

ICES IDENTIFICATION LEAFLETS FOR DISEASES AND PARASITES OF FISH AND SHELLFISH

Leaflet No. 61

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Recommended format for purposes of citation:

Feist, S. W., and Lang, T. 2014. Liver tumours in flatfish. ICES Identification Leaflets for Diseases and Parasites of Fish and Shellfish. Leaflet No. 61. 5 pp.

Series Editor: Stephen Feist. Prepared under the auspices of the ICES Working Group on Pathology and Diseases of Marine Organisms.

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ISBN 978-87-7482-147-2

ISSN 0109–2510

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Susceptible species

Liver tumours (neoplasms) in flatfish have been reported from several species from North America (Myers *et al.*, 1987, 1990, 1998a, b; Moore and Stegeman, 1994), including the English sole (*Parophrys vetulus*) and starry flounder (*Platichthys stellatus*), and European waters (Bucke and Feist, 1984; Vethaak and Jol, 1996; Vethaak and Wester, 1996) where the principle species exhibiting liver tumours are the European flounder (*Platichthys flesus*) and the dab (*Limanda limanda*).

Disease name

“Liver nodule” is the term used for macroscopic lesions visible on the surface of the liver which are, according to standard technical guidelines, greater than 2 mm in diameter (Bucke *et al.*, 1996; Feist *et al.*, 2004). Microscopic examination of histological sections of these nodules is used to eliminate the possibility that they may be inflammatory lesions attributable to parasitic infections and to discriminate between non-malignant neoplasms (hepatocellular adenoma, cholangioma, hemangioma, pancreatic acinar cell adenoma) and malignant neoplasms (hepatocellular carcinoma, cholangiocarcinoma, hemangiosarcoma, pancreatic acinar cell carcinoma). Using the OSPAR terminology, cases of liver nodules histologically confirmed as non-malignant or malignant tumours are called “macroscopic liver neoplasms” (OSPAR, 2008).

Aetiological agent

Liver tumours and their pre-stages (foci of cellular alteration) are associated with long-term exposure to anthropogenic carcinogenic contaminants, in particular polycyclic aromatic hydrocarbons (PAHs) and polychlorinated biphenyls (PCBs) and their metabolites. Route of exposure is thought to be direct via exposure to contaminated sediments, but more likely through the diet via invertebrates which are unable to metabolize and thereby bioaccumulate these compounds.

Geographical distribution

Liver tumours have been recorded in European flounder, which are commonly found in inshore and estuarine locations along North Sea coasts but have rarely been seen in Baltic flounder (Stentiford *et al.*, 2003; Lang *et al.*, 2006). Lesions in dab have routinely been recorded throughout the North Sea, but particularly in the Dogger Bank and German Bight regions. However, the prevalence has declined during the past decade in the North Sea (Vethaak *et al.*, 2009). Dab exhibiting liver tumours and pre-neoplastic lesions have also been detected in the Irish Sea Liverpool Bay region.

Associated environmental conditions

The occurrence of liver tumours and pre-neoplastic lesions does not appear to be directly influenced by environmental conditions such as salinity or temperature.

Significance

It has been demonstrated that the occurrence of liver tumours increases with age but also that there are clear differences in prevalence between regions and that ‘age at

onset' for pre-neoplastic and neoplastic lesions also differs (Stentiford *et al.*, 2010). Prevalence of liver neoplasia can reach 40% in dab ≥ 7 years of age (Stentiford *et al.*, 2010), but the prevalence in dab and flounder populations in the North Sea has steadily declined in recent years (Vethaak *et al.*, 2009). The reason for this has not been established but numbers of older dab of larger size classes (≥ 20 cm) known to be more susceptible to lesion occurrence have been declining in most North Sea areas and in Dogger Bank and German Bight areas in particular.

Gross clinical signs

Liver nodules appear as discrete macroscopic lesions on or raised above the surface of the liver. Larger lesions often have conspicuous vasculature and different colouration to the surrounding liver tissue. Multiple lesions can occur and in extreme cases, many lesions can be present throughout the liver. There are no external macroscopic signs in fish with liver nodules although co-occurrence with skin ulcers, hyperpigmentation, epidermal hyperplasia/papilloma and emaciation has been recorded.

Control measures and legislation

There is currently no evidence to support an infectious aetiology. Macroscopic liver neoplasms, pre-neoplastic lesions and other histopathological liver changes are incorporated in the OSPAR JAMP guidelines for general and contaminants-specific biological effects monitoring for the OSPAR Coordinated Environmental Monitoring Programme (CEMP; OSPAR, 1997, 2005, 2008) and the current suite of biological effects of contaminants tools for use in the assessment of Good Environmental Status (GES) under Descriptor 8 (contaminants are not at levels giving rise to pollution effects) of the Marine Strategy Framework Directive (MSFD; Lyons *et al.*, 2010).

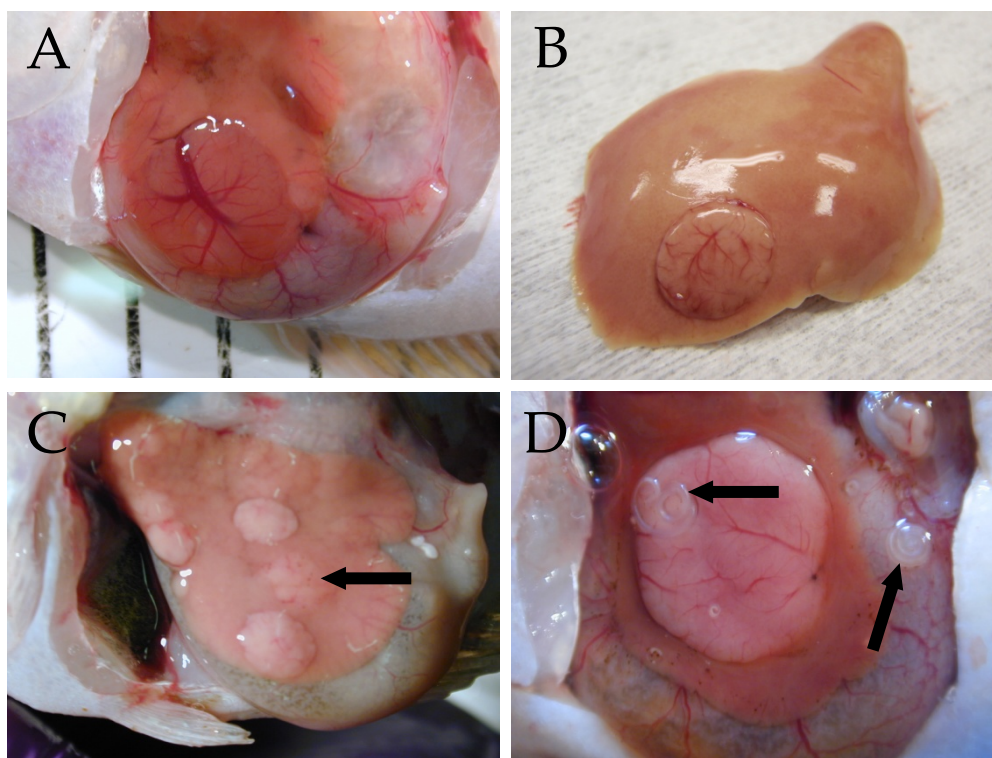
Diagnostic methods

Methods for sampling, macroscopic examination, histological processing and evaluation are provided by Feist *et al.* (2004). Guidelines for quality assurance for the diagnosis and reporting of data on liver pathology are provided under the Biological Effects Quality Assurance in Monitoring (BEQUALM) programme (<http://www.bequalm.org/>).

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Figures A-D showing the macroscopic variability of liver tumours in dab. A: Discrete 'nodule' with relatively dark colouration compared to the rest of the liver and with characteristically prominent vascularisation. B: Single nodule protruding from the surface of a dissected liver, again showing increased and enlarged blood vessels. C: Multiple pale staining nodules protruding from the surface of the liver or with the majority of the lesion embedded in the liver (arrow). D: Large discrete 'nodule' of pale colouration compared to the rest of the liver. Note the presence of anisakid nematodes on the surface of the lesion and intestine (arrows).

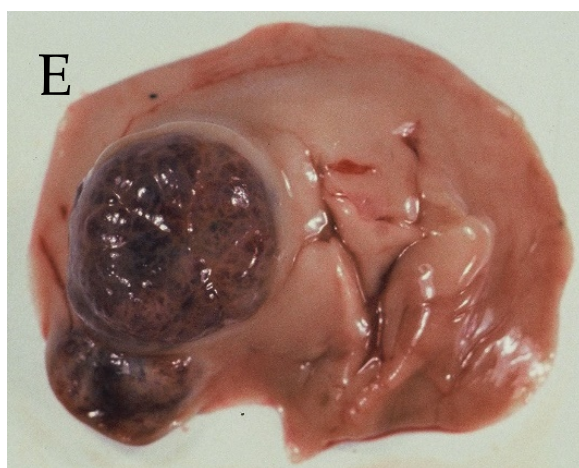


Figure E shows a large, rarely occurring dark variant of liver nodule with prominent protrusion of neoplastic tissue on the underside of the liver.

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