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Abstract: 25-30% of families fulfilling the criteria for hereditary diffuse gastric cancer have germline mutations of the CDH1 (E-cadherin) gene. In light of new data and advancement of technologies, a multidisciplinary workshop was convened to discuss genetic testing, surgery, endoscopy and pathology reporting. The updated recommendations include broadening of CDH1 testing criteria such that: histological confirmation of diffuse gastric criteria is only required for one family member; inclusion of individuals with diffuse gastric cancer before the age of 40 years without a family history; and inclusion of individuals and families with diagnoses of both diffuse gastric cancer (including one before the age of 50 years) and lobular breast cancer. Testing is considered appropriate from the age of consent following counselling and discussion with a multidisciplinary team. In addition to direct sequencing, large genomic rearrangements should be sought. Annual mammography and breast MRI from the age of 35 years is recommended for women due to the increased risk for lobular breast cancer. In mutation positive individuals prophylactic total gastrectomy at a centre of excellence should be strongly considered. Protocolised endoscopic surveillance in centres
with endoscopists and pathologists experienced with these patients is recommended for: those opting not to have gastrectomy, those with mutations of undetermined significance, and in those families for whom no germline mutation is yet identified. The systematic histological study of prophylactic gastrectomies almost universally shows pre-invasive lesions including in situ signet ring carcinoma with pagetoid spread of signet ring cells. Expert histopathological confirmation of these early lesions is recommended.