

Ministry of Defence

Synopsis of Causation

Cancer of the Pancreas

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September 2008

Disclaimer

This synopsis has been completed by medical practitioners. It is based on a literature search at the standard of a textbook of medicine and generalist review articles. It is not intended to be a meta-analysis of the literature on the condition specified.

Every effort has been taken to ensure that the information contained in the synopsis is accurate and consistent with current knowledge and practice and to do this the synopsis has been subject to an external validation process by consultants in a relevant specialty nominated by the Royal Society of Medicine.

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1. Definition

- 1.1. The pancreas is an elongated gland that stretches across the posterior abdominal wall and comprises endocrine and exocrine tissue. It secretes various substances including digestive enzymes and the hormones insulin and glucagon. The organ comprises a head, body and tail and contains a main duct that runs its length, draining smaller ducts and emptying into the duodenum.
- 1.2. **Non-endocrine cancer.** 95% of pancreatic tissue is non-endocrine, i.e. exocrine. More than 75% of non-endocrine pancreatic cancers are adenocarcinomas of the pancreas. Other rare non-endocrine cancers include adenosquamous, acinar, giant cell and pancreaticoblastomas. There is also a group of cystic non-endocrine tumours of the pancreas; serocytic, mucinous, intraduct papillary mucinous and acinar cell cystadenocarcinoma. Of these the mucinous type has a strong malignant potential.¹
- 1.3. **Endocrine cancer.** Endocrine tumours of the pancreas are uncommon. At least 50% of endocrine cancers are not associated with active hormone production.

2. Clinical Features

- 2.1. Symptoms are not usually sufficiently specific to make a confident diagnosis of pancreatic cancer without supporting laboratory, radiological and pathological examinations. The most frequent site of pancreatic tumours is the head of the pancreas.
- 2.2. Tumours of the head of the pancreas often present with jaundice, often painless. This develops as the tumour encroaches on the common bile duct. The presence of jaundice necessitates urgent investigation. A small tumour may be diagnosed early giving the best opportunity for operative treatment.
- 2.3. Abdominal pain is present in two thirds of patients with pancreatic cancer. Initially it may be subtle for one or 2 months but becomes epigastric and constant with increasing severity and eventually may be unremitting. It may radiate to the back and is thought to be due to the invasion of the coeliac plexus of nerves, although the data are inconsistent.²
- 2.4. As many as 80-90% of patients presenting with pancreatic cancer have weight loss, most are in the advanced stage of the disease. This weight loss is often profound and up to 10% of body weight may be lost in one month. It is associated with chronic abdominal pain causing anorexia. Less frequently patients may have steatorrhoea due to malignant obstruction of the pancreatic duct.³ *De novo* diabetes in an older patient or increasing insulin requirement in an established diabetic may be the first presentation of an underlying cancer of the pancreas.
- 2.5. Cancer of the body and tail of the pancreas often have an insidious presentation – vague pain increasing with time, accompanied by back pain, malaise, weight loss, and steatorrhoea, and the diagnosis is often delayed until the tumour has become inoperable.
- 2.6. **Endocrine tumours** These tumours present with symptoms relating to their mass, i.e. pain or a palpable mass, and sometimes with bleeding. The tumours which actively secrete hormones, insulinoma and gastrinoma usually present when they are still tiny.

3. Aetiology

- 3.1. **Age** Eighty percent of cases of pancreatic cancer occur between the ages of 60 and 80 years.⁴
- 3.2. **Smoking** The most prominent and constant risk factor in pancreatic cancer is cigarette smoking, the relative risk of smokers being at least 1.5. The risk increases as the level of cigarette smoking increases. The highest risk ratio, tenfold, has been seen in males who consume over 40 cigarettes daily.^{5,6,7}
- 3.3. **Diet** A second important risk factor for pancreatic cancer is probably diet, although the data for diet is not as consistent as those for smoking. Increased risks have been associated with a diet high in animal protein and fat consumption and decreased risks with high intake of vegetables and fruit. It has been speculated that the increased incidence in Japan is related to dietary factors. Obesity is a risk factor for pancreatic cancer. The relationship between body mass index and calorie intake suggests that energy balance is important in pancreatic carcinogenesis. The way food is prepared has some association with the incidence of the disease with greater risk in those with a high intake of salt, smoked meat, dehydrated food, fried food and refined sugar. There is an inconclusive association with high carbohydrate intake and cereals.^{3,4}
 - 3.3.1. An association has been proposed between coffee consumption and cancer of the pancreas. Available published evidence is not supportive. The association between alcoholism and pancreatic cancer is weak and inconsistent. However, there is agreement that a high intake of alcohol with smoking leads to an increased risk. The association cannot be quantified.⁹
- 3.4. **Occupation** Excessively high rates of pancreatic cancer have been reported in some occupational groups; including chemists, coal and gas exploration workers and those in metal industries. High rates in other industries such as leather tanning, textile manufacturing and aluminium milling have also been reported although the risk has not been quantified.^{9,10,11}
- 3.5. **Medical conditions** Several medical conditions have been associated with pancreatic cancer, although no causal link has been established. An example is diabetes mellitus. Whether there is an increased risk in diabetes or whether diabetes and pancreatic cancer are related in some other way is not known. Patients with chronic pancreatitis, which itself is associated with chronic alcoholism, and biliary tract disease have an increased risk of pancreatic cancer after 10 years of heavy exposure to alcohol.⁸ This may mean that there is a common risk factor for both alcoholism and chronic biliary tract disease.¹²
- 3.6. **Ionising Radiation** The effects of ionising radiation were studied in the survivors of the Hiroshima and Nagasaki atomic bombings.¹³ No radiation link was noted for pancreatic cancer. Similarly no radiation effect on pancreatic cancer was noted in a study at Sellafield in the UK.¹⁴ However, there were excess deaths in patients who had therapeutic irradiation to the spine for ankylosing spondylitis.¹⁵ This 1965 study surveyed 14,554 patients who had irradiation of the spine for ankylosing spondylitis and follow-up was from 5-25 years. The commonest deaths were those related to disease of the blood and lymphatic systems, however in reviewing causes related to the gastrointestinal tract the authors did find 200 patients, classed as 'other deaths', which included

pancreatic cancer. The expected deaths for that population would have been 3.78 for normal causes of death but the observed number who had pancreatic cancer was 9, suggesting a 2.4 fold increased risk. The treatment dose used was not detailed in this paper but the Tayside Region was recording dosages very accurately in those who had this treatment at the time, and the dose would have been between 150 and 180 centigrays given in 10 fractions.

- 3.7. The most widely studied occupations are the petroleum and chemical industries although studies are by no means conclusive.¹⁶ One paper¹⁷ describes a risk of 5:1 while another describing the effects of 25 years of exposure to large amounts of oil quantifies the increased risk as 9.9:1 in machinists and 3.2:1 in grinders.¹⁸ However a study in the Du Pont company¹⁹ involving 3,686 employees found no increased risk of the disease, as did a UK death certificate study linking cause of death and occupation.²⁰

4. Prognosis

- 4.1. About 6,900 patients are diagnosed with cancer of the pancreas each year in the United Kingdom. This is 3% of all cancers and makes it the 11th commonest cancer in the United Kingdom in women and the 9th commonest cancer in men. Two thirds of the patients (63%) diagnosed are over 70 years of age.
- 4.2. Outcomes for this disease are poor and resection (proximal pancreatic duodenectomy) is the only curative treatment. Results of surgery in terms of complications and death have improved considerably over the last 20-30 years. Factors relevant to this include specialist centres, earlier diagnosis and better perioperative support. Of all the patients diagnosed with pancreatic cancer fewer than 13% are alive at one year and less than 2-3% at 5 years.⁴ Even after successful resection less than 1% are alive at 10 years.
- 4.3. Most patients with unresectable cancer of pancreas receive chemotherapy. It may also be used as an adjuvant to resection. As there is no clear survival benefit, radiotherapy is used less nowadays. However, it may have a role in palliating pain or as 'consolidation' treatment in patients who respond to chemotherapy but still have a visible mass on CT scan.
- 4.4. As the pancreas has a capacity to activate carcinogens and DNA abnormalities are detected in pancreatic cancer tissue, genotoxic compounds might be involved in causing this malignant change. There is also in pancreatic cancer a wide spectrum of mutation of genes.
- 4.5. Advances in molecular biology will be necessary before any high risk group can be identified or in whom targeted prevention might be successful.

5. Summary

- 5.1. The severity of pancreatic cancer and the scarcity of information on its aetiology means that much more research will be needed to improve the prognosis.
- 5.2. Rates of the condition increase with age and are higher in males than females. Epidemiological studies showed increased incidences of this condition in earlier decades of this century and rates have now levelled off. Thus, both genetic and environmental factors may play a role in exposure to carcinogens which increase the risks of pancreatic cancer.
- 5.3. All forms of present management, diagnosis and treatment have failed to alter the prognosis to a significant extent. Life expectancy has been increased in a few patients who have undergone radical resectional surgery but long-term cure is very rare.

6. Related synopses

Cancer of the Stomach

Peptic Ulcer

7. Glossary

| | |
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| acinar | Pertaining to the minute sacs that compose secreting glands, such as the pancreas. |
| adenocarcinoma | Cancer involving cells from the lining of organ walls. |
| anorexia | The lack or loss of appetite for food. |
| endocrine | Secreting directly into the bloodstream. |
| epigastric | Relating to the upper central part of the abdomen. |
| exocrine | Of a glandular structure; secreting outwardly via a duct. |
| gastrinoma | Tumour of the G-cells of the stomach antrum and the pancreas which produce gastrin. This causes overproduction of gastric acid and may lead to ulceration of the stomach and bleeding and/or perforation. |
| insulinoma | Insulin-producing tumour of the pancreas. |
| intraduct | Within the duct or ducts of a gland. |
| jaundice | Yellowing of the tissues, especially the skin and whites of the eyes by bilirubin, a pigment produced by the liver, often caused by liver disease. |
| mucinous | Relating to or containing mucin (mucus). |
| pancreas | A tongue-shaped glandular organ situated below and behind the stomach. The pancreas secretes hormones that regulate blood sugar (insulin, glucagon) and also produces pancreatic enzymes involved in the digestion of fats and proteins in the small intestine. |
| resection | Excision of some or all of an organ. |
| steatorrhea | Frothy, foul-smelling faecal matter that floats due to high fat content, associated with metabolic dysfunction. |

8. References

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