Journal of the Academic Society for Quality of Life (JAS4QoL)

2023 Vol. 9(1) 5:1-5

Recent Developments and the Incidences of Cancers in Japan: Focal Emphasis on Breast Cancer and the Use of Food Ingredients and Plant-Part Extracts for Prevention

Anthony FW FOONG

R&D Department, Imex Japan Co. Ltd., Kyoto, 3F Imex Japan Bldg, 22 Simomidori-cho, Shichiku, Kita-Ku, Kyoto 603-8425, Japan 78imexfw@gmail.com

Citation: FOONG, F. W.; Recent Developments and the Incidences of Cancers in Japan: Focal Emphasis on Breast Cancer and the Use of Food Ingredients and Plant-Part Extracts for Prevention *JAS4QoL* **2023,** *9(1) 5*:1-5.
Online: http://as4qol.org/?p=3845

Received Date: Dec. 18, 2023 Accepted Date: Dec. 19, 2023 Published: Dec. 24, 2023

JAS4QoL

Mini review

Recent Developments and the Incidences of Cancers in Japan: Focal Emphasis on Breast Cancer and the Use of Food Ingredients and Plant-Part Extracts for Prevention

Anthony FW FOONG

R&D Department, Imex Japan Co. Ltd., Kyoto, 3F Imex Japan Bldg, 22 Simomidori-cho, Shichiku, Kita-Ku, Kyoto 603-8425, Japan (78imexfw@gmail.com)

According to recent analysis in Japan (2020), the mortality rate of males is higher than that of females: i.e. 368 (males) vs 248 (females) per 100,000 population. With regards to the affected sites, the mortality trend traces a similar pattern of males > females in the following order (with approximately 2-fold higher rate in males): oral cavity, larynx, esophagus, stomach, liver, pharynx, lung, and bladder. However, mortalities attributable to thyroid cancer appear to be higher in females. Regarding the site-related mortalities, males tend to be more susceptible to succumbing to following cancers, in decreasing order: colon/rectum, lung, stomach, colon, pancreas, and liver; while susceptibility of females traced the following pattern, in decreasing order: colon, lungs, pancreas, breasts, and stomach.

According to the Japan Cancer Registry System (2016), cancer incidences approximated 981,000. Incidence in males was over 1.3 times that of females. In the 2018 survey, males suffered the highest proportion of prostate cancer, followed by stomach (15.6%), colon/rectum (15.5%), lungs (14.7%), and liver (22.2%) cancers, while females suffered the highest incidence in breast cancer (BC), followed by colon/rectum (15.6%), stomach (9.3%), and uterus (6.8%) cancers.

Based on 2018 survey, the site distribution of cancer cases varies across age groups. For males, aged 40 years old (yo) and above, cancers of the lower digestive tract (stomach, colon/rectum) and liver account for 50-60% of cancer cases, while those of lungs and prostate are higher among those aged 70yo and above. For females aged 40-49yo, ca. 50% of cancer cases occur in the breast, and ca. 20% in the uterus and ovary; however, the proportion of those 3 sites decreases with age, and instead they suffer from cancer in other sites such as the lower digestive tract (stomach, colon/rectum), liver, and lung. Fore males under 40yo, the cancer incidences of intestine and lung are lower than those aged 40 and above. For females under the age 40, the incidence of cervix uteri is higher than those 40yo and above. Accordingly, attention needs to focus on the high proportion of BC (ca. 50%) in females, and the incidence of BC in younger ages is increasing.

The predominance of BC in women in the 2018 survey requires attention. It is true that recent analyses (2013) have shown the ratio of BC in normal Japanese female patients is 1:12 compared with the US (1:7). None-

Citation: FOONG, F. W.; Recent Developments and the Incidences of Cancers in Japan: Focal Emphasis on Breast Cancer and the Use of Food Ingredients and Plant-Part Extracts for Prevention. *JAS4QoL* ***2023***, *9(1) 5*:1-5.

Available online at
http://as4qol.org/?p=3845

Received: Dec. 18, 2023
Accepted: Dec. 19, 2023
Published: Dec. 24, 2023

theless, although the highest incidence of BC occurred in the 45-49Yyo age-group, followed by the 40-44yo group, an increase in incidence is found in the 15-39yo group (2018). This trend indicates that the incidence of BC is fast increasing in the younger females below 40yo. It is therefore vital to understand this shift in the incidence of BC in younger females by looking at etiological factors, early detection, disease onset and development, and the fatality rate of BC by adopting useful preventive measures to extend survival rates and avoid preventable deaths.

To account for reasons in the trend towards increased incidence of BC in younger aged women, there are 6 possible relevant factors:1) younger females are more aware of the disease, and they are taking increased precautions by going for screening earlier and more frequently than their elders; 2) younger females are more educated in detecting the disease by doing self-examinations such as examining their breasts for signs of lumps and noting other relevant symptoms; 3) Innovations in screening examinations have made them more reliable and less expensive allowing improved detection of the signs of BC; 4) better surgical approaches to conserve affected breasts to keep up the moral and confidence of the patients; 5) more effective drugs with less adverse effects have been developed; and 6) knowledge on the detection and management of BC has been more easily accessed and disseminated more widely through the internet.

This review focuses foremost on the etiological factors, and probes the possible preventions and treatments that may reduce the incidence of BC.

Etiological factors of BC

Epidemiological risk factors for a disease can provide important clues to the etiology or causal relationships of a disease. Analogous to other cancers, BC is now considered to be the outcome of the following environmental and hereditary factors:

- Lesions to DNA (the human genome map) such as genetic mutations via cellular exposures to free radicals and superoxides derived from improperly prepared meals, and radioactive exposures from hazardous environment and certain occupations. Certain hormonal therapies, etc. that can lead to BC have been experimentally linked to estrogen exposure. Beyond the attribution of estrogen, research has implicated viral oncogenesis and ionizing radiation in inducing genetic mutations.
- Failure of immuno-surveillance, a theory in which the immune system removes malignant cells throughout an individual's lifetime.
- Abnormal growth factor signaling via the interaction between stromal cells and epithelial cells can facilitate malignant cell growth: e.g. tumors can induce blood vessel growth (i.e. angiogenesis) by secreting various growth factors to further facilitate cancer growth.
- Inherited defects in DNA repair genes (e.g. BRCA1, BRCA2, p53, etc.) have been suggested.
- Although many epidemiological risk factors have been identified, the cause of any individual BC may not be known. In short, epidemiological research informs the patterns of BC incidence across certain populations, but not in any given individual. The primary risk factors that have been identified are: gender (male, female, etc.), age (adolescence, adulthood, aging, etc.), body developmental status (e.g. childbearing, pre- and post-menopausal stages, etc.), body change (hormones, metabolism, etc.), foods/diets (burnt/charred proteins, high-fat, high-carbohydrate, etc.), lifestyle (tobacco/alcohol intake, etc.), body maintenance status (underweight, overweight, obese, etc.), and environmental factors (polluted air, tobacco use, etc), work (low-, high-stress, etc.), workplace, profession/job-related factors (easy, stressful, hazardous, etc.).

Etiology is not known in 95% of BC cases, with the remaining BC cases being attributed to hereditary syndromes. Particularly in carriers of BC-susceptible genes (e.g. BRCA1, BRCA2, etc.), and certain hitherto unknown genes increase the risk of breast and ovarian cancers by 30-40%, depending on the site of protein where the mutation occurs. Although the hereditary gene factor may account for about 5% of BC development, the other above-mentioned factors seem to be the even more critical factors for inducing

BC in our modern society.

The Destructive Events of BC (and cancers in general)

BC does not kill per se; early detection is critical and important in extending and saving lives. More important than cures/treatments, prevention is the foremost important treatment and is the frontline defense for BC. Abnormal growth in cells to form tumors is initiated by DNA distortions. Once a tumor is formed on a site in the breast, functions of surrounding cells are impaired to subsequently degrade to abnormal and decaying tissues to induce discomfort and pain. When benign tumors are surgically removed on site in the breast, the damage may be restricted for some time; however, malignant tumors may cause more and extensive damage even with surgical intervention. On-site malignant tumors (which eventually form cancerous tissues) are characterized as abnormal cells that eventually destroy the living system as a whole via 4 typically destructive mechanisms: 1) abnormal on-site growth per se, 2) angiogenesis of abnormal cells, 3) non-apoptosis of tumor cells, and 4) metastasis from on-site growth to remote sites. These 4 events need to be inhibited or totally prevented to control destruction of the living system by cancers.

These malignant tumor cells with impaired or distorted DNAs grow abnormally. Therefore to control and/or terminate cancer growth and destruction of the living system requires the following approaches for the above 4 mechanisms/events: 1) destroying on-site abnormal cells per se is the first line of defense in cancer control; 2) reversing the phenomenal apoptosis lacking in cancer cells to recover and therefore to return to the normal cell cycle of growth-death phenomenon; 3) terminating angiogenesis and therefore inhibiting cell access to enhanced blood and nutrient supplies for further growth; and finally 4) inhibiting or mitigating remote metastasis of cancer cells by neutralizing certain 'X' oncogenic factors released by these abnormal cells to remote sites of the living system that lead to further destruction throughout the rest of the living system. The above-mentioned measures can involve substances - certain ingredients of foods and extracts from plant-parts – that can be used in preventing formation of abnormal cells and/or inhibiting and eventually mitigating their destructive events via their intrinsic mechanisms of action.

Preventive measures

--- with a healthy lifestyle

Active smoking, which is strongly discouraged, is penetrating fast among the young female population. Passive smoking alone increases BC risk by 70% in younger, primarily menopausal women. Exposure to tobacco smoke is most problematic between puberty and first-child birth: viz., breast tissues appear most sensitive to chemical carcinogens during this phase, because breast cells are not fully differentiated until lactation.

--- with surgical intervention of certain reproductive organs

Removal of ovaries, or prophylactic oophorectomy, in high-risk individuals with various previous childbirths reduces the risk of developing BC by 60% as well as reducing the risk of developing ovarian cancer by 96%.

--- with medications

Hormonal therapy has been used for chemo-prevention in individuals at high risk for BC; chemoprevention in women with high risk of BC and low risk for adverse drug reactions is recommended.

--- with screening x-ray mammography / breast MRI

BC screening is an attempt to find undetected cancers. The most common screening methods are self and clinical breast examinations, X-ray mammography, and breast magnetic resonance imaging (MRI). Although controversial to some, recent technical improvements have promoted mammography to be the modality of choice for screening for early BC, since it is non-invasive, relatively fast, reasonably accurate, and widely available in many countries. Interpreting mammograms in younger women (<50yo) is more difficult due to the issue of breast density. Radiographically, a dense breast has a preponderance of glandular tissues, and younger age or estrogen hormone replacement therapy contributes to mammographic breast density. Mammographic interpretation after menopause is much more accurate, because

the breast glandular tissue is gradually replaced by fatty tissue. Note that breast density is an independent adverse prognostic factor on BC prognosis. MRI can detect cancers not visible on mammograms; however, it has been regarded to have disadvantages: e.g. although >25 to <40% more sensitive, it is less specific than mammography.

--- with genetic testing

Women with a family history associated with an increased risk for deleterious mutations in BRCA1 or BRCA2 genes may be referred by clinicians for genetic counseling and evaluation for BCRA genetesting.

--- with use of selective estrogen receptor modulators (SERMs)

Based on guidelines on studies of SERMs, studies have demonstrated that the relative risk reduction for Roloxifene is 76%, while Tamoxifen can prevent BC in high-risk individuals. The relative risk reduction was up to 50% of new BCs, although the BCs prevented were more likely estrogen-receptor positive (interestingly, this is analogous to the preventive effect of finasteride on prostate cancer). Additional randomized controlled trials (2006) have demonstrated Raloxifene is able to yield efficacy equal to Tamoxifen in preventing BC, and there are fewer side-effects (uterine cancer) with the former.

--- with food/diet ingredients and plant part extracts

Foods/Diets: Ancient Chinese medicine is based on crude extracts from foods and plants with the original philosophical foundation of "Foods and medicines are of the same source". The living system is composed of units called cells. Each cell has various organelles, and the deoxyribonucleic acid (DNA) is the major controlling unit that regulates and dictates the fate and wellbeing of cells whereby the various systems are coordinated globally to form the whole of a living system. Therefore, when abnormalities occur in cells, the various systems cease to coordinate and function as a wholesome system, and that is when the living system suffers from sickness, a disease or death itself.

Based on the philosophy of Chinese medicine, various food/plant ingredients have useful activities, which are attributable to their properties, such as supplemental nutritional value, repair as well as potential and powerful antioxidation, cytolytic and other intervening properties in overcoming abnormal cell growth, which exacerbates to a diseased state if not intervened.

Apart from supplemental and repair properties of foods and plants derived by boiling and mixing herbal mixtures/preparations, recent experimental studies have given insight to more refined and concentrated forms of intake: Certain functional properties of the various specifically useful food ingredients and health-promoting plant-part (leaf, bark, root, etc.) extracts. More than the basic supplemental and repair mechanisms, these recently more specifically isolated food ingredients and properly extracted ingredients (with purposeful properties) provide specific and powerful properties to perform higher levels of normalizing cell abnormalities. Additionally, certain substances found in foods can prevent abnormal cell growth in affected organs such as the breast, ovary, and other organs in the living systems.

The following food ingredients and plan-part extracts are of recent importance in treating cancers, including women disease, especially BC in this review.

1. **Phytoestrogens and soy**: From recent studies, food and diet play a critical role in inducing abnormal cell growth for diseases such as BC and other cancers. Animal and human studies have revealed that phytoestrogen found in soybeans may be useful: the intake of plant estrogens (e.g. from soy products) in early adolescence may protect against BC later in life.
2. **Folic acid**: Studies have found that folate intake counteracts alcohol-induced BC risk, and women who drink alcohol and have a high folate intake are not at increased risk of BC. A prospective study of over 17,000 women has found that those who consume 40g of alcohol (about 3-4 drinks) per day have a higher risk of BC; and a daily intake of 200mg folate (folic acid or vitamin 9) decreases the BC risk. Folate is involved in the synthesis, repair, and functioning of DNA, and foliate deficiency may result in DNA damage and may lead to cancer. In addition to BC, studies have also associated diets low in folate with increased risk of pancreatic and colon cancers. Folate-rich foods include citrus fruits/juices, dark green leafy vegetables (e.g. spinach), dried beans, and peas. Vitamin 9 can also be taken in a multivitamin pill.

3. **Tocotrienols (3e)**: These are basically vitamin E derivatives from plant sources. Three double-bond 3e has potent antioxidant action that neutralizes free radicals and superoxides in blood to protect cell DNA from damage, thus preventing abnormal cell formation. In vitro studies using BC cell lines have demonstrated the indiscriminate inhibitions of 3e on estrogen-sensitive and estrogen-nonsensitive BC cell growth, and its potentiation effect on the inhibitory effects of tamoxifen (the chemotherapeutic specifically used for BC treatment) on these 2 BC cell lines.

4. **Propolis:** An extract derived from the beehive: This natural substance directly and selectively destroys abnormal cells such as BC cells without affecting normal body cells. Additionally, this extract has potently powerful antioxidation effects that can neutralize harmful free radicals and superoxides in the living system to prevent DNA damage. Furthermore, this extract prevents angiogenesis and apoptosis. All in all, propolis counteracts the 4 destructive mechanisms of cancers and BC action in destroying the living system.

5. **Fucoidan:** This is a polysaccharide (largely made up of l-fucose and sulfate groups) extracted from marine brown algae (e.g. Sargassum spp.). Apart from its antimicrobial activity, it has multiple useful anticancer and anti-inflammatory properties, amongst other benefits. This marine extract exhibits immunodefense system enhancement, and has antioxidant, cytolytic, antiangiogenic, and apoptosis-inductive properties, and therefore is very useful in restricting BC cell growth and metastasis.

6. **Sea cucumber extract:** Extracts from this marine invertebrate species have been demonstrated to elicit suppressive effects on BC: in vitro experiments have shown the extracts to boast the immunodefense systems (triggering natural killer (NK) cells, other leucocytes, etc.), inhibit angiogenesis, induces apoptosis, and elicit anti-inflammatory effects in rats and BC cell lines, albeit the extracts have also been demonstrated to mimic excellent healing effect of diabetes-induced complications such as limb/philange amputations.

7. **Plant-part extracts**: Recent experimental studies and literature on Asian Folklore medicine has claimed that extracts of leaf/stem extract of Strobilanthes crispus (black face general or pecah beling in Malay), leaf extract of fragrant screwpine or pandan in Malay (Pandanus amaryllifolius) and rind/peel extract of mangosteen (Garcinia mangostena) elicit anticancer effects beside many other useful properties for the human body. Their anticancer effects – especially on BC – are believed to have derived from their potent antioxidant properties and enhancement effect on the immunodefense systems.

8. **Miscellaneous**: There are many more natural ingredients useful against cancers: e.g. lycopene from tomatoes is effective against prostate enlargement and cancer. Therefore, many more candidates have yet to be discovered in nature. Continuous efforts to explore and discover useful food ingredients and plant extracts may serve as useful treatment choices other than chemotherapeutics or natural food/plant ingredients may be used as adjuvants for complementing effects/actions of chemotherapeutics for treatment against cancers, including BC.