A disease affecting the exocrine pancreas of Atlantic salmon has been found in the stock of several sea farms. The effects of the disease vary from site to site and from year to year but experience now indicates this disease has a significant economic impact. The acute stage of the disease, characterised by a generalised exocrine pancreatic necrosis, has been observed between the third and tenth months after entry to sea water. Most fish recover from the acute stage (>95%) but survivors fall into two groups, one where fish regenerate exocrine tissue rapidly and subsequently show no evidence of the disease and the other (20-30%) where destruction of the exocrine is complete leaving either a fibrotic strand of tissue or a complete absence of pancreas over a large caecal area. The latter group do not feed for 2-3 months and become emaciated. At the end of this period a proportion regenerate the pancreas, start feeding and in consequence growing again. The remainder (~15%) of the original population have to be culled. An account of the pathology, epidemiology and progress in studies of the cause of the disease is given.
INTRODUCTION

An apparently unrecorded disease of farmed Atlantic salmon has become noticeably prevalent in sea cage sites since it was first investigated in January 1977. The number of known affected sites is now nine out of 46 recorded sea farm sites and may be more. The severity of the disease which has some unusual features is quite variable. However, because it affects fish in their first sea year it inevitably has economic consequences which can be severe.

This report describes the disease condition and discusses the continuing investigation of its causes.

Pathology

Sequential studies of gross signs and histological changes by light and electron microscope have been made of Atlantic salmon smolts from entry to sea water to recovery, culling or death from this disease at a sea cage site in the Western Isles. The pathogenesis of the disease has been divided into three main phases based on light microscopy of histological changes in the pancreas, a pre-acute phase, an active phase involving (often haemorrhagic) pancreatic necrosis and a post-acute phase.

1. Pre-acute phase. Smolts are transferred to sea water mostly in May. There were no gross signs of abnormality during this phase which lasted until August or September. The only organ architectural changes considered pathological involved the pancreas in which two changes were observed. The relationship of one to the other has not been established.

The first change was noticed approximately 4-6 weeks after entry to sea water. Pancreas acinar cells had a shrunken appearance, were densely basophilic with limited amounts of zymogen granules which also appeared abnormal by having condensed into larger globules. By July and August this change was not evident.

The second change was noticed prior to the onset of phase two. Significant numbers of acinar cells developed non-staining vacuoles. Concurrently, other groups of acinar cells had become very weakly basophilic, swollen, and ultimately the cell margins disappeared to give syncitial formations.

Electron microscopy of these weakly basophilic, swollen cells revealed two distinctive features, loss of spherical endoplasmic reticulum to extensive plate-like formations and a response by local fibrocytes to produce collagen apparently in response to breaks in the acinar cell membrane.

Other elements of the pancreas including fat cells, Islets of Langerhans, blood vessels, nervous tissue, exocrine ducts, ductal cells and fibrocyte elements appeared within the normal range. However, comparing the organ as a whole with sections from older and younger salmon there is an impression that the numbers of acinar cells are less than expected and we judged this a hypoplasia of the acinar elements.

2. The active phase. This phase commonly occurred in August or September but has been seen to occur in some years at this site as late as November and at other sites early in the following year. In some years it is marked by morbidity which has never been more than 5% and is commonly less than 1% and sometimes not apparent at all. Affected cage populations are inappetant at this time. Excessive jumping behaviour often characterises this phase.
Internal examination of moribund fish showed a line of haemorrhage between each caecum where pancreas tissue is situated and which discoloured the adjacent body cavity wall. Histology of moribund animal tissues revealed an acute and generalised haemorrhagic pancreatic necrosis. The gut was often filled with the necrosing pancreatic elements which had presumably discharged through the pancreatic ducts to the common duct and into the duodenum. Random sampling of one population over a four week period indicated all fish were suffering the disease but the severity differed markedly between fish. In some, the necrosis was much slower and less generalised, haemorrhage was absent and it was never clear if all acinar elements were subject to necrosis. In such fish leucocyte responses could sometimes be seen.

The effects of acinar cell necrosis on other pancreas elements was considered proportional to the acuteness and generalised degree of the necrosis. At the extreme the whole organ disappeared between individual caeca while at the other extreme islets, blood vessels and exocrine ducts were preserved in a fibrotic stringy matrix in which an occasional acinar cell or group of cells might be found.

The livers showed an occasional clearly delineated eosinophilic body in individual cells, but at most only 10% of liver cells in individual fish were so affected at the peak of the acute phase. Although these bodies stained positive by Feulgen stain commonly used for detection of virus inclusion bodies, electron microscopy revealed continuous amorphous material devoid of any structure and it was concluded they were hyaline bodies. There was marginal evidence of leucocyte hyperplasia in the head and mid-kidney. Erythrocyte cell morphology was normal.

3. Post-acute phase. As indicated in phase 2 a wide range of responses were observed in surviving fish. Those fish returning to feeding behaviour in late September and October had near normal pancreas tissues. Approximately 70-80% of the population recovered although individual cage populations were often much more severely affected eg only 50% feeding. Non-feeding fish were characterised by a total absence of pancreas tissues or a fibrotic strand of tissue containing varying amounts of islet tissue, blood vessels, leucocytes engaged in clearing necrotic debris and acinar ducts complete with epithelial cells lining them. These fish become progressively thinner throughout the winter although the farm reported that by spring approximately 50% of thin fish would return to feeding and start growing. After four years of the disease the farm staff had learned that by April/May remaining thin fish were unlikely to recover and they are culled at that time.

It is difficult to generalise about losses from this disease because the pattern is different in successive years at this site. Farm staff consider losses due to mortality during the acute phase are less than 2%. Culling may account for 15% and another 15% may lose 6-8 months growth. The remainder may lose 1-2 months growth. Seen in these terms it is of significant economic consequence.

Epidemiology

Since the disease was first recognised in December 1976 it has been seen in another eight sea cage sites. Once recognised it is seen as an annual event at sea farm sites in salmon in their first sea year. At the site where most studies have been conducted, it occurs between late July and December. In 1983 it occurred later in the 1982 stock but precisely when is uncertain because thin fish were not recognised until March. Other sites have experienced the disease later than December and as early as June. One site has been abandoned because of the severity of the condition whereas at others the numbers of thin fish are perhaps less than 5%.
No obvious common factors are shared between sites except all are cage sites and all are in the northern half of the salmon farming area.

It has been proposed that the most severely affected sites, and the more severely affected cage populations within those sites are the most exposed but at present this cannot be verified.

Investigation of Communicable Causes

Histopathology by light and electron microscope of fish tissues has not revealed signs of an infectious agent. Bacteriological techniques have also failed to consistently culture a common species from systemic organs. However, culture from the duodenum of phase 3 fish regularly produced a *Vibrio* sp. In healthy feeding fish it is unusual to culture any species from this area. Trials involving feeding and injection of these isolates are in progress but do not show promise of reproducing the disease. However, healthy fish all possess agglutinating factors (assumed to be antibody) to these isolates whereas thin fish with fibrotic pancreas do not show this response.

An intensive effort has been made to culture virus from all three stages of the disease without avail. The following cell lines have been challenged with filtrates of tissues, rainbow trout gonad (RTG-2), Atlantic salmon (As), fat head minnow (FHM), Menhaden kidney (MK), brown bullhead (BB), blue gill fry (BF), and carp epithelioma (CE) without obvious production of cytopathic effect. RTG-2 and As lines have subsequently been challenged with IPN and VHS virus and showed cytopathic effect indicating absence of interfering virus.

Transmission by ip route using organ homogenates from diseased fish in phases 2 and 3 to salmon and rainbow trout and by feeding viscera of phase 3 fish has failed to reproduce the disease in these fish.

**DISCUSSION**

Currently the cause(s) of this condition remain unknown. Despite the failure to grow or see virus or to transmit the condition to experimental fish the epidemiological evidence is not inconsistent with a virus aetiology. Smolts going to sea are novices in that environment to any new pathogens they may meet. Apparently fish surviving the condition do not have a second occurrence consistent with, but not proof of, many virus diseases. However, in three other virus diseases of salmonids, infectious pancreatic necrosis (Roberts and McKnight, 1976), infectious haemopoietic necrosis (Yasutake and Amend, 1972) and 13p2 reovirus (Meyers, 1983) where pancreatic necrosis is a feature of the clinical picture, necrosis is characteristically focal rather than generalised, while other organs also show significant pathology. In the present disease pancreas is acutely affected while other organs show only minor changes the significance of which is difficult to determine.

The consistent isolation of *Vibrio* sp. from the duodenum of phase 3 fish is enigmatic but may represent no more than a commensal population colonising the gut of non-feeding sickly fish.

The apparent ease of discharge of the necrosing pancreas into the intestine suggests that blockage of the duct or reflux of bile into the pancreas via blockage of the common duct, a cause of acute pancreatic necrosis in humans (Robbins, 1974), is an unlikely cause.
Donaldson (1943) reported significant pancreatic lesions in young chinook salmon (Oncorhynchus tschawytscha) during dietary trials. Unfortunately the poorly defined diets of that period did not allow identification of the principle involved in lesion production although it was reported diets high in salmon oil promoted pancreas destruction and choline or extracts of pancreas ameliorated the condition. Current salmon diets do not have a similar composition to those used by Donaldson but the fish oil content of about 17-20% is similar.

Exocrine pancreas degeneration and fibrosis similar to that described by us are characteristic of selenium deficient diets fed to young chicks (Gries and Scott, 1972). However, no mention of pancreas lesions was made by Poston et al. (1976) in a study of experimental selenium deficiency in first feeding Atlantic salmon fry. The four commercial diets commonly used to feed salmon in Scottish farms contain sufficient ingredients like herring meal, yeast extract, wheat, brewers grains, possibly soya meal and even supplemental selenite for the selenium requirement to be met 10-20 times (Cantor et al., 1975). If selenium deficiency were a factor in this disease then impaired absorption, perhaps caused by the greatly increased level of mineral intake when smolts are transferred to sea water may be a causal factor. The 12-16 week period taken for the disease to commonly be observed bears a similarity to the time taken for many nutritional diseases to be expressed.

The pathology of the salmon exocrine cells described here is analagous to descriptions of cell hypoxia seen in cells of other animals involved in high levels of energy utilisation and in which energy transfer mechanisms are disrupted (Halvor, 1982). Unfortunately there are several points at which disruption can occur by the presence of interfering materials eg ethionine (Goldberg et al., 1950) the absence of essential components eg selenium, vitamin E, or pantothenate (Poston and Page, 1982) or the presence of excesses eg dietary lipids (Tasman-Jones and Abraham, 1973). The histopathology of the present condition is therefore insufficient in itself to allow diagnosis indicating further studies are necessary.

REFERENCES


Meyers, T R 1983 Serological and histopathological responses of rainbow trout, Salmo gairdneri Richardson, to experimental infection with the 13p2 revirus. Journal of Fish Diseases 6, 277-292.


