# SALTED FISH

## 1. Exposure Data

### 1.1 Production

Salted fish (salt fish) are treated by brining, dry-salting, pickle curing or a combination of these treatments, increasing the amount of salt in the fish substantially beyond that ordinarily found in the fresh product. Brining is the process of placing fish in a solution of salt (sodium chloride) in water for a period of sufficient length for the fish tissue to absorb the required amount of salt. Dry-salting is the process of mixing fish with dry salt and allowing the resultant brine (from dissolution of the salt in the water present in the fish) to drain away. Pickling or pickle curing is the process whereby fish is mixed with salt and is stored under the brine (pickle) which is formed when the salt dissolves in the water extracted from the fish tissue.

Processes for the preparation of salted fish have been reviewed by the FAO/WHO Codex Alimentarius Commission (1983). The following general description is taken from that review, unless otherwise noted. Salt acts upon fish as upon other foods by withdrawing water from the tissue. Fish flesh contains 75–80% water (in the case of very fatty fish, 60–65%), and this water can be replaced partly by salt. In the preparation of salted fish, water diffusing from the fish becomes saturated with the surrounding salt and is termed 'pickle'. Dry-salting results in a rapid loss of the weight of the fish, while with 'wet' salting, after an initial weight loss, there is a gradual weight gain. Salt uptake and water loss are influenced by the fat content of the fish, the thickness of the flesh, freshness, temperature, the chemical purity of the salt and other factors. Fat acts as a barrier to both the entry of salt and withdrawal of water; thus, water loss is slower from more fatty fish. The salting process may be terminated when the fish have achieved the required salinity and acquired the desired taste, consistency and odour.

Salting may be divided into salt preservation, as such, and ripening. Ripening, which is desirable for some fatty fish products, is a process that causes changes in the chemical and physical characteristics of fish flesh, generally by some enzymatic process. The rate of ripening depends on the fish, the salt composition employed, the temperature and the amount of salt absorbed by the fish tissues. These variables give rise to many different and uniquely characteristic products. Spoilage of fish is brought about chiefly by autolysis and microbial decomposition. Most enzymes and micro-organisms are inactivated by high salt concentrations, and the reduced moisture content of salted fish also results in an unfavourable environment for the multiplication of micro-organisms. If poor quality raw fish is used and/or salting takes place at elevated temperature, however, decomposition may proceed faster than the penetration of salt into the tissues, and spoilage of the fish will occur.

While salting reduces the rate of autolysis, it does not completely stop enzymatic action, which increases with increasing temperature. Salting enhances fat oxidation, and fat hydrolysis and the development of rancidity may contribute to the spoilage of fish. Certain halophilic micro-organisms can multiply under the conditions of dry-salting and can also spoil the product. Salted fish should therefore be cured and stored under cool conditions, and some fatty fish should be kept in the absence of air.

The origin, and thus the composition, of the salt used in the salting process in different countries varies. Mine salt or rock salt is usually almost pure sodium chloride, but solar salt of marine origin (sea salt) contains several impurities, including calcium sulfate, magnesium sulfate, magnesium chloride and nitrates or nitrites (Armstrong & Eng, 1983). Too much calcium ( > 0.35%) may reduce the rate of salt penetration to the extent that spoilage occurs. Magnesium salt levels above 0.15% may lead to an unpleasant flavour and/or spoilage.

The commercial processing of salted fish, as practised in Europe and North America, has been described by the FAO/WHO Codex Alimentarius Commission (1983), Anon. (1986) and Bjarnason (1987). Figure 1 is a flow chart of the commercial processes. Ripening is not a part of the process. A number of steps, including heading and splitting, are largely done by machines, and the fish are moved through the processes on conveyor belts (FAO/WHO Codex Alimentarius Commission, 1983).

Traditional processes used in the preparation of salted fish in various regions have been described. Almost 30% of the fish caught in Southeast Asia is preserved by curing (salting, drying or smoking) (Ah-Weng *et al.*, 1985).

### 1.1.1 *South China*

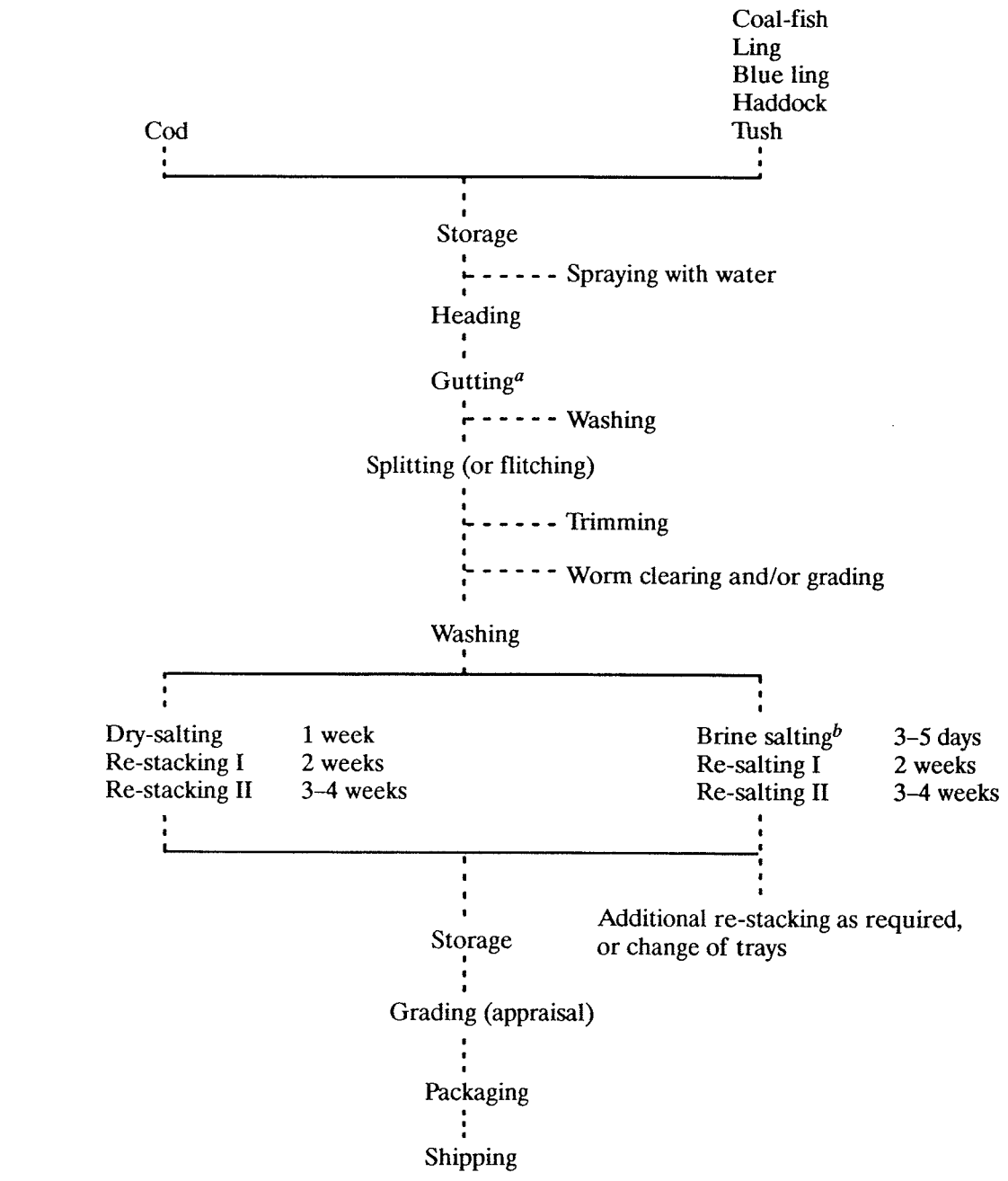
In South China, fish are generally not gutted prior to salting, and only when bigger fish such as red snapper are salted are the guts drawn out through the throat, without making an incision in the belly of the fish. Salting is done in wooden vats, and the fish are arranged in alternate layers with coarse rock salt. After a few days, the fish are immersed in brine and weights (often large stones placed on top of grass mats) are placed on the surface to prevent the fish from floating. The length of salting ranges from one to five days, after which the fish are taken out to dry in direct sunlight, usually spread on woven grass mats. They are turned every few hours and left out for one to seven days, depending on the size of the fish and the weather. During drying, insect infestation can be a serious problem, especially in damp weather. Unfortunately, in South China, the relative humidity is over 80% for about eight months of the year, and it often reaches 96–99% during the summer months.

Sometimes, fish is allowed to soften by decomposition before salting, to produce *muihurn* salted fish. Fish that is not previously decomposed is known as *sud yoke* (literally, tough meat) salted fish (Tannenbaum *et al.*, 1985).

### 1.1.2 *Malaysia*

In Malaysia, fish is usually gutted and cleaned by fishermen in the port. The degree of cleaning of the fish varies considerably and is generally unregulated; refrigeration is virtually non-existent between the point of catching the fish and selling it on the market. Salted fish is prepared only when the markets have enough fresh fish, when there is a failure of transport

**Figure 1. Flow chart for the commercial processing of salted fish**




From Bjarnason (1987)
[a]During the summer fishing season in Iceland, gutting is done aboard the fishing vessels.
[b]Brine salting in Iceland is dry-salting and keeping the fish in the resultant brine (pickling).

between the port and the market or some other delay. Thus, fresh fish undergoes varying degrees of deterioration before it is salted down for pickling. Most fish for salting are sprinkled and stuffed with crude sea salt and placed in a tank. When the tank is full, the fish are covered and compressed with bricks or stones. After two to three days of pickling, the fish are either smoked or left as is and put to dry in the sun. The more expensive varieties of salted fish are sometimes marinated in jars of cooking oil (usually palm or coconut oil) before dispatch to market. Depending on the weather, the process before the fish go into storage or to market takes about a week (Armstrong & Eng, 1983).

Malaysian Chinese have a distinct preference for what is known locally as 'Kuantan salted fish'—salted red snapper which takes its name from the port that first gained the reputation for supplying the best quality, although today an equivalent product may come from other ports in Malaysia. Salted red snapper is processed and sold in three ways, chiefly for Chinese consumers. The bulk of the fish is salted, smoked and dried in the usual way to produce 'Kuantan hard fish' or *ikan merah jerok*. Smaller proportions are preserved in salt chips for three days, rather than two, before drying, to produce an exceptionally salty fish (*ikan merah jerok asin*). Another small proportion is first preserved for two to three days in tanks of vinegar and salt and then dried in the sun. An alternative, perhaps older, procedure is to allow the fish to soften by decomposition then stuff it with salt, compress for three days and dry in the sun. The latter two processes yield the expensive and famous *moi heong* (literally, 'red plum') or 'Kuantan soft-type' salted fish (*ikan merah jerok asam*). The procedures vary widely among fish handlers. In salting inferior, less expensive grades of fish, only enough salt to prevent gross deterioration may be used while the fish is drying (Armstrong & Eng, 1983).

Although smoking of salted fish is common in Malaysia, duration of smoking and kinds of smokehouses and fuels used have not been studied (Armstrong & Eng, 1983).

### 1.1.3 *Northeastern Thailand*

Salted fish consumed in northeastern Thailand can be placed in one of three categories, according to the type of fish (fresh-water or sea-water) and curing process used. *Pla-ra* is a fresh-water fish that has been left to ferment in salted water for at least one month. This is the traditional salted-fish dish of northeastern Thailand and is prepared at home and kept wet. Other fresh-water fish undergo shorter fermentation (usually one week) and may be kept wet or dried. The third type comprises sea fish fermented with salt for several weeks and allowed to dry: This typical Chinese-style fish is purchased on the market rather than prepared at home (Sriamporn *et al.*, 1992).

### 1.1.4 *Tunisia*

In Tunisia, salted anchovies and sardines are prepared by alternating layers of salt and fish in glass or earthernware containers, which are then sealed and stored for up to three years. The fish is used mainly in salads (Hubert, 1984).

### 1.1.5 *Egypt*

In Egypt, sand-salted fish is prepared by covering the gills and body of fish with salt, wrapping it in canvas and burying it in sand for 15–30 days. Tin-salted fish is made by covering

the gills and body with salt and then leaving the fish for several hours in the sun until the body has swollen; the salt is then renewed, and the fish is arranged in alternate layers with salt in a special tin or barrel. Treated fish is consumed after at least 10 days' storage (Elmossalami & Sedik, 1972).

### 1.1.6 *Sudan*

*Alestes baremose* is the fish species most commonly used for producing wet-salted fish in the Sudan. Salting is done by fishermen in small, temporary sheds or huts made of reed mats. Whole fish are washed and placed on mats made of palm leaves, sometimes in perforated wooden or steel barrels, with layers of fine-grain salt (solar sodium chloride). The fish are then covered with a thick layer of salt and wrapped with the same mats; weights are placed on top to press down the fish. The fluid formed is allowed to run off. Depending on climatic conditions, and especially the ambient temperature, the fish are left for three to five days to ferment. They are then transferred to tins in which heavy layers of salt are alternated with layers of fish. After about three days, the fluid is decanted and additional layers of fish and salt are applied. The process is continued for 7–10 days, after which time the tins are sealed. At this stage, the fish has lost about one-third of its initial weight. The average amount of salt needed to ferment 1 kg of fresh fish is about 0.1 kg. The final product is called *fassiekh*. The technique is believed to have been introduced from Egypt during the Turkish rule in the nineteenth century (Yousif, 1989).

## 1.2 Worldwide production, trade and consumption

### 1.2.1 *Production and import/export*

About 15% of the world fish catch is preserved by curing, i.e., salting, drying or smoking, or a combination of those treatments (Ah-Weng *et al.*, 1985). World production of salted fish in 1980–89 is presented in Table 1.

Global production (by region) of dried, salted and smoked fish in 1989 was 2 621 757 tonnes in Asia, 769 300 tonnes in the USSR, 514 316 tonnes in Europe, 342 892 tonnes in Africa, 106 063 tonnes in North America, 72 921 tonnes in South America and 10 175 tonnes in Oceania (FAO, 1989).

World production of salted (and dried) cod and related products is on average 300–400 thousand tonnes per annum. Europe produces about two-thirds of the total, the largest producers in order of importance being Norway, Iceland, Spain, Portugal, the Faroe Islands and France. The most important producing countries outside Europe are Canada and the USA. Curing of salted fish is a traditional industry in Iceland, and exports of salted dried fish in 1980–82 were 2539, 840 and 1460 tonnes, respectively. Major importers of Icelandic salted dried fish in those years were Brazil, France, Martinique, Panama, Portugal and Zaire (Bjarnason, 1987).

Almost 40% of the total annual fish catch in Indonesia is converted into dried salted products. In 1985, the fish catch in Indonesia was about two million tonnes (Esser *et al.*, 1990). Approximately 34% of fish from inland waters and 48% of marine fish were cured, 71% of the cured fish being processed by salting and drying (Buckle *et al.*, 1988). The major

**Table 1. World production of salted fish, 1980–89**

| Year | Production (thousand tonnes) | |
|---|---|---|
| | Dried, salted or smoked | Dried, salted or in brine |
| 1980 | 3997 | 3103 |
| 1981 | 3892 | 2951 |
| 1982 | 4031 | 3079 |
| 1983 | 4032 | 3091 |
| 1984 | 4025 | 3075 |
| 1985 | 4194 | 3232 |
| 1986 | 4203 | 3223 |
| 1987 | 4312 | 3313 |
| 1988 | 4287 | 3408 |
| 1989 | 4437 | 3432 |

From FAO (1989)

producing islands are Sumatra, South Kalimantan and South Sulawesi. In 1987, 4200 tonnes of dried salted fish from Jakarta were exported to Saudi Arabia, and small amounts are regularly exported to Australia (Wibowo *et al.*, 1990).

Production of wet-salted fish in the Sudan in 1986 was estimated to have been 1160 tonnes. Nearly 80% of the product was exported to Egypt (Yousif, 1989).

The growth of the Asian populations of Europe, the USA and Australia is expected to stimulate importation of dried salted fish from the traditional producing regions (Wibowo *et al.*, 1990).

### 1.2.2 *Consumption*

Chinese-style ('Cantonese marine') salted fish is a favourite dish along the South China coast and in Southeast Asian countries. In Selangor, Malaysia, over 90% of Chinese households and about 40% of Malay and Indian households reported regular consumption of salted fish (Armstrong & Eng, 1983). Although the amount consumed at any one time is small (not more than 10 g), the dish may appear at every meal; some people actually prefer the spoiled parts (Fong & Chan, 1973a).

Some populations are exposed to Chinese-style salted fish from weaning. Seventeen mothers in Guangzhou (Canton City), China, reported that they fed salted fish mixed with rice at least five times a week to their children both during and after weaning. The median ratio of salted fish to rice was 1:9 (Yu *et al.*, 1989a). In a study of nasopharyngeal carcinoma in Hong Kong Chinese, 250 Chinese controls were interviewed regarding their dietary habits three years previously and at the age of 10, and the mothers of 155 controls were questioned about the diets of the study subjects at the age of 10, between the ages of one and two and during weaning (Yu *et al.*, 1986; Yu & Henderson, 1987). The frequency of consumption of Chinese-style salted fish in this population is shown in Table 2.

**Table 2. Frequency of salted fish consumption among Chinese in Hong Kong**

| Frequency | No. of subjects |
|---|---|
| Three years previously | |
| Rarely | 164 |
| Monthly[a] | 66 |
| Weekly[b] | 19 |
| Daily | 1 |
| At age 10 | |
| Rarely | 108 |
| Monthly | 101 |
| Weekly | 39 |
| Between ages 1–2 | |
| Never | 83 |
| Sometimes | 34 |
| Often[c] | 8 |
| During weaning | |
| Never | 96 |
| Ever | 31 |

From Yu *et al.* (1986); Yu & Henderson (1987)
[a]Once a month to less than once a week
[b]Once a week to less than daily
[c]Considered by mothers to be a typical meal

Poirier *et al.* (1987) reported that the frequency of consumption of salted fish varied from once or twice a week to more than three times a week in Tunisia and South China.

Consumption of salted fish more than 10 times a month was reported by 52 and 70% of the adult farm populations and 36 and 57% of the adult non-farm populations of Hiroshima and Miyagi, Japan, respectively (Haenszel *et al.*, 1976). The Japanese National Nutrition Surveys for 1975 indicated that the daily per-caput dietary intake of salted fish was 6.2 g (Omura *et al.*, 1987). In Indonesia, fish provides approximately 70% of the per-caput dietary protein intake (Esser *et al.*, 1990).

### 1.3 Regulations and guidelines

The FAO/WHO Codex Alimentarius Commission (1983) adopted the Recommended International Code of Practice for Salted Fish in December 1979. The Code covers the technological and essential hygienic requirements for the preparation of high-quality salted fish products, but the drying of salted fish is not covered. Pirimiphos methyl has been cleared by FAO/WHO for use on salted–dried fish to protect against blowfly infestation during processing and against further insect infestation during storage (Esser *et al.*, 1990).

## 1.4 Compounds present in salted fish

### 1.4.1 *Nitrosamines and related contaminants*

Ho (1972) speculated some time ago that the presence of nitrosamines in salted fish might be significant. Fish are rich sources of secondary and tertiary amines, and nitrate and possibly nitrite occur in the crude sea salt used to pickle them. Furthermore, pickling and drying are done in the open, so that the fish are susceptible to bacterial contamination which might contribute to nitrosation (Fong & Chan, 1976a,b). Subsequent analyses revealed the presence of nitrosamines in salted fish; levels of *N*-nitrosodimethylamine (NDMA) (see IARC, 1978a, 1987) are summarized in Table 3.

Kawabata *et al.* (1984) conducted a survey of the occurrence of total *N*-nitroso compounds, total *N*-nitrosamides, volatile *N*-nitrosamines (NDMA) and nitrite in the Japanese diet. No appreciable amount, or only trace quantities, of nitrosamines were detected in uncooked fish products, but the content of volatile nitrosamines (especially in dried squid samples) increased upon broiling on a city gas range. Table 4 presents the occurrence of the four groups of compounds in salt-dried fish.

Samples of uncooked, steamed and fried salted yellow croaker, purchased at three southern Chinese markets on six occasions were analysed for volatile nitrosamines. The mean levels found were: NDMA, 100–600 ng/kg (uncooked fish and steamed fish), 200–1400 ng/kg (fried fish); *N*-nitrosodiethylamine (see IARC, 1978b, 1987), not detected to 50 ng/kg (uncooked fish), not detected to 100 ng/kg (steamed fish), not detected to 10 ng/kg (fried fish); *N*-nitrosodi-*n*-propylamine (see IARC, 1978c, 1987), mean in one batch, 50 ng/kg (steamed fish), 30 ng/kg (fried fish); *N*-nitrosodi-*n*-butylamine (see IARC, 1978d, 1987), same batch, 50 ng/kg (fried fish); and *N*-nitrosomorpholine (see IARC, 1978e, 1987), 200 ng/kg (uncooked fish). NDMA and *N*-nitrosodiethylamine were found in both uncooked salted fish heads (60–100 ng/kg) and soups prepared from them (10–60 ng/l); NDMA was found in all batches, and *N*-nitrosodiethylamine in only one batch (Huang *et al.*, 1981).

Samples of seven species of salt-dried fish purchased in the Tokyo area were analysed for nitrosamines before and after broiling. Levels of NDMA in uncooked samples ranged from not detected to 5.0 μg/kg, while levels in cooked samples ranged from trace to 26.1 μg/kg. *N*-Nitrosopyrrolidine (see IARC, 1978f, 1987) was not detected in either uncooked or cooked samples. The NDMA content of the samples apparently increased after broiling on a gas range; however, considerable variation in the increase was observed, depending on the species of fish. It has been reported that covering fish with aluminium foil or broiling it in an electric range decreases NDMA formation during cooking (Kawabata *et al.*, 1980).

Food extracts from high-risk areas for nasopharyngeal carcinoma (NPC) were analysed for nitrosamines; and, since *N*-nitroso compounds can be formed from ingested foods and nitrate or nitrite, aqueous food extracts were also examined after acid-catalysed nitrosation *in vitro*. Samples of hard salted and dried grouper from China contained 388 μg/kg NDMA, 81 μg/kg *N*-nitrosopiperidine (see IARC, 1978g, 1987) and 30 μg/kg *N*-nitrosopyrrolidine. After nitrosation *in vitro*, the samples contained 1191 μg/kg NDMA, a trace amount of *N*-nitrosopiperidine and 98 μg/kg *N*-nitrosopyrrolidine. Volatile nitrosamines were not detected before nitrosation in soft salted and dried Japanese mackerel from China; after nitrosation, 377 μg/kg NDMA and 20 μg/kg *N*-nitrosopyrrolidine were found. Salted

anchovies from Tunisia contained NDMA at 299 μg/kg before and 43 μg/kg after nitrosation (Poirier *et al.*, 1989).

**Table 3. *N*-Nitrosodimethylamine (NDMA) levels in uncooked salted fish**

| Fish product[a] (place of purchase) | No. of samples | NDMA level (μg/kg) | Analytical method | Reference |
|---|---|---|---|---|
| Salted fish (Hong Kong) | | ND–300 | GC or GC–MS | Fong & Chan (1973a) |
| White herring | 7 | 40–300[b] | | |
| Yellow croaker | 5 | 10–200 | | |
| Anchovies | 2 | 20–100 | | |
| Croaker | 2 | 20–30 | | |
| Pomfret | 1 | ND | | |
| Salted fish (Hong Kong) | | < 1–35 | GC–MS | Huang *et al.* (1978a) |
| Anchovy | 2 | 2–35 | | |
| Croaker | 3 | ND–8 | | |
| Red snapper | 4 | < 1 | | |
| White herring | 4 | < 1–8 | | |
| Yellow croaker | 6 | < 1–18 | | |
| Salted fish (Hong Kong) | | ND–2.8 | GC–TEA | Tannenbaum *et al.* (1985) |
| Yellow croaker | 1 | 0.64 | | |
| Mackerel | 1 | ND | | |
| Croaker | 1 | 2.0 | | |
| Red snapper | 1 | ND | | |
| Black pomfret | 1 | ND | | |
| White croaker | 1 | ND | | |
| Unknown import from Japan | 1 | 2.8 | | |
| Salted-dried fish (China) | | < 0.1–133 | HPLC–TEA | Poirier *et al.* (1987) |
| Grouper | 1 | 133 | | |
| Croaker | 4 | < 0.1–2 | | |
| Japanese mackerel | 1 | 1.1 | | |
| Spotted mackerel | 1 | 1.0 | | |
| Silver pomfret | 1 | 0.2 | | |
| Dolphin fish | 1 | 9.2 | | |
| Soldier croaker | 1 | 0.3 | | |
| Ribbon fish | 1 | 6.4 | | |
| Sprats, small fry | 1 | 1.5 | | |
| Ribbon, small fry | 1 | 14 | | |
| Croaker, small fry | 1 | 1.0 | | |
| Salted fish[c] (China) | 27 | ND–24.4 | GC–TEA and/or GC–MS | Song & Hu (1988) |
| Hard-salted and dried grouper (China) | 1 | 388 | GC–TEA | Poirier *et al.* (1989) |
| Soft-salted and dried Japanese mackerel (China) | 1 | ND | GC–TEA | Poirier *et al.* (1989) |

**Table 3 (contd)**

| Fish product[a] (place of purchase) | No. of samples | NDMA level (μg/kg) | Analytical method | Reference |
|---|---|---|---|---|
| Salted fish (China) | | 13–323 | GC-TEA | Zou *et al.* (1992) |
| Sihui County | 5 | 45–323 | | |
| Guiping County | 4 | 15–36 | | |
| Henshan County | 3 | 14–188 | | |
| Changsha City | 2 | 91–112 | | |
| Shanghai City | 6 | 13–59 | | |
| Salt-dried fish (Japan) | | < 0.5–5 | GC | Kawabata *et al.* (1980) |
| Horse-mackerel | 3 | 1.0–4.9 | | |
| *Shishyamo* | 2 | 0.5–4 | | |
| Pacific saury | 1 | trace | | |
| Flounder | 1 | < 0.5 | | |
| Chub mackerel | 1 | 0.5 | | |
| Round herring | 1 | 5 | | |
| Salted/dried fish (Canada) | | 0.4–4.2 | GC-MS or GC-TEA | Sen *et al.* (1985) |
| Cod | 3 | 0.4–0.9 | | |
| Hake | 1 | 4.2 | | |
| Caplin | 1 | 0.9 | | |
| Salted fish (Canada) | | 0.2–1.1 | GC-MS or GC-TEA | Sen *et al.* (1985) |
| Mackerel | 2 | 0.2 each | | |
| Herring | 5 | 0.4–1.1 | | |
| Turbot | 2 | 0.6–0.8 | | |
| Cod | 1 | 0.3 | | |
| Salted anchovies (Tunisia) | 1 | 299 | GC-TEA | Poirier *et al.* (1989) |

ND, not detected; GC, gas chromatography; HPLC, high-performance liquid chromatography; MS, mass spectrometry; TEA, thermal energy analysis

[a]Author's terminology used

[b]Level reached 1 ppm (mg/kg) in one sample of spoiled herring

[c]Squid, octopus, cuttlefish, hairtail fish and fish sauce

Fong and Chan (1973b) reported an increase in the level of NDMA in fish broth after it was inoculated with *Staphylococcus aureus* isolated from salted fish obtained from a Chinese market. They suggested that the amount of NDMA present in salted fish was dependent on storage conditions, degree of contamination by nitrate-reducing bacteria and the levels of precursors present.

Fong and Chan (1976a,b) investigated the effects on the presence of NDMA in salted fish of preservation with crude sea salt containing 40 ppm (mg/kg) nitrate or with sodium chloride. The NDMA levels in two species of marine fish were 25–40 μg/kg after treatment with crude salt and 6–7 μg/kg after preservation with sodium chloride. The levels in two species of freshwater fish were 19–20 μg/kg after treatment with crude salt and not detected to 5 μg/kg after treatment with sodium chloride.

**Table 4. Levels of total *N*-nitroso compounds (TNC), total *N*-nitrosamides (TNAd), volatile *N*-nitrosamines (VNA) and nitrite in the Japanese diet**

| Dietary item | TNC (μg NO/kg) | TNAd (μg NO/kg) | VNA (NDMA, μg/kg) | Nitrite (mg/kg) |
|---|---|---|---|---|
| **Salt-dried fish** | | | | |
| Sardine, *maruboshi iwashi* (uncooked) | 0.86 | 0.63 | 0.6 | < 0.05 |
| Sardine, *maruboshi iwashi* (city gas-broiled) | 4.53 | 2.04 | 6.1 | < 0.05 |
| Pacific saury, *samma hiraki* (uncooked) | 1.87 | 1.58 | 0.7 | < 0.05 |
| Pacific saury, *samma hiraki* (city gas-broiled) | 6.74 | 5.42 | 3.3 | 0.28 |
| Mackerel, *aji hiraki* (uncooked) | 1.45 | 1.14 | 0.9 | < 0.05 |
| Mackerel, *aji hiraki* (city gas-broiled) | 6.61 | 3.62 | 7.4 | 0.40 |
| Air-dried squid, *hoshi surume* (uncooked) | 26.6 | 22.6 | 9.9 | < 0.05 |
| Air-dried squid, *hoshi surume* (city gas-broiled) | 37.7 | 22.5 | 37.5 | 0.77 |
| **Other products** | | | | |
| Salted-fermented squid, *ika shiokara* | 15.8 | - | 3.5 | < 0.05 |
| Fish sausage 1 | 2.5 | - | 2.1 | 0.07 |
| Fish sausage 2 | 3.4 | - | 2.6 | < 0.05 |

From Kawabata *et al.* (1984). Detection limits: TNC and TNAd, 0.5 μg/kg NO equivalent; VNA, 0.1 μg/kg; nitrite, 0.05 mg/kg; –, not analysed

### 1.4.2 *Micro-organisms and toxins*

Fong and Walsh (1971) obtained viable cultures on salt-agar of nitrate-reducing halobacteria and salt-tolerant *S. aureus* from all samples of Cantonese salt-dried fish that they examined. Onishi *et al.* (1980) isolated a variety of halophilic bacteria from salted fish, including salmon, salmon roe, codfish, cod roe and guts of cuttlefish.

Bacteria isolated from Egyptian sand-salted fish included micrococci, gram-positive bacilli, *Proteus vulgaris*, *P. mirabilis* and *Aeromonas liquefaciens*. All of the same micro-organisms except *A. liquefaciens* were isolated from tin-salted fish; *Serratia marcescens*, *P. rettgeri*, *P. morganii*, *Enterobacter aerogenes* and *Corynebacterium freundii* were isolated from tin-salted fish only. Total bacterial counts were lower in sand-salted fish than in tin-salted fish (Elmossalami & Sedik, 1972).

Species of fungi isolated from Indonesian dry salted fish included *Paecilomyces variotii*, *Eurotium amstelodami*, *Aspergillus candidus* and *A. sydowii* (Wheeler & Hocking, 1988).

Aflatoxin $B_1$, produced by the fungi *A. flavus* and *A. parasiticus*, was reported in cured fish (see also the monograph on aflatoxins). Okonkwo and Nwokolo (1978) found a mean aflatoxin $B_1$ concentration of 650 μg/kg in Nigerian dried fish. Stockfish, a dried imported fish from Scandinavia, contained no aflatoxin. Shank *et al.* (1972) identified aflatoxins in 5% of 139 samples of dried fish/shrimp purchased in markets in Thailand but in none of 35 samples purchased in Hong Kong. In the contaminated samples, the mean aflatoxin ($B_1$, $B_2$, $G_1$ and $G_2$) concentration was 166 μg/kg.

Total bacterial count and coliforms were estimated in fresh Egyptian *bolti* fish after brining, after drying and during storage at room temperature for three months. The total bacterial count decreased after drying, owing to the high salt content and the lack of free water in fish tissues. Coliforms were not present after brining, drying or throughout storage (Zaki *et al.*, 1976).

#### 1.4.3 *Other*

Polynuclear aromatic hydrocarbons were identified by high-performance liquid chromatography in uncooked, salted and sun-dried fish commonly consumed in South India. Chrysene (see IARC, 1983a, 1987) was found at 3.6–18.6 μg/g and benzo[*a*]pyrene (see IARC, 1983b, 1987) at 5.7–60.8 μg/g; one sample contained 1,2:5,6-dibenz[*a*]anthracene [dibenz[*a*,*h*]anthracene] (see IARC, 1983c, 1987) at 12.34 μg/g (Sivaswamy *et al.*, 1990).

The mean concentration of sodium ion in five samples of salted fish purchased in Hong Kong was 46.5 mg/g of fish (Yu *et al.*, 1989a).

### 1.5 Analysis

Selected methods for the analysis of *N*-nitroso compounds in various matrices have been reviewed (Walker *et al.*, 1978, 1980; Bartsch *et al.*, 1982; Preussmann *et al.*, 1983; O'Neill *et al.*, 1984).

## 2. Studies of Cancer in Humans

### 2.1 Chinese-style salted fish

A number of studies considered the effects of salted fish, as traditionally prepared in southern China, in different Chinese population throughout the world. As this preparation is quite different from preparations of salted fish elsewhere in the world, epidemiological studies in those populations were considered separately. It cannot be excluded, however, that salted fish products consumed by other populations are similar to Chinese preparations.

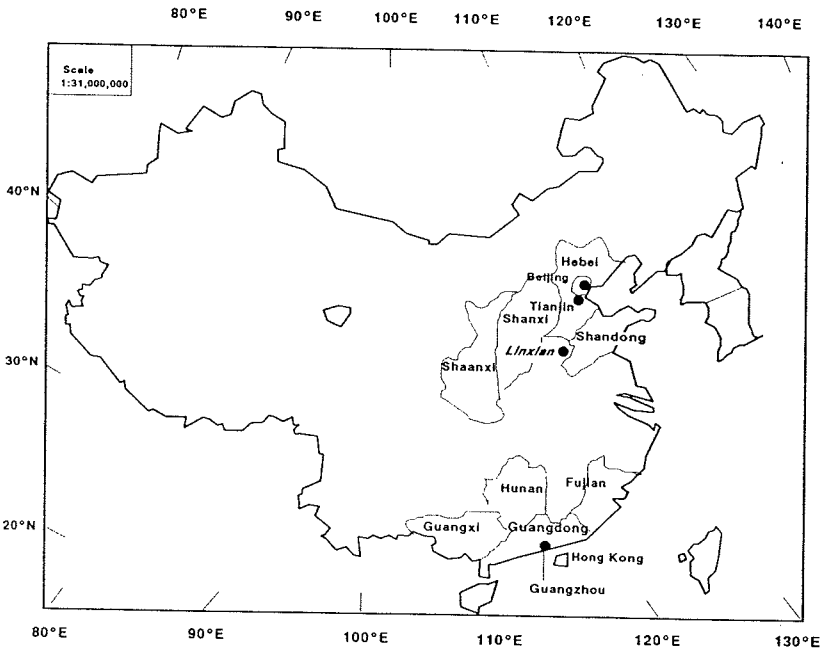
#### 2.1.1 *Nasopharyngeal carcinoma*

##### (*a*) *Correlation (ecological) studies*

Nasopharyngeal carcinoma (NPC) is a rare cancer in most parts of the world; the annual age-standardized incidence rate for either sex is generally less than 1 per 100 000 population (Hirayama, 1978; Muir *et al.*, 1987; Ning *et al.*, 1990). A few populations, however, have very high rates of NPC; these include Chinese living in China and in other parts of world (e.g., Hong Kong, Malaysia, Singapore, USA). Nevertheless, there is substantial variation among the rates of NPC within China: The incidence rates generally increase from North (2–3/100 000) to South China (25–40/100 000), so that rates in the southernmost province of Guangdong may be 10–20 times higher than those in the northernmost provinces (Chinese National Cancer Control Office/Nanjing Institute of Geography, 1979; Yu *et al.*, 1981; Muir

*et al.*, 1987). The three regions in which rates of NPC are particularly high are Guangdong Province, Guangxi Autonomous Region and Fujian Province (Fig. 2).

**Fig. 2. Map of China, showing the provinces and other areas that have been studied with respect to consumption of salted fish**




From Li *et al.* (1985)

This north–south gradient in NPC rates in China corresponds to a traditionally low intake of salted fish in northern China and a high intake of this food in southern China (Yu & Henderson, 1993). There are also distinct differences in rates of NPC by ethnic and dialect groups of southern Chinese. Among the Cantonese in Hong Kong, the highest rates of NPC are observed among the Tankas (boat people), representing 1–2% of the Cantonese population, who are fishermen and consume large quantities of salted fish in their daily diet. The rates of NPC among the Tankas are about twice those of the land-dwelling Cantonese (Ho, 1967, 1971a, 1978; Li *et al.*, 1985). In turn, the rate of NPC among the land-dwelling Cantonese is twice that of the Hakka and Chiu Chau (Teochew) dialect groups who reside in north-eastern Guangdong (Ho, 1967, 1971b; Yu *et al.*, 1981; Ho, 1975; Li *et al.*, 1985). It is noteworthy that the people of Fujian Province, who are culturally similar to the Chiu Chau people in Guangdong Province, have similar rates of NPC. Hakkas, who originated from northern China many years ago, also have rates of NPC that are similar to those of their Chiu Chau neighbours and not to those of their low-risk ancestors in the north (Ho, 1971a, 1975; Li *et al.*, 1985). Thus, the distinct pattern of NPC incidence among different ethnic or dialect groups in southern China coincides with the pattern of their consumption of salted fish (Ho, 1978; Yu *et al.*, 1981). Cantonese who migrate to other parts of southeast Asia continue to exhibit a risk for NPC that is twice that of Hakkas, Chiu Chaus and Fujianese who have migrated (Armstrong *et al.*, 1979; Armstrong & Eng, 1983).

The high rates of NPC in provinces that neighbour Guangdong Province are probably due to the adoption of some of the dietary habits of people in Guangdong. Guangxi Autonomous Region, which borders Guangdong Province on the west, has the second highest rates of mortality from NPC in China. These high rates are observed mainly among the Han people of the Guangxi Region (Yu *et al.*, 1988), who are ethnically similar to the Cantonese in Guangdong; the Zhuang people in western Guangxi have about one-fifth the rates of Cantonese. In areas of Hunan Province that border Guangxi and Guangdong to the north, the rates of NPC are, not surprisingly, also high (Yu & Henderson, 1993).

Among the high-risk southern Chinese, people in the lower social strata have higher rates of NPC than those in the higher social strata (Armstrong *et al.*, 1978; Geser *et al.*, 1978; Yu *et al.*, 1981). Exposure to salted fish may explain this observed inverse association, as salted fish is traditionally one of the cheapest foods in southern China.

The incidence of NPC in southern Chinese peaks at the ages of 45–54 and declines clearly thereafter (Ho, 1971b). This observation suggests that exposure to the etiological agent occurs early in life and that either exposure declines or the target tissue becomes less susceptible (or both) at older ages. Salted fish mixed with soft rice is commonly, and sometimes the only food, fed to infants in the weaning and post-weaning period (Topley, 1973). Exposure to this food item very early in life is thus consistent with the age distribution of NPC (Ho, 1979; Yu & Henderson, 1993).

(*b*) *Case–control studies* (see Table 5)

Since Ho published his hypothesis in the early 1970s, eight case–control studies have been conducted to investigate the association between consumption of salted fish and the occurrence of NPC among Chinese living in different parts of the world and displaying distinct risks for NPC. The evidence is derived from studies conducted among the very high-risk Cantonese Chinese in Hong Kong (Geser *et al.*, 1978; Yu *et al.*, 1986) and Guangzhou (Yu *et al.*, 1989b), among southern Chinese in Guangxi Autonomous Region, who have intermediate rates of this disease (Yu *et al.*, 1988), and among Chinese in Tianjin, who have relatively low rates (Ning *et al.*, 1990). In addition, the association between consumption of salted fish and NPC has been observed among southern Chinese living outside of China or Hong Kong but who have maintained this custom (Henderson *et al.*, 1976; Henderson & Louie, 1978; Armstrong *et al.*, 1983).

A case–control study of NPC was conducted among Chinese, whites and other ethnic groups in California, USA (Henderson *et al.*, 1976). Cases were identified in 1971–74 from the population-based tumour registries of Los Angeles County (n = 150) and the San Francisco Bay area (n = 53 Chinese); a further 27 cases originally diagnosed in 1960–70 were obtained from the California Tumor Registry. Of the 230 cases, 156 were interviewed; 74 were Chinese, 65 of whom had been born in China. Controls were identified from hospitals and clinics in the same geographical areas as the cases; 267 were interviewed, 110 were Chinese, of whom 91 had been born in China [response rates not given]. Questions on life style, medical and family histories and use of salted fish (for Chinese subjects only) were included in the interview. More cases than controls currently used salted fish (odds ratio [OR], 2.1; 95% confidence interval [CI], 0.6–6.3), and a significant, positive association was found between intake frequency and risk for NPC: OR, 1.6 for at least monthly use, 2.1 for

weekly use and 3.1 for more than weekly use as compared to no use ($p$ for trend = 0.02) (Henderson & Louie, 1978). [The Working Group noted that it is not clear whether consumption of salted fish was adjusted for other risk factors for NPC.]

Geser *et al.* (1978) conducted a hospital-based case–control study of NPC in Hong Kong which included 150 cases selected 'by rotation' from among about 350 cases and an equal number of controls (mainly with other cancers), matched to cases by sex, age (plus or minus five years) and hospital ward. The NPC patients were identified at one of two major hospitals in Hong Kong while undergoing radiotherapy treatment for this disease between 1973–74. Interviews were conducted with each case and control and also with senior women in the households of 108 cases and 103 controls, in order to determine socioeconomic conditions, religious practices and dietary habits in the households. Current intake of salted fish was similar for cases and controls [details not presented]; however, significantly more senior women in the households of NPC cases (75%) reported having fed their babies salted fish after weaning than in those of controls (53%) (OR, 2.6; $p < 0.01$). The effect of intake of salted fish remained after adjusting for traditional life style practices. [The Working Group noted that it is not clear how the 150 NPC patients were selected from the 350 admissions or whether the information about weaning referred directly to the study subjects or was an indication of general household practice.]

Armstrong *et al.* (1983) conducted a case–control study of NPC (100 cases, 100 controls) among Chinese residing in 27 census districts in Selangor, Malaysia. Controls were individually matched to cases on sex, age and neighbourhood of residence. All cases were histologically confirmed, had been resident in the study area for at least five years and had been diagnosed between 1973 and 1980 in the only hospital that offered radiotherapy treatment for NPC in Malaysia. The interviews covered information on use of alcohol, tobacco and nasal ointments and dietary habits. Current intake of salted fish as well as intake during childhood and adolescence were assessed. Salted fish consumption during childhood was a significant risk factor (OR for any consumption *versus* no consumption, 3.0; $p = 0.04$); the OR was 17.4 (95% CI, 2.7–111.1) for daily intake compared to no intake. Salted fish intake during adolescence was also a risk factor, but its effect was weaker than that observed for childhood intake. The OR for daily consumption of salted fish compared to less than weekly consumption during adolescence was 3.5 (95% CI, 1.2–10.7). Current intake of salted fish was not a risk factor. The effect of salted fish intake remained when the effects of other risk factors (i.e., occupational exposure to smoke and/or dust) were accounted for in the analysis.

Yu *et al.* (1986) conducted a population-based case–control study of NPC in Hong Kong. Eligible cases were Chinese residents of Hong Kong with histologically confirmed NPC diagnosed when they were less than 35 years of age, identified from four hospitals in Hong Kong covering over 90% of all new cases in the area. A total of 266 cases were identified, and interviews were successfully completed with 250 (245 confirmed histologically; 16 refused). Controls were friends of cases, and each was matched to the index case by sex and date of birth (within five years); in two instances, the first control refused and a second eligible control was interviewed. In addition, 182 case and 155 control mothers participated in the study. The index subjects and their mothers were interviewed by one interviewer (one of the authors of the study), who could thus not be blinded to the status of the respondent.

Consumption of salted fish three years before interview/diagnosis and at the age of 10, as reported by the index subjects, and at the age of 10, between the ages of one and two and during weaning, as reported by the mothers of index subjects, was significantly associated with the occurrence of NPC, and a strong dose–response relationship was observed, based on frequency of consumption. For the four time periods assessed, the risk for NPC was up to 38 times higher for people with the highest frequency of intake than for those who had never or rarely ate the food. The association was stronger for consumption in childhood than in adulthood, and the strongest association was with intake before the age of two. There was strong concordance in the pattern of intake of salted fish at age 10 as reported by the index subject and by mothers of index subjects. The consumption patterns of male and female controls were similar, and the ORs for corresponding levels of consumption were alike. The ORs for salted fish intake remained highly significant after account was taken of domestic and occupational exposure to smoke, dust or fumes. A number of preserved foods were significantly associated with the occurrence of NPC, but none remained significant after salted fish intake was adjusted for.

Yu *et al.* (1988) conducted a case–control study in Yulin Prefecture in Guangxi Autonomous Region, China, among Han Chinese under the age of 45. This study area was chosen because it borders Guangdong Province and represents an intermediate-risk population within southern China. Eligible cases were residents of Yulin Prefecture with histologically confirmed incident cases of NPC (231 cases), diagnosed between 1984 and 1986 in one of eight hospitals located in Yulin and neighbouring prefectures. Controls of the Han race were chosen from the general population of Yulin Prefecture and matched to cases by sex, age (within five years) and neighbourhood; about 60% of the controls were the first that were eligible. Interviews were conducted with 128 case and 174 control mothers of the 231 cases and 231 controls identified, giving a total of 109 matched case–control mother pairs. All interviews were conducted by trained interviewers, who used a structured questionnaire to enquire about dietary habits, use of nasal oils, incense and mosquito coils and other life style practices. Mothers were asked about the index subjects' consumption of 10 food items during weaning, of 19 food times between the ages of one and two and of 42 food items at around the age of 10. The mother's own pattern of consumption of salted fish during pregnancy with and lactation of the index subject was also assessed. Mothers were asked to describe consumption patterns at the different time points using three frequency categories: rarely, at least once a month to less than once a week, once a week to less than daily. Subjects' intake of salted fish during weaning as well as the mothers' intake during pregnancy and nursing was significantly related to the occurrence of NPC. When compared to mothers who rarely ate salted fish during pregnancy and nursing, mothers who ate this food weekly during pregnancy had an OR of 3.1 (95% CI, 1.1–8.8) (which was reduced after adjustment for other dietary factors to 1.7 [$p = 0.017$]), and those who ate it weekly during lactation had an OR of 4.9 (95% CI, 1.5–15.9). Subjects' consumption of salted fish during weaning was associated with about a three-fold increase in risk (OR, 2.6; 95% CI, 1.2–5.6). Consumption of salted fish between the ages of one and two years and consumption around the age of 10 were also positively associated with risks for NPC, but these results did not reach statistical significance. The findings clearly suggest that early exposure (before the age of two years) is more important than later exposure (around the age of 10 years). Because of the extremely close

correlations between mothers' intake during pregnancy and nursing and subjects' intake during weaning, however, it was not possible to assess the relative importance of exposure during the three time periods.

Yu *et al.* (1989b) conducted a case–control study of NPC in Guangzhou (Canton City), China, where most of the population are Cantonese and from where most of the Chinese in Hong Kong originated. The rates of NPC in Guangzhou are believed to be comparable to those in Hong Kong. In the primary treatment facility for NPC in Guangzhou, 329 histologically confirmed incident cases diagnosed under the age of 50 were identified between 1983 and 1985, of whom 306 (209 men, 97 women) were alive and were interviewed. An equal number of age-, sex- and neighbourhood-matched controls were identified and interviewed. The mothers of 110 cases (71 men, 38 women) and 139 controls (90 men, 49 women) who were under the age of 45 were interviewed in person about dietary habits by four trained interviewers using structured questionnaires; subjects were also interviewed. Intake of salted fish by mothers during pregnancy and nursing and by subjects during weaning, at the ages of one to two, at the age of around 10 and three years before interview were significantly associated with the risk for NPC. At the highest frequency of intake at each time period (i.e., daily intake during nursing and pregnancy for mothers; daily intake for subjects at the age of around 10 and three years previously; weekly intake for subjects at the ages of one to two; and during weaning), there was a significant, two-fold increased risk. The effect of salted fish was independent of other significant dietary risk factors—mouldy bean curd and *chan pai mui* (salted, dried plums).

Ning *et al.* (1990) conducted a case–control study of NPC in Tianjin City, in northern China, a low-risk region for NPC, with rates of about 2–3 per 100 000. Cases were identified through the population-based tumour registry of Tianjin. Subjects were considered to be eligible if they were aged 64 or less at the time of diagnosis and had histologically confirmed NPC diagnosed on or after 1 January 1981. Three neighbourhood controls were matched individually to the patients for age (within five years), sex and race (Han). Of the 163 eligible cases identified, 100 patients (68 men, 32 women) and 300 controls were interviewed about diet, mostly by one of the authors of the study. Exposure to salted fish was significantly associated with an increased risk for NPC (OR, 2.2; 95% CI, 1.3–3.7). Four characteristics of exposure to salted fish contributed independently to the increased risk: decreasing age at first exposure, increasing duration of consumption, increasing frequency of consumption at the age of 10 and consumption of salted fish after steaming (OR, 4.2; 95% CI, 2.2–8.3) rather than after frying, grilling or boiling (OR, 1.6; 95% CI, 0.8–3.2). The effect of salted fish intake was independent of the increased risk associated with consumption of salted shrimp paste. [The Working Group noted that the study population was older than those in the studies of Yu *et al.* and that no information was available on exposure to salted fish at weaning or in early childhood.]

A further case–control study of NPC was conducted in a hospital in north-eastern Thailand, a region in which the risk for this neoplasm is intermediate (Sriamporn *et al.*, 1992). Data on current salted fish consumption, cigarette smoking, alcohol drinking and occupational exposure to smoke or dust were collected for 120 NPC cases diagnosed during 1987–90 (67.5% males) and for the same number of hospital controls matched by sex and age. As consumption of *pla-ra* (freshwater fish left to ferment in salted water) was reported by

all but four study subjects, it could not be evaluated. After adjustment for alcohol and cigarette consumption, occupation, level of education, residence, age and sex, consumption of Chinese-style sea-salted fish less than once a week gave an OR of 1.5 (95% CI, 0.6–3.5), and consumption at least once a week gave an OR of 2.5 (95% CI, 1.2–5.2), when compared to no consumption.

[The Working Group noted that the case–control studies on NPC and consumption of salted fish did not examine the concomitant role of Epstein-Barr virus (EBV) infection in the etiology of this cancer. Although NPC patients, regardless of ethnic or geographic origin, show a characteristic EBV antibody pattern and the presence of viral fingerprints in tumour cells, the nature of the association between EBV and NPC is unclear (de-Thé *et al.*, 1982). Southern Chinese at high risk for NPC do not differ from low-risk populations in China or elsewhere in the prevalence of EBV infection or in the age at primary infection with EBV (Zeng, 1985). The dissimilarities in the geographical and racial distributions of EBV infection and NPC thus suggest that the observed effect of salted fish cannot be explained by EBV infection.]

### 2.1.2 *Stomach cancer* (see Table 5)

The role of salted fish in the etiology of stomach cancer was investigated in a study, described in detail in the monograph on pickled vegetables (p. 97), conducted in 1984–86 in a high-risk area in China (Linqu, a rural county in Shandong Province) (You *et al.*, 1988). People who had the highest level of intake of salted fish (> 1 kg/year; about 2.8 g/day) had a nonsignificant increase in risk compared with people who consumed 0.5 kg or less per year. The authors noted that the effect of salted fish was enhanced in logistic regression analyses when the effects of other risk factors were accounted for [details not given].

### 2.1.3 *Oesophageal cancer* (see Table 5)

The role of salted fish in the etiology of oesophageal cancer was investigated in a study, described in detail in the monograph on pickled vegetables (p. 99), conducted among Chinese in Hong Kong in 1989–90 (Cheng *et al.*, 1992). Current intake of salted fish was associated with an increased risk for oesophageal cancer, reaching an OR of 4.73 (95% CI, 2.11–10.60) for daily or more frequent intake. The association observed in univariate analyses was, however, greatly weakened [details not given] when the effects of other dietary variables (e.g., pickled vegetables) were accounted for. The authors proposed that the dilution of the effect of current intake of salted fish might have been related to a stronger effect of exposure in early childhood than currently and to the generally smaller amounts of salted fish consumed compared to pickled vegetables.

**Table 5. Summary of case–control studies of cancer and consumption of Chinese-style salted fish**

| Geographical area (reference) | No. of cases and no. and type of controls | Intake | Odds ratio | 95% CI or *p* value | Comments |
|---|---|---|---|---|---|
| **Nasopharyngeal cancer** | | | | | |
| USA, California (Henderson *et al.*, 1976; Henderson & Louis, 1978) | Chinese subjects: 74 cases and 110 hospital/clinic controls | Any current use | 2.1 | 0.6–6.3 | Chinese subjects represented 47% of cases and 41% of controls interviewed. |
| | | At least 1/month } *vs* never | 1.6 | | |
| | | 1/week } *vs* never | 2.1 | | |
| | | > 1/week } *vs* never | 3.1 | | |
| | | *p* for trend = 0.02 | | | |
| Hong Kong (Geser *et al.*, 1978) | Chinese subjects: 150 cases and 150 hospital controls | Current use | No association | | Analysis of use around weaning based on interview of senior women in 108 case and 103 control households |
| | | Salted fish after weaning | 2.6 | $p < 0.01$ | |
| Malaysia (Armstrong *et al.*, 1983) | Chinese subjects: 100 cases and 100 population controls | *Childhood use*: | | | Mean age of cases and controls: 45 years |
| | | Yes *vs* no | 3.0 | $p = 0.04$ | Effect of salted fish remained when occupational exposures were accounted for. |
| | | < 1/day | 2.8 | | |
| | | 1/day | 17.4 | | |
| | | | *p* for trend < 0.001 | | |
| | | *Adolescent use*: | | | |
| | | < 1/week | 1.0 | | |
| | | 1/day | 3.5 | 1.2–10.7 | |
| | | Current use | No association | | |
| Hong Kong (Yu *et al.*, 1986) | Chinese subjects: 250 cases and 250 friend controls; 182 case and 155 control mothers also interviewed | *Three years before interview* | | | Subjects aged < 35 years; interviewer aware of status of patient. |
| | | 1/month–< 1/week } *vs* rarely | 2.3 | 1.5–3.5 | Effect of salted fish remained when effects of potential confounders (including other foods, domestic/occupational exposures to smoke, dust or fumes) were accounted for. |
| | | ≥ 1/week but < 1/month } *vs* rarely | 3.2 | 1.7–6.1 | |
| | | 1/day } *vs* rarely | 7.5 | 0.9–65.3 | |
| | | *At 10 years of age* | | | Intake of salted fish was important during all time periods, particularly during childhood. |
| | | 1/month but < 1/week } *vs* rarely | 15.0 | 6.0–37.2 | |
| | | ≥ 1/week } *vs* rarely | 37.7 | 14.1–100.4 | |
| | | *Between age 1 and 2 years* (reported by mother) | | | |
| | | Sometimes } *vs* never | 6.1 | 3.0–12.5 | |
| | | Often } *vs* never | 20.2 | 6.8–60.2 | |
| | | *During weaning* (reported by mother) | | | |
| | | Ever *vs* never | 7.5 | 3.9–14.8 | |

**Table 5 (contd)**

| Geographical area (reference) | No. of cases and no. and type of controls | Intake | Odds ratio | 95% CI or *p* value) | Comments |
|---|---|---|---|---|---|
| Guangxi Region, China (Yu *et al.*, 1988) | 231 cases and 231 population controls; 128 case and 174 control mothers also interviewed | *Mothers' intake*<br>During pregnancy:<br>1/month } *vs* rarely<br>1/week } *vs* rarely<br>During nursing:<br>1/month } *vs* rarely<br>1/week } *vs* rarely<br>*Subjects' intake*<br>During weaning: yes *vs* no<br>Between ages 1 and 2:<br>1/month } *vs* rarely<br>1/week } *vs* rarely<br>Around age of 10:<br>1/month } *vs* rarely<br>1/week } *vs* rarely | <br><br>1.9<br>3.1<br><br>1.3<br>4.9<br><br>2.6<br><br>1.2<br>2.2<br><br>1.5<br>1.5 | <br><br>1.0–3.6<br>1.1–8.8<br><br>0.6–2.6<br>1.5–15.9<br><br>1.2–5.6<br><br>0.5–2.7<br>0.7–7.6<br><br>0.9–2.7<br>0.5–4.3 | Subjects < 45 years of age. Risks adjusted for subject's sex and age (< 35, ≥ 35 years). 1/month = at least 1/month–< 1/week; 1/week = at least 1/week to < 1/day. Intake of many salted and preserved foods during weaning and between ages 1 and 2 was assessed: intake of salted fish during weaning, strongest risk factor; intake during pregnancy remained significant after adjustment for other foods in regression analyses. Other foods with a significant effect on risk included salted ducks' eggs, salted mustard greens and *chung choi* during weaning; dried fish, fermented black bean paste and fermented soya bean paste between ages 1 and 2 |
| Guangzhou, China (Yu *et al.*, 1989b) | 306 cases and 306 population controls; 110 case and 139 control mothers also interviewed | *Subjects' intake*<br>(reported by mothers)<br>During weaning: yes *vs* no<br>Between ages 1 and 2:<br>1/month } *vs* rarely<br>1/week } *vs* rarely<br>Around age 10:<br>1/month<br>1/week } *vs* rarely<br>1/day | <br>2.1<br><br>1.6<br>2.0<br><br>1.3<br>1.1<br>2.4 | <br>1.2–3.6<br><br>0.8–3.4<br>1.1–3.6<br><br>0.6–2.8<br>0.5–2.3<br>1.0–6.0 | Subjects < 50 years of age. 1/month = at least 1/month to < 1/week. 1/week = at least 1/week to < 1/day. Only intake of salted fish during weaning was significant when intakes during other time periods were examined simultaneously. Results for salted fish remained significant when intake of other foods was accounted for. |

**Table 5 (contd)**

| Geographical area (reference) | No. of cases and no. and type of controls | Intake | Odds ratio | 95% CI or *p* value) | Comments |
|---|---|---|---|---|---|
| Guangzhou, China (Yu *et al.*, 1989b) (contd) | | *Subjects' intake* (reported by subjects) | | | Other foods with an independent effect on risk included mouldy bean curd and *chan pai mui*. Intake prevalence among cases was similar to that in Hong Kong (Yu *et al.*, 1986), but intake among controls was twice as common in Guangzhou as in Hong Kong. |
| | | Around age 10: | | | |
| | | 1/month } *vs* rarely | 1.1 | 0.7–1.9 | |
| | | 1/week } *vs* rarely | 1.4 | 0.9–2.2 | |
| | | 1/day } *vs* rarely | 2.1 | 1.2–3.6 | |
| | | Three years previously: | | | |
| | | 1/month } *vs* rarely | 0.9 | 0.6–1.4 | |
| | | 1/week } *vs* rarely | 1.4 | 0.9–2.1 | |
| | | 1/day } *vs* rarely | 1.8 | 0.9–3.6 | |
| | | *Mothers' intake* | | | |
| | | During pregnancy: | | | |
| | | 1/month } *vs* rarely | 0.9 | 0.4–1.8 | |
| | | 1/week } *vs* rarely | 1.7 | 0.9–3.2 | |
| | | 1/day } *vs* rarely | 2.2 | 1.1–4.6 | |
| | | During nursing: | | | |
| | | 1/month } *vs* rarely | 0.8 | 0.4–1.7 | |
| | | 1/week } *vs* rarely | 1.1 | 0.6–2.2 | |
| | | 1/day } *vs* rarely | 2.3 | 1.1–4.6 | |
| Tianjin, China (Ning *et al.*, 1990) | Han Chinese subjects: 100 cases and 300 neighbourhood controls | *Any intake* | | | Subjects were < 65 years of age; mean age: cases, 44.9 years; controls, 45.2 years. 39% (63/163) cases could not be interviewed. Most interviews were conducted by one of the authors of the study. The effect of salted fish remained when other factors were adjusted for. Intake of salted shrimp paste was another risk factor. |
| | | Ever *vs* never | 2.2 | 1.3–3.7 | |
| | | *Age at first exposure (years)* | | | |
| | | ≥ 21 | 1.5 | 0.7–3.3 | |
| | | 11–20 | 1.9 | 0.9–4.0 | |
| | | 1–10 | 2.6 | 1.5–4.6 | |
| | | *Duration of consumption (years)* | | | |
| | | 1–10 | 1.6 | 0.9–3.1 | |
| | | 11–20 | 2.8 | 1.4–5.4 | |
| | | ≥ 21 | 2.8 | 1.4–5.6 | |

**Table 5 (contd)**

| Geographical area (reference) | No. of cases and no. and type of controls | Intake | Odds ratio | 95% CI or *p* value) | Comments |
|---|---|---|---|---|---|
| Tianjin, China (Ning *et al.*, 1990) (contd) | | *Frequency of consumption at age of 10:* | | | |
| | | 1/year | 1.6 | 0.8–3.2 | |
| | | 1/month | 3.5 | 1.6–7.4 | |
| | | 1/week or 1/day | 6.7 | 2.2–20.7 | |
| | | *Cooking method for consumption at age 10:* | | | |
| | | Steaming | 4.2 | 2.2–8.3 | |
| | | Other (frying, grilling or broiling) | 1.6 | 0.8–3.2 | |
| North-eastern Thailand (Sriamporn *et al.*, 1992) | 120 cases and 120 hospital controls | No consumption | 1.0 | | Logistic estimates adjusted for occupation and area of residence, alcohol intake, type of cigarettes smoked and level of education |
| | | < 1/week | 1.5 | 0.6–3.5 | |
| | | ≥ 1/week | 2.5 | 1.2–5.2 | |
| **Stomach cancer** | | | | | |
| Shandong, China (You *et al.*, 1988) | 564 cases and 1131 population controls | ≤ 1 kg/year } *vs* ≤ 0.5 kg/year | 1.0 | 0.8–1.4 | Questionnaire included 85 food items; intake habits about 1965 and 1980; adjusted for sex, age and family income |
| | | > 1 kg/year } *vs* ≤ 0.5 kg/year | 1.4 | 0.8–1.5 | |
| **Oesophageal cancer** | | | | | |
| Hong Kong (Cheng *et al.*, 1992) | Chinese subjects: 400 cases and 1598 controls (800 hospital, 798 general practice) | < 1/year | 1.0 | | Adjusted for age, level of education and birthplace. Univariate analysis much weakened by adjustment for other variables. |
| | | < 1/month | 0.99 | 0.56–1.77 | |
| | | 1–3/month | 1.17 | 0.72–1.92 | |
| | | 1–3/week | 2.03 | 1.23–3.34 | |
| | | 4–6/week | 3.15 | 1.58–6.29 | |
| | | 1/day or more | 4.73 | 2.11–10.60 | |

CI, confidence interval

## 2.2 Other salted fish

### 2.2.1 *Nasopharyngeal carcinoma*

*Case–control studies* (see Table 6)

Jeannel *et al.* (1990) carried out a case–control study on all incident cases of NPC that had been histologically confirmed and treated at the Institute of Cancer in Tunis, Tunisia, in 1986–87. Eighty cases and 160 age- and sex-matched neighbourhood controls were interviewed about socioeconomic conditions, diet during the year preceding diagnosis and, with the help of their families, diet during the first month of life, weaning, childhood and adolescence. Tunisian families live under the same roof, and in most households there is someone of an older generation who can answer questions about childhood diet and weaning. Living conditions, such as living in a *gourbi* (makeshift one-room dwelling) without separate beds for parents and children and without windows, and cooking in the main room during childhood, were significantly associated with risk for NPC. All of these variables were pooled in a single score for multivariate matched analysis of dietary variables. Subjects who had been weaned directly from mother's milk on to an adult diet were at higher risk, regardless of living conditions. Intake of salted anchovies during childhood was associated with a small increase in risk (crude OR, 2.6; $p = 0.08$), but this association was no longer significant when living conditions were accounted for in the analysis (adjusted OR, 1.5; $p = 0.5$).

In a study of NPC among Alaskan native populations (Eskimos, Indians and Aleuts), Lanier *et al.* (1980) collected information on the dietary habits of 13 of 31 cancer patients diagnosed during 1966–76 and 13 controls individually matched on age, sex, ethnic group and residence. More cases than controls reported having eaten salted fish frequently in childhood (four *versus* one discordant pairs).

### 2.2.2 *Stomach cancer*

Most of the available studies on salted fish and stomach cancer were conducted in populations at high risk for cancer at this site.

(*a*) *Correlation studies*

Two of three correlational studies conducted in Japan suggested that consumption of salted fish is positively associated with risk for stomach cancer. (For a detailed description of the studies, see the monograph on pickled vegetables, pp. 90–91.) The two studies with positive results used the rates of mortality from stomach cancer and dietary information from 46 prefectures. In the study of Hirayama (1971), standardized death rates for stomach cancer in 1955 were correlated with marketing data obtained in 1959 and nutritional survey data obtained in 1958 by the Ministry of Agriculture. A significant positive association was found between salted fish intake and stomach cancer mortality (salted salmon, $p < 0.01$; salted trout, $p < 0.05$; other salted fish, $p > 0.10$). In a later study (Hara *et al.*, 1985), cancer mortality data for 1969–79 were related to consumption data obtained from a national survey in 1974 [specific type of dietary data obtained not described]. Of the many categories of foods compiled in the survey, 26 food items were selected for this correlation study. The

standardized mortality ratio (SMR) for stomach cancer was significantly associated with intake of salted or dried fish ($p < 0.05$). In a study in which mortality rates for 1969–74 were related to dietary data from 1040 census tracts in Japan sampled in 1974, 1975 and 1976 (Nagai *et al.*, 1982), consumption of dried or salted fish was not associated with risk for stomach cancer ($r = 0.052$ for men; $r = -0.026$ for women). In this study, the nutritional data were based on foods consumed over a three-day period by approximately 70 people in about 20 households in 300 areas of Japan.

Kolonel *et al.* (1980, 1981, 1983) conducted a series of correlation studies among Japanese and other ethnic groups in Hawaii. The results of these studies support a positive association between intake of salted or dried fish and risk for stomach cancer. A decreasing gradient in the rates of stomach cancer was seen for Japanese in Japan, first-generation Japanese in Hawaii, second-generation Japanese in Hawaii and Caucasians in Hawaii. A corresponding gradient was seen for intake of salted or dried fish.

(*b*) *Cohort studies* (see Table 7)

In a cohort study conducted on Hawaiian men of Japanese ancestry (Chyou *et al.*, 1990), described in detail in the monograph on pickled vegetables (p. 93), incident cases of stomach cancer identified in 1966–83 were compared with a random sample of the cohort who had not developed cancer at the end of the follow-up period. The two groups did not differ significantly in their intake of dried fish: the mean daily intake was 0.4 g for cases and 1.3 g for the subcohort. [The Working Group noted that it was not clear whether salted fish was included in the category of dried fish. The authors describe the study as a case–cohort study; however, the controls were not selected from the total cohort at its inception.]

Kneller *et al.* (1991) investigated the effect of salted fish in a cohort of 17 633 white US men aged 35 and older, mainly of Scandinavian and German descent, who responded to a mailed questionnaire in 1966. After 20 years of follow-up, 23% of the cohort (4027 respondents) were lost to follow-up, and there were 1033 cancer deaths, including 75 from stomach cancer. The questionnaire covered demographic factors, use of tobacco and alcohol, dietary pattern (including 35 food items) and other factors. After control for age and smoking status, salted fish emerged as a risk factor for stomach cancer. Subjects who ate salted fish at least once a month showed about a two-fold increase in risk over those with less frequent intake. This increase was most apparent among residents of the north-central states (relative risk, 2.1; 95% CI, 1.08–4.13) and among immigrants and first-generation Americans (relative risk, 2.2; 95% CI, 0.97–4.77). The results for salted fish were adjusted for year of birth and current smoking habits but not for other significant dietary factors.

(*c*) *Case–control studies* (see Table 6)

Intake of dried and salted fish emerged as a risk factor for stomach cancer in a study conducted among Japanese in Hawaii (Haenszel *et al.*, 1972), described in detail in the monograph on pickled vegetables (pp. 93–94). About a two-fold increase in risk for stomach cancer was associated with eating dried or salted fish at least four times per month, when compared with nonconsumers; however, the risks associated with intake once or two to three times per month were not significantly different from those of nonconsumers. The risk associated with consumption of dried and salted fish combined was no higher than the risks

associated with eating dried and salted fish individually. Analyses were not conducted for dried and salted fish simultaneously, so that it is difficult to determine the independent effect of each of these food items. The association between dried/salted fish and stomach cancer was observed among both migrants (Issei) and second-generation (Nisei) Japanese Americans, but the effects were slightly more pronounced among the Issei. The effects of other foods were not accounted for in the analysis.

In a study conducted in Hiroshima and Miyagi prefectures in Japan (see Figure 3) (Haenszel *et al.*, 1976), described in detail in the monograph on pickled vegetables (p. 94), intake of salted/dried fish was associated with a small, nonsignificant increased risk for stomach cancer in both study areas. The ORs were 1.06 and 1.20, respectively, for consumption four to nine and 10 or more times per month compared to less than four times per month. When the results were examined separately for the two prefectures, the increase was somewhat higher in Miyagi (where traditional customs persisted) than in Hiroshima. The association between intake of salted fish and stomach cancer risk was similar for diffuse and intestinal types of stomach cancers. The effects of other foods were not accounted for in the analysis.

**Figure 3. Map of Japan showing the islands, prefectures and cities that have been studied with respect to consumption of salted fish**


From Hara *et al.* (1985)

In a study conducted in Nagoya, Japan (Tajima & Tominaga, 1985), described in detail in the monograph on pickled vegetables (p. 94), a significant, two-fold increase in risk for stomach cancer was associated with intake of dried or salted fish at least once a week compared with less frequent intake, after adjustment for sex and age (1.99; $p < 0.05$). [The Working Group noted that although multivariate analyses were conducted, it is not clear whether the results for salted fish were adjusted for other dietary factors.]

In a study described in detail in the monograph on pickled vegetables (pp. 94, 97), conducted in Saga Prefecture, a low-risk rural area in Kyushu, Japan (Kono *et al.*, 1988), intake of salted fish did not differ between gastric cancer patients and the two control groups (hospital and population controls).

Buiatti *et al.* (1989) conducted a population-based case–control study of stomach cancer in Italy, comprising seven centres in two high- and two low-risk areas displaying a three-fold range of rates for stomach cancer mortality. Eligible subjects were aged 75 or less, residents of the study areas and with histologically confirmed gastric cancers diagnosed in 1985–87 in one of the hospitals in the study areas. Personal interviews were conducted with 1016 of 1229 eligible patients. Of the 1159 general population controls of similar age, sex and study area, 266 were second controls. The interviews were extensive, covering the intake of 146 food items and beverages consumed during a 12-month period approximately two years before the interview. Over 90% of patient interviews were conducted in hospital, whereas over 60% of interviews with controls took place at home. Risk increased with increasing tertile of intake of salted and dried anchovies, cod and herring (ORs, 1.0, 1.1, and 1.4, respectively, for tertiles; $p$ for trend = 0.001), even after adjustment for matching variables and the main potential confounders (excluding other dietary variables). The ORs for stomach cancer and intake of salted/dried fish were not reported separately for the high- and low-risk areas, but intake of these products was not consistent in the two areas.

In a subsequent analysis by histological type of stomach cancer, a significantly increased risk was found to be associated with the highest compared to the lowest tertile of intake of salted/dried fish for both intestinal (OR, 1.5; 95% CI, 1.1–1.9) and diffuse (1.5, 1.1–2.1) types of stomach cancer (Buiatti *et al.*, 1991). In a further analysis, 68 cases of cancer of the cardia were separated from the remaining sites (Palli *et al.*, 1992). No difference was seen in the risk associated with consumption of salted/dried fish from that of gastric cancer at other sites.

*(d) Precursor lesions*

Nomura *et al.* (1982) conducted a study in Japan, described in detail in the monograph on pickled vegetables (pp. 97–98), to identify risk factors for intestinal metaplasia of the stomach, an established precursor stage of stomach cancer. The dietary item most strongly related to metaplasia score was dried fish ($p = 0.002$, multiple linear regression analysis), consisting mainly of dried sardine, cod, mackerel or herring, with salt added. This finding was made only among males.

### 2.2.3 *Other cancers* (see Table 6)

The association between salted fish and oesophageal cancer was investigated in a number of correlation studies conducted in Japan, described in detail in the monograph on pickled vegetables (pp. 98–99). In the study of Nagai *et al.* (1982), dried or salted fish was one

**Table 6. Summary of results of case–control studies on consumption of salted fish other than Cantonese-style**

| Geographical area (reference) | No. of cases and no. and type of controls | Intake level | Odds ratio | 95% CI or *p* value | Comments |
|---|---|---|---|---|---|
| **Nasopharyngeal carcinoma** | | | | | |
| Tunisia (Jeannel *et al.*, 1990) | 80 cases and 160 neighbourhood controls | *During childhood* Salted anchovies: yes *vs* no | 1.5 | $p = 0.5$ | Adjusted for living conditions; crude RR was 2.6 ($p = 0.08$) |
| USA, Alaska (Lanier *et al.*, 1980) | 13 cases and 13 controls | *During childhood* Salted fish | 4 *vs* 1 | | Discordant pairs |
| **Stomach cancer** | | | | | |
| USA, Hawaii (Haenszel *et al.*, 1972) | Japanese subjects: 220 cases and 440 hospital controls | *Dried fish* | | | Questionnaire included a number of Japanese and western foods. RR adjusted for sex and place of birth. Any use significant for Issei not Nisei. Results elevated but not significant for Issei and Nisei separately |
| | | Any use *vs* no use | 1.8 | $p < 0.05$ | |
| | | 1/month *vs* no use | 1.5 | $p > 0.05$ | |
| | | 2–3/month *vs* no use | 1.6 | $p > 0.05$ | |
| | | ≥ 4/month *vs* no use | 2.8 | $p < 0.05$ | |
| | | *Salted fish* | | | |
| | | Any use *vs* no use | 1.6 | $p < 0.05$ | |
| | | 1/month *vs* no use | 1.4 | $p > 0.05$ | |
| | | 2–3/month *vs* no use | 2.0 | $p < 0.05$ | |
| | | ≥ 4/month *vs* no use | 2.0 | $p < 0.05$ | |
| | | *Dried and salted fish combined* | | | Results significant for Issei |
| | | Use of both *vs* no use | 2.0 | $p < 0.05$ | |
| | | Total, 2/month *vs* no use | 1.5 | $p > 0.05$ | |
| | | Total, 3–5/month *vs* no use | 2.5 | $p < 0.05$ | |
| | | Total, 6/month *vs* no use | 2.6 | $p < 0.05$ | |
| Japan, Hiroshima and Miyagi (Haenszel *et al.*, 1976) | 783 cases and 1566 hospital controls | *Salted/dried fish* | | | Questionnaire included a number of Japanese and western foods. Increase greater in Miyagi than in Hiroshima |
| | | ≥ 4/month *vs* < 4/month | 1.12 | $p > 0.05$ | |
| | | 4–9/month *vs* < 4/month | 1.06 | | |
| | | ≥ 11/month *vs* < 4/month | 1.20 | $p > 0.05$ | |

**Table 6 (contd)**

| Geographical area (reference) | No. of cases and no. and type of controls | Intake level | Odds ratio | 95% CI or *p* value | Comments |
|---|---|---|---|---|---|
| Japan, Aichi Cancer Center, Nagoya (Tajima & Tominaga, 1985) | 93 cases and 186 hospital controls | *Dried/salted fish*<br>≥ 1/week *vs* < 1/week | 1.99 | $p < 0.05$ | Questionnaire included a list of specific foods and eating frequencies. Results adjusted for sex and age. Increase greater for dried or salted fish in 40–45 age group than in 56–70 age group. |
| Japan, northern Kyushu (Kono *et al.*, 1988) | 139 cases, 2574 hospital controls, 278 general population controls | *Salted fish*<br>1–3/month } *vs* none<br>≥ 3/month } *vs* none | 0.9<br>1.0 | $p > 0.05$<br>$p > 0.05$ | Questionnaire pertained to current habits only (year preceding interview); 25 food items. Some differences in the administration of questionnaire, even though all interviewers were trained together. |
| Italy (Buiatti *et al.*, 1989) | 1016 cases and 1159 population controls | *Salted and dried fish*<br>Tertiles of weekly intake:<br>Intermediate } *vs* low<br>High } *vs* low | <br><br>1.1<br>1.4<br>*p* for trend = 0.001 | | Questionnaire included frequency of intake of 146 food items. OR adjusted for age, sex, study area, social class, residence, migration, family history and Quetelet's index |
| (Buiatti *et al.*, 1991) | | *By histological type*<br>Highest *vs* lowest tertile:<br>Intestinal<br>Diffuse<br>Unclassified | <br><br>1.5<br>1.5<br>1.3 | <br><br>1.1–1.9<br>1.1–2.1<br>0.8–2.0 | Salted/dried fish included anchovies, cod, herring. Tertile cutoffs not presented |
| **Brain tumour** | | | | | |
| Canada, southern Ontario (Burch *et al.*, 1987) | 215 cases and 215 hospital controls | *Salted fish*<br>≥ 1 *vs* < 1/month | 1.4 | 0.4–4.4 | Only 58 cases were self-respondents. Only 124 case–control pairs were included in the analysis for salted fish, owing to missing information. |

**Table 6 (contd)**

| Geographical area (reference) | No. of cases and no. and type of controls | Intake level | Odds ratio | 95% CI or *p* value | Comments |
|---|---|---|---|---|---|
| **Liver cancer** | | | | | |
| Thailand, north-east (Parkin *et al.*, 1991) | 103 cases and 103 hospital controls | *Salted fish* ≥ monthly *vs* < monthly | 0.5 | 0.2–0.9 | Dietary information pertains to one year prior to interview; 54 dietary items included. Results no longer significant in multivariate analysis. |

CI, confidence interval

**Table 7. Summary of cohort studies on stomach cancer and consumption of salted or dried fish**

| Geographical area (reference) | No. of subjects, no. of cases and length of follow-up | Intake level | Relative risk | 95% CI or *p* value | Comments |
|---|---|---|---|---|---|
| USA, Hawaii (Chyou *et al.*, 1990) | 8006 men of Japanese descent<br>111 stomach cancers<br>(361 cancer-free controls)<br>18 years of follow-up | *Dried fish: Mean intake*<br>Cases: 0.4 g/day<br>Controls: 0.5 g/day | | $p = 0.44$ | 24-h dietary intake data were recoded to allow comparison by specific foods or food groups. *p* values calculated by comparing two mean values, adjusting for age |
| USA (Kneller *et al.*, 1991) | 17 633 men of Scandinavian and German descent<br>75 stomach cancers<br>20 years of follow-up | *Salted fish*<br>< 1/month } *vs* never<br>≥ 1/month } *vs* never<br>Used previously but not currently | 1.0<br>1.9<br>1.3 | 0.6–1.8<br>1.0–3.6<br>0.6–2.6<br>*p* for trend, NS | Mailed questionnaire, 35 food items included. Results adjusted for year of birth and current cigarette smoking. Salted fish primarily a risk factor for immigrants and second-generation Americans and for residents of north-central states |

CI, confidence interval

of three of the 20 foods or food groups investigated which was significantly and positively correlated with the occurrence of oesophageal cancer in both men and women. The standardized partial regression coefficient was 0.09 ($p < 0.01$) for men and 0.069 ($p < 0.05$) for women. Hara *et al.* (1985) correlated cancer mortality rates in 46 Japanese prefectures and data on food consumption from a national survey. Of the 26 food items investigated, salted or dried fish was significantly associated with SMRs for oesophageal cancer ($p < 0.01$).

Burch *et al.* (1987) conducted an exploratory study of brain tumours in adults in southern Ontario, Canada, between 1979 and 1982. A total of 328 histologically confirmed brain tumours diagnosed during 1977 and 1981 were identified through the medical record departments of 33 hospitals in the study area; 247 patients were selected for interview, but a high proportion of the interviews were conducted with relatives (only 58 were self-respondents). One hospital control without cancer was matched to each case on the basis of sex, area of residence, marital status, year of birth (within five years), date of diagnosis (within one year) for live cases and date of death (within one year) for deceased cases, resulting in 215 appropriately matched case–control pairs. Intake of a variety of processed meat and fish products containing nitrite was investigated. A small, nonsignificantly increased risk for brain tumour (OR, 1.4; 95% CI, 0.4–4.4) was found to be associated with regular consumption (at least once a month) of salted fish compared to less frequent consumption.

Parkin *et al.* (1991) conducted a case–control study of cholangiocarcinoma of the liver in north-eastern Thailand, described in detail in the monograph on aflatoxins (p. 262). In a univariate analysis, there was a significant deficit of cases who were frequent (monthly or more) consumers of salted fish; this result was no longer significant in a multivariate analysis.

In the study of Tajima and Tominaga (1985), described above and in detail in the monograph on pickled vegetables (p. 94), nonsignificant increases in risk for cancers of the colon and rectum were associated with consumption of dried or salted fish.

In the study of Lanier *et al.* (1980), described above, no difference in intake of salted fish in childhood was found between 17 patients with tumours at sites other than the nasopharynx (salivary glands and other cancers of the head and neck, excluding thyroid) and their matched controls.

## 3. Studies of Cancer in Experimental Animals

### 3.1 Oral administration

#### 3.1.1 *Rat*

Ten female and 10 male inbred WA albino rats, one month of age and weighing 150 g, were each given 30 g per day of steamed Chinese-style salted fish for six months and then 20 ml of an extract of Cantonese salted fish heads as drinking-water (500 g of salted fish heads boiled in 1 l of water to give a final concentration of 500 ml of extract, which was diluted 1:5 with fresh drinking-water to give a sodium chloride concentration of 0.9 g/l) on five days per week. A group of three males and three females served as controls. The animals

were sacrificed after one to two years or when moribund [number of animals alive at the time of diagnosis of the first tumour and number sacrificed at each time period not given]. The heart, lung, liver, spleen, kidney, trachea, oesophagus, stomach and six sections of nasal cavity were examined. In the treated group, 4/10 females developed carcinomas in the nasal or paranasal regions: two developed adenocarcinomas of the nasal cavity after 12 and 24 months, respectively, one an undifferentiated carcinoma of the paranasal sinus after 15 months and another a squamous-cell carcinoma of the bucco-alveolar sulcus after 24 months. No nasal or paranasal tumour was seen in treated males or in controls. The two rats with nasal adenocarcinomas also developed a mammary adenocarcinoma and a nodular liver, respectively (Huang *et al.*, 1978b). [The Working Group noted the small number of animals.]

Groups of 37 female and 37 male inbred Wistar-Kyoto rats, aged 21 days, were fed a powdered diet to which one part of Chinese-style salted fish (from Hong Kong; 48% soft-type fish and 52% hard-salted fish of nine common species) was added to five parts of diet (low dose) or to three parts of diet (high dose) for 18 months. A group of 37 males and 36 females given only rat chow served as controls. The salted fish was air-mailed to the study site (Los Angeles, USA) and then kept frozen; every two weeks, fish was thawed, steamed for 45 min, dried in a laminar flow hood, then ground to form a powder which was mixed with the rodent diet. After 18 months, all rats were given standard rat chow pellets, and at three years of age all remaining rats were killed and examined. Lung, kidney, liver, stomach and nasal cavity were examined. Median lengths of survival were 121, 123 and 127 weeks for low-dose, high-dose and control females and 131, 130 and 129 weeks for males. Three of 74 rats given the high dose of salted fish had epithelial tumours of the nasal cavity: a squamous-cell carcinoma during week 97 in a female, an undifferentiated carcinoma during week 44 in a male and a spindle-cell carcinoma during week 99 in a female. One low-dose male had a spindle-cell tumour of the nasal cavity [not otherwise specified] during week 118 of the experiment. Nasal cavity tumours were not found in low-dose females or in controls of either sex. No significant difference in the occurrence of other tumours was observed between treated and control animals (Yu *et al.*, 1989a). [The Working Group noted the limited number of tissues examined.]

### 3.1.2 *Hamster*

Six female and eight male Syrian golden hamsters, aged one month and weighing 100 g, were each given 20 g per animal of steamed Chinese-style salted fish for six months and then 20 ml of an extract of Cantonese salted fish heads as drinking-water (prepared as described in section 3.1.1) on five days per week. Three male and three females served as controls. The animals were sacrificed after one to two years or when moribund [numbers sacrificed at each time period not given]. The incidences of tumours of the heart, lung, liver, spleen, kidney, trachea, oesophagus, stomach and nasal cavity were not increased (Huang *et al.*, 1978b). [The Working Group noted the small number of animals.]

### 3.2 Administration with known carcinogens

*Mouse*

A group of 19 female mice (weighing 20–22 g) was given *N*-nitrososarcosine ethyl ester at 20 ml/kg bw in the diet five times over 200 days, and a group of 22 mice was fed the nitrosamine plus Chinese-style dry-salted fish [concentration of salted fish unspecified]. Carcinomas of the forestomach developed in 6/19 mice (31.6%) given the nitrosamine alone and in 14/22 (63.6%) also given the salted fish ($p < 0.05\%$). All mice had papillomas and carcinomas of the forestomach (Lin *et al.*, 1986).

## 4. Other Relevant Data

### 4.1 Absorption, distribution, metabolism and excretion

No data were available to the Working Group.

### 4.2 Toxic effects

No data were available to the Working Group.

### 4.3 Reproductive and developmental toxicity

No data were available to the Working Group.

### 4.4 Genetic and related effects

4.4.1 *Humans*

The urine of four nonsmoking Japanese became mutagenic to *Salmonella typhimurium* on days 2–3 and 6–7 following meals of fried, salted salmon. The urine was tested over seven consecutive days. Urinary mutagenicity increased up to 12–14 h after initial intake, reached a plateau at about 20 h and remained at that level up to 24 h. The excretion of mutagenic substances thus appeared to be complete within about 20 h (Ohyama *et al.*, 1987).

4.4.2 *Experimental systems* (see also Table 8 and Appendices 1 and 2)

In one study, rats fed dried salted fish from southern China produced urine that was mutagenic to bacteria. A variety of extracts prepared from several different kinds of salted fish from various countries were mutagenic to bacteria. In one study of salmon, cooking rather than salting produced bacterial mutagens.

## Table 8. Genetic and related effects of salted fish

| Test system | Result | | Dose (LED/HID; standardized to weight of original material) | Reference |
|---|---|---|---|---|
| | Without exogenous metabolic system | With exogenous metabolic system | | |
| **Hawaiian dried salted fish** | | | | |
| ERC, *Escherichia coli rec* strains, differential toxicity | – | – | 100 µl fish extract | Ichinotsubo & Mower (1982) |
| SA7, *Salmonella typhimurium* TA1537, reverse mutation | – | – | 1000 µl fish extract | Ichinotsubo & Mower (1982) |
| SA0, *Salmonella typhimurium* TA100, reverse mutation | + | – | 400 µl fish extract | Ichinotsubo & Mower (1982) |
| SA9, *Salmonella typhimurium* TA98, reverse mutation | – | – | 1000 µl fish extract | Ichinotsubo & Mower (1982) |
| EC2, *Escherichia coli* WP2, reverse mutation | – | – | 1000 µl fish extract | Ichinotsubo & Mower (1982) |
| **Southern Chinese salted fish** | | | | |
| SA0, *Salmonella typhimurium* TA100, reverse mutation | + | + | 1.25 mg (aqueous) | Ho *et al.* (1978) |
| SA9, *Salmonella typhimurium* TA98, reverse mutation | + | + | 1.25 mg (aqueous) | Ho *et al.* (1978) |
| BFA, Urine from rats, microbial mutagenicity | + | + | Not given | Ho *et al.* (1978) |
| **Japanese salted salmon (fried)** | | | | |
| SA0, *Salmonella typhimurium* TA100, reverse mutation | – | + | 1 g[a] | Ohyama *et al.* (1987) |
| SA5, *Salmonella typhimurium* TA1535, reverse mutation | – | – | 1 g[a] | Ohyama *et al.* (1987) |
| SA8, *Salmonella typhimurium* TA1538, reverse mutation | (+) | + | 1 g[a] | Ohyama *et al.* (1987) |
| SA9, *Salmonella typhimurium* TA98, reverse mutation | (+) | + | 50 mg[a] | Ohyama *et al.* (1987) |
| BFH, Urine from humans, microbial mutagenicity | + | + | Not given | Ohyama *et al.* (1987) |
| **Chinese salted fish (*pak wik*) from Canada** | | | | |
| SA5, *Salmonella typhimurium* TA1535, reverse mutation (suspension assay) | – | 0 | 500 mg/ml (methanol extract) | Stich *et al.* (1982) |

+, positive; (+), weakly positive; –, negative; 0, not tested

[a]Dichloromethane–XAD-2 ion-exchange resin eluate of aqueous extract

# 5. Summary of Data Reported and Evaluation

## 5.1 Exposure data

Salted fish is prepared by treating fish with dry salt or an aqueous salt solution and is often subsequently dried in the sun. It is produced and consumed primarily in Southeast Asia and northern Europe. Chinese-style salted fish is usually softened by partial decomposition before or during salting. High levels of *N*-nitrosodimethylamine have been reported in some samples of Chinese-style salted fish.

## 5.2 Human carcinogenicity data

The pattern of nasopharyngeal carcinoma incidence in China reflects the pattern of consumption of salted fish. Eight case–control studies consistently demonstrate that consumption of Chinese-style salted fish is strongly related to risk for nasopharyngeal carcinoma. The effect remained in studies that controlled for other risk factors. A significant dose–response relationship is seen between frequency of intake and risk for nasopharyngeal carcinoma, and the association is especially strong for intake of salted fish during childhood. Two further case–control studies, on oesophageal cancer and stomach cancer, found nonsignificant associations with consumption of Chinese-style salted fish.

The association between cancer and the consumption of other types of salted fish was examined in several studies. A study in Tunisia and one in Alaska suggested a relationship between intake of salted fish and nasopharyngeal carcinoma. Ecological studies in Japan showed a correlation between consumption of dried or salted fish and cancers of the stomach and oesophagus. One cohort study in the USA and three case–control studies in Hawaii, Japan and Italy showed positive associations between intake of dried or salted fish and risk for stomach cancer; a cohort study from Hawaii and two case–control studies from Japan found no association. In none of these studies was the effect of salt consumption evaluated independently.

Studies on cancers at other sites were not considered informative for the evaluation.

## 5.3 Animal carcinogenicity data

Chinese-style salted fish was tested in two studies in rats by administration in the diet or in the diet and drinking-water. A small number of carcinomas was oberved in the nasal, paranasal and oral cavities in each of the studies in rats, mostly in females.

## 5.4 Other relevant data

Extracts of Chinese-style salted fish are mutagenic to bacteria.

### 5.5 Evaluation[1]

There is *sufficient evidence* in humans for the carcinogenicity of Chinese-style salted fish.

There is *inadequate evidence* in humans for the carcinogenicity of other salted fish.

There is *limited evidence* in experimental animals for the carcinogenicity of Chinese-style salted fish.

**Overall evaluation**

Chinese-style salted fish *is carcinogenic to humans (Group 1).*

Other salted fish *is not classifiable as to its carcinogenicity to humans (Group 3).*

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[1]For definition of the italicized terms, see Preamble, pp. 26–29.

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