations causing MSI in sporadic cancers.

Synchronization of examination methods with regard to laboratory possibilities and functional cooperation with clinicians, especially surgeons, internists, oncologists and clinical geneticists are the most important factors in LS diagnosis and management of the patient and his family members.