Cancer in Japan from the View Point of Geographical Pathology

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Upon looking through the list of age-adjusted death rates for cancers in different sites in Japan, we note that some items are excessively higher than the corresponding rates in Western countries, while some are exceptionally low. This peculiarity can be clearly noticed in the results of our calculations based on the data directly furnished by the central statistics administrations of 24 countries, and in the results of calculations by Stocks' simple method. We will hereunder give some results of statistical studies on cancer in Japan made chiefly by the staff members of our department from the view point of geographical pathology.

Fig. 1. Trend of age-adjusted death rates for stomach cancer in Japan, England and Wales, and United States (White) (Standard population: 46 countries in 1950)
1. Gastric Cancer

The most notable specificity of cancer in Japan is the high prevalence of gastric cancer. Gastric cancer is frequent in Finland, Chile and Iceland also, but it must be noted that in Japan, the death rate for gastric cancer is still increasing year by year—a phenomenon not to be observed in any Western country as far as we are aware of. The death rate for this cancer is rising in the age-classes of 65-70 and above and remains nearly stationary in the age-classes of 60-64 and below. The trend of the age-adjusted death rates for gastric cancer in England and Wales, U.S.A. (Whites) and Japan is as shown in Fig. 1. The death rates here have been adjusted by age with the total population of 46 countries in 1950 as standard (as is always the case herein-under, unless specially noted otherwise. The composition of the standard population is as given on page III of a separate publication1 of ours).

Haviland3 pointed out a century ago that the geographical distribution of cancer is rather markedly uneven, even within the limits of one country. Following the path of this illustrious pioneer, many researchers in England, the Netherlands and so forth have tackled the problem of geographical difference in the frequency of cancers. In particular, Stocks' in England and Tromp and Diehl5 in the Netherlands have gone deep into the study of the relation between the frequency of gastric cancer and the quality of soil. More recently, Haenszel6 has reported on the distribution of gastric cancer in the United States. The remark that the gastric cancer shows a curious distribution within the realms of a country seems to apply to many a land.

![Fig. 2. Map of prefectures in Japan](image-url)
We will hereunder describe some features in the geographical distribution of gastric cancer in Japan, basing ourselves on the age-adjusted death rates calculated by Hiraide\(^7\) and Suganuma\(^8\) of our department.

Japan is divided into 46 prefectures for local administration. The age-adjusted death rate for gastric cancer in 1955 was the highest in Yamagata Prefecture and the lowest in Kagoshima Prefecture. The rate in Yamagata was higher than the average rate of all Japan by about 30%, both among men and among women, and lower by about 50% than the all Japan rate in Kagoshima. (Fig. 3)

The 46 prefectures in Japan are subdivided into 1,027 city and county areas in total. We have computed the age-adjusted death rates for gastric cancer of every area in 1955 by direct method. The numbers of deaths of each area have been specially tabulated for us by the Statistical Department, Welfare Ministry, as itemized by sex and age-class. (Fig. 4, 5)

There are 4 districts with particularly high death rates for gastric cancer in Japan as follows:

1. The district facing the Japan Sea in Northern Honshu
   (Marked A in Fig. 5)

The district washed by the Sea of Japan on the west and lying between the
40° and 36° parallels shows high rate of deaths for gastric cancer all over and Yamagata Prefecture, the prefecture with the highest death rate to show among all the prefectures in Japan, lies in this district. This district is an outstanding rice-producing center in Japan but produces little else of agricultural crops. Winter is rigorous and snowy, and cloudy weather prevails in the colder season admitting little sunshine. The soil is humid.

(2) Tokyo and its neighborhood (Marked B in Fig. 5)

Several prefectures including the capital city and surrounding it constitute this district. A number of city and county areas with average death rates are

Fig. 4. Ratios of age-adjusted death rates for stomach cancer by city and county areas, 1955. (Standard population: 46 countries in 1950)
included in this district so that the district cannot be called a dense-packed aggregation of high-rated areas, as the District A above. Besides rice, wheat, barley and green vegetables as well as much sweet potatoes are produced in this district. In the list by prefectures, Tokyo ranks the twelfth for men and the seventh for women.

(3) Osaka and its neighbourhood (Marked C in Fig. 5)

The two prefectures of Osaka and Nara are included in this district. The age-adjusted death rate in Nara Prefecture for men ranks the second and that for women the sixth of all the prefectures. This prefecture had been generally accepted as the area with the highest frequency of gastric cancer in all Japan. The habit of eating steaming rice gruel has prevailed for centuries in this prefecture and some authors are inclined to see a correlation between this habit and the high frequency gastric cancer here.

(4) The Northern Kyushu District (Marked D in Fig. 5)

This district containing many high-rated city and county areas lies in the northern part of the Kyushu Island, the southern-most of the four major islands of Japan.

The three following are the districts consisting of areas with low death rates for gastric cancer.

(1) The northern part of Honshu facing the Pacific Ocean (Marked X in Fig. 5)

This district includes Iwate Prefecture with the lowest death rate for men
as well as women next only to Kagoshima Prefecture in District Z below. Lime stone is the prevailing bed-rock in this district. It has cold winter but snow is far less copious than in District A above lying to the west. The land is hilly and dry in most parts.

(2) Shizuoka prefecture and its neighbourhood (Marked Y in Fig. 5)

This district comprises the largest center of orange and tea production in Japan.

(3) Western Japan (Marked Z in Fig. 5)

The portion of Honshu lying west to the 135° meridian, east longitude, Shikoku Island and Kyushu Island, contain many areas with low death rates for gastric cancer, except the District D above of high rate in Northern Kyushu. Kagoshima Prefecture in the southern-most extremity of Kyushu shows the lowest rate for men and women in all Japan. Sweet potato is the staple food in this prefecture.

We have the impression that the correlation between the nature of soil and the frequency of gastric cancer in the same area as propounded by Haviland3), Stocks4), Tromp and Diehl5) are observable in some areas at least in Japan too. Low, ill-drained and watery lands and alluvial lands, which constitute the largest rice-producing centers in Japan, usually show high cancer death rates. Districts over limestone bed-rocks, for example, the northern Pacific coastland, show low death rates for gastric cancer, but on this point, there are some exceptions. Haviland3) has presumed that the acidity of soil frequently induced by repeated floods may be correlated with the frequency of gastric cancer. Hirayama9) has also pointed out that gastric cancer is particularly frequent in areas with acidic soil in Japan.

According to the calculated rates by Ogata10) of this department, in the 282 counties in Japan in which more than the half of the land under cultivation in the county is acidic, the percentage of the acidic soil and the death rate for gastric cancer was found significantly correlated at the rejection level of 0.1%, the correlation coefficient amounting to +0.214. But when also the county areas with less than half of the arable land acidic were included in the computation, no significant correlation was observable. Of the abovementioned 4 districts with high cancer death rates, the District A in northern Honshu is rich in acidic soil, but in the districts comprising Tokyo and Osaka and their neighbouring prefectures, no perceptible correlation could be established between the prevalence of acidic soil and the death rates for gastric cancer.

We have drawn up a map of Miyagi Prefecture, in which our Tohoku University is situated, indicating the age-adjusted death rates of the cities, towns and villages for the ten years from 1948 to 1957. (Fig. 6). Prof. Fujiwara of Agricultural Agrology of our University, seeing this map, remarked that he was
impressed by a possibility of some correlation between the nature of soil and the
distribution of gastric cancer. In the northern portion of the prefecture, there
lies an area in which communes with high cancer death rates are aggregated.
This area is covered by a soil consisting of old volcanic ash, from which the basic
components have been washed out in a long age, resulting in a strong acidification
of the soil, so that the soil has to be neutralized with a large quantity of lime
before planting rice. The cancer death rate is also high in peaty lands. Also
in the middle part of the prefecture, where the death rate is average or lower,
the surface soil consists of volcanic ash, but the acidity is weaker here, the basic
components being yet better conserved.

Volcanoes are abundant in Japan and many parts of the land are covered
under volcanic ash, but these parts do not show necessarily high death rates for
gastric cancer. In the areas of volcanic ash, where the soil is not humid, gastric
cancer tends to be rather infrequent. We may suppose that unless the soil is
humid, the human body is not subject to the bad influence of volcanic ash. We
can say nothing definite on the relation between volcanoes and gastric cancer, but
as the activity of a volcano may possibly change the chemical composition of the
surface soil, the frequency of gastric cancer may be more or less correlated with volcanic activity, at least in some cases. In this connection, it must be noticed that Iceland, Chile and Japan, three of the countries with highest gastric cancers, are rich in volcanoes.

The age-adjusted death rate for gastric cancer in Japan is higher in the major cities with above 1,000,000 population than the national average, except in the average-rated Kyoto. If Western mode of living act in lowering the frequency of gastric cancer, the rates in these major cities should be lower than the average, but the actuality seems to contradict this premise. Areas with particularly high or exceptionally low death rates for gastric cancer are both found in the countryside. The major cities are still absorbing rural population, but the particularly high-rated and low-rated counties are now sending out their natives to the urban areas. Most of the subjects contracting gastric cancer in the rural areas are born natives of the villages, and can be looked upon as having been long under some influence of the living conditions of the native lands encouraging cancer formation. Such rural residents are supposed to show heavy dependence on the food produced in the respective districts. The position occupied by canned, refrigerated and such preserved foods in Japan, especially in rural areas, is lower than in the Western countries.

The postulate that gastric cancer is frequent in areas with high underground water level and with humid soil holds to considerable extent in Japan, too. Generally speaking, the humidity of soil is low in western Japan, while the principal rice producing centers in Japan are situated on alluvial plains, where the humidity is generally high. It is a miraculous coincidence that in the northern hemisphere, the cold and humid lands show high frequency of gastric cancer.

The Japanese take rice as staple food, and rely for 57% of calories and 32% of protein on rice (National Nutrition Census, 1958). In a rice grain, the part richest in fat and vitamin is the embryonic bud but the Japanese usually throw away this part while polishing the rice. As rice is washed with water rather thoroughly before boiling it, unlike in the case of baking bread of wheat flour, the water-soluble substances, such as vitamin B1, are nearly all washed away before going into the pot.

In our epidemiological survey\textsuperscript{11}, we have once obtained the result that the rate of gourmands of rice was higher among the subjects with gastric cancer than among the non-cancerous controls. In this survey, however, we did not go into the details of actual daily menus but took down only the answers to our general questions, and the value of the data is limited in this respect. Wherever rice is produceable in quantity, it is economically most advantageous and secure for the farmers to produce rice, of which the producer price is officially kept at a protective level. In the District A (Fig. 5) where snow lies deep on the fields
through winter, a single crop of rice in autumn is the usual farming calendar and shortage in protein and vitamins A, B, C and D is rampant. But in the southwestern part of Japan west to Tokyo it is the common practice to cultivate wheat and barley on the paddy-fields in winter besides dry-farm vegetables, beans and potatoes. Winter in these districts is warmer and less snowy so that the paddy-fields can be utilized for cultivating winter wheat and barley harvested in late spring. Moreover, green vegetables are easy to procure even in the coldest season here.

In the great rice-producing districts, where rice alone is the main source of nutrition, overconsumption of rice is the natural sequence, for the protein content of rice is very small. Some Japanese scientists are inclined to find a correlation between this heavy rice consumption and gastric cancer.

But it is clear that rice cannot be the universal chief cause of gastric cancer in the world, for gastric cancer seems to be not frequent among all the nations of southeastern Asia where it constitutes the staple food. Gastric cancer is apparently not frequent in Taiwan (Formosa). The age-adjusted death rate for gastric cancer in Ryukyu (Okinawa) was found to be low, according to the data recently supplied by Ogasuku. (Okinawa is an area with well-developed limestone bed-rocks.) Some Western countries where rice is rarely consumed as food have rather high rates of gastric cancer to show.

According to our epidemiological survey\(^1\), irregular meal times showed significant relation with the frequency of gastric cancer. I heard from Meinsma that similar observations have been made in Netherlands, too.

Dutch and Japanese are both great fish-eater, but in Japan, fish-meat is rarely smoked for preservation and in particular, in the rural areas, smoked fish is nearly unknown. In former days, salted fish was rather largely consumed, but at present, this habit is on the wave. In Japan, fish-meat is mostly boiled or broiled before serving. It is our impression that the areas with particularly high consumption of fish hardly coincide with the areas with particularly high frequency of gastric cancer in Japan.

The death rate for cerebral hemorrhage is also high in Japan. Tohoku District comprising the northernmost six prefectures of Honshu where this rate is particularly high in Japan has a cold climate and the inhabitants consume much salty food. Some say that the Japanese relying much on vegetable food have to consume much NaCl to keep the equilibrium of K and Na in their body. Sato\(^1\) has inferred the possibility of the mucous membrane of a stomach damaged by concentrated saline may be afflicted by cancer. The age-adjusted death rates for cerebral hemorrhage and gastric cancer in the individual cities, towns and villages in Miyagi Prefecture were found to show a geographical correlation at the level of significance of 0.5%\(^1\), but when viewed in nation-wide scope, it is doubtful whether such a parallelism can be established in Japan. In
Iwate Prefecture, the rate for gastric cancer is exceptionally low, but that for cerebral hemorrhage is especially high.

In his intermediate report on epidemiological survey in England, Stocks reports that a high content of Zn was found in the garden soil of stomach cancer cases. Hirayama says that some gastric cancer areas are situated in the basin of rivers washing zinc deposits, but our observations have revealed too many exceptions. We have measured the Zn content in the drinking water used by a few of the gastric cancer cases in some rural areas of Miyagi Prefecture, but found it smaller than that in the city water of Sendai. This problem, however, is of importance for us, since the city water conduits are zinc-plated on the inside in Japan.

We drink with preference an alcoholic drink brewed from rice, the notorious sake, in Japan. This sake has a content of alcohol of 12–13%. At dinner parties, sake and/or beer is consumed, sometimes singly and sometimes in mêlée. Not a few Japanese regularly enjoy 200–300 cc or even more of sake every evening. According to our survey, the rate of such habitual bibbers was found higher among the patients of gastric cancer than among the controls. Many of the heavy sake bibbers lose appetite for other food and are said to be apt to suffer from hepatic cirrhosis due to deficiency in protein.

Many authors in Japan believe in the close etiological correlation between gastric ulcer and gastric cancer. The death rate for gastric ulcer in Japan is far higher than in Western countries. Some are inclined to believe that the frequency of gastric cancer is heightened by the rate of gastric cancer induced in relation with gastric ulcer in Japan. Mori says to have had a similar impression during the survey instituted among the Japanese in Hawaii.

The death rate for gastric ulcer rose to an extremely high level in wartime and in the immediate post-war years when consumption of animal food was drastically restricted. The facts that the death rate for gastric ulcer rose to the highest in the period when the nutritive partiality was most severely accentuated and that gastric ulcer and gastric cancer are widely believed to be pathogenetically correlated, at least in Japan, leads to the inference that the partiality in alimentary habits among the Japanese may be somewhat responsible for the prevalence of gastric cancer. But this inference falls through in the case of Western countries, for much animal food is consumed in Finland and Iceland. According to the investigation at Prof. Kurokawa’s Clinic of Internal Medicine, one half of the cancer cases had been in good health in the past and the other half had gastric ulcer or chronic gastritis or complaints of habitually weak stomach. In our survey too, we found cases with past experience of gastric ulcer or gastritis more frequently among the gastric cancer cases than among the control cases.

In summary of the above, we have not yet come upon a factor apparently
of high probability as pathogenic cause of the high prevalence of gastric cancer in Japan. Even though we can point to some possible factors, these factors are only rarely deemed effective in the North European countries where gastric cancer is comparatively frequent. The mainly effective causes of gastric cancer may be not the same in different countries or in different parts of the same country. However it may be, we do not despair of finding some better clues to approach the problem of the pathogenesis of gastric cancer, if we go on with our epidemiological survey on gastric cancer.

2. Esophageal Cancer

The death rate for cancer of the esophagus in Japan is on the same level as that in the European countries. The sex ratio of the death rate for this cancer shows large differences by countries. According to the survey by Stocks19) in 41 major cities in England and Wales and our age-adjusted death rates in 23 countries (1956-57)20), the death rate for this cancer, unlike that for cancers of many other sites, shows a lack of geographical intersex correlation, as a common characteristic.

We have calculated the age-adjusted death rates for esophageal cancer with the statistics for 1952-1956 published by WHO19) as data and the total population of 46 countries in 1950, and examining the possible geographical correlation be-
between this rate and the similarly calculated rate for pharyngeal cancer, obtained
the positive coefficients of 0.55 for males and 0.30 for females. These results
indicate that, where esophageal cancer is frequent, pharyngeal cancer is also
frequent, among males, at the level of significance of 1%; among females, the
correlation is significant at the level of 5%, except in Venezuela where the death
rate for pharyngeal cancer is exceptionally high.

The geographical distribution of deaths for esophageal cancer in Japan\textsuperscript{1)}
is dissimilar to that of deaths for gastric cancer. (Fig. 7) The latter has been
found high-rated in the District A above (in Fig. 5) of Northern Honshu facing
the Japan Sea, but in the case of esophageal cancer, the district lying east to the
District A and facing the Pacific Ocean contains prefectures with high death
rates. In some prefectures, for example, Nara Prefecture, however, both the
death rates for stomach cancer and for esophageal cancer are high.

In Japan, it is generally believed that esophageal cancer is frequent among
the subjects used to eating hot fares and those with unhealthy teeth, and in fact
we experience frequent cases of esophageal cancer in subjects addicted to hot
courses. But we have not yet confirmed this impression in a statistical study.
In Nara Prefecture, where cancers of both the stomach and the esophagus are
particularly frequent, the habit of eating bowlfuls of steaming rice gruel has been
the tradition. In recent days however, the provincial peculiarities in alimentary
habits are rather rapidly falling into oblivion and so, in Nara Prefecture, the
time-honored “Narachagayu”, the hot rice gruel, is losing popularity. At any
rate, the high rates of deaths for gastric cancer as well as for esophageal cancer
in this prefecture of oldest civilization in Japan is a notable case.

3. Intestinal Cancer

In Japan, intestinal cancer is extremely infrequent. In Japan, where cases
of postmortem examination are limited in number, the danger of intestinal cancer
cases to be misdiagnosed as cases of some other diseases is not excluded, but
taking the past operation and autopsy results into account, it is beyond doubt
that intestinal cancer is not frequent and at least much less frequent than
stomach cancer in Japan. In Japan, the death rate is slowly rising owing to the
rise in the death rate among the high-aged of 70 years and above.

Our calculated death rates show that, in the countries with high death
rate for intestinal cancer, the death rate for duodenal ulcer is also high\textsuperscript{17}).
Intestinal cancer rarely produced in the duodenum, but may this finding not
interpreted as indicating that a state of “weakened organ” contributes to the
occurrence of cancer? For example, in Japan where gastric ulcer, gastritis and
such stomach diseases are frequent, gastric cancer is also frequent, while in
England where chronic bronchitis is prevalent, pulmonary cancer is also fre-
quent. Of course, nothing definite is known anent the pathogenic correlation
between these pairs of diseases. It may be that some factor causing cancer is also a cause of other diseases in the same or neighbouring site.

4. Rectal Cancer

It is the general belief that hemorrhoids are prevalent in Japan and also rectal cancer is also believed to be frequent here by many, but in fact the age-adjusted death rate for this cancer does not rise beyond the level common in Western countries. The rate is rising in the age-classes above 65 years, but is falling off in the younger age-classes.

5. Hepatic and Choledochal Cancers

The age-adjusted death rate in Japan for hepatic cancer among males is the highest and among females the 5th among the 24 countries cited in our study. It is noted that the death rate among the female population is the highest and particularly high among the high-aged women in Western Germany. As in Japan, gastric cancer is so frequent, that the possibility of gastric cancer metastatised to the liver to appear as hepatic cancer on death certificates is not deniable, but it is believed that hepatic cancer has been prevalent in Japan for the long past.

In the statistics by prefectures in Japan\(^8\), we see that the death rate for

![Fig. 8. Standardized mortality ratios for cancer of liver and biliary passages by prefectures, 1954–1956](image)
hepatic cancer is high in Yamanashi and Saga Prefectures (Fig. 8). In Japan, almost only these two prefectures are infested by schistosoma japonicum. The death rate for hepatic cirrhosis is also high in Yamanashi Prefecture and in Kyushu Island, on which Saga Prefecture is situated.

The death rates for hepatic cancer per prefecture is positively correlated with that for gastric cancer at the level of significance of 5%.

6. Pancreatic Cancer

It seems that the death rate for pancreatic cancer is steeply rising in all age-classes in most countries. In Japan too, the rate has markedly risen, perhaps partly due to the improved accuracy of diagnosing the cancer, but a real increase in the cases seems to be indicated in all probability.

The rates for deaths for cancers of specified sites in Japan generally show a similar trend of rise or fall in frequency, except that for gastric cancer cited above and a few others. The cancers showing substantial rise in frequency in Western countries in recent years are generally perceptibly rising in frequency in Japan, too, as fitly exemplified by the parallel rise in the rates for pancreatic and pulmonary cancers.

7. Mammary Cancer

The lowness of the rate in Japan has drawn the attention of medical scientists. In these 20 years, the rate of deaths for mammary cancer has risen among the high-aged of 70 years and above, but that among the lower classes has remained stationary.

According to the results of our epidemiological survey\textsuperscript{11) in Japan, significant differences were obtained in the following points. Breast cancer was found more frequent in the left mamma at the level of significance of 5%. The age of first matrimony was found higher among the breast cancer cases than among the controls both in urban and rural areas, at the level of significance of 1%. The age of first child birth was also higher among the former at the same level. The number of children of married breast cancer patients is smaller than that of average married women as given in the national census.

The age of first menstruation is lower among the breast cancer cases than among the controls, both in urban and rural areas, at the level of significance of 1%. Fifteen years ago the mean age of first menstruation in Japan was somewhat above 14 years, but recently, it has fallen to less than 14 years.

In Japan, it is generally accepted the cancer of the breast is more frequent among the higher social classes.

In Japan, the rate of breast cancer patients with anamnesis of mastitis is probably higher than in the Western countries. According to the data\textsuperscript{11) we
have collected, among the 917 cases of breast cancer with experience of childbirth, 152 (16.6%) had experienced mastitis. Mastitis is naturally apt to occur among mothers who have more frequent chances for lactation. When only the cases with anamnesis of mastitis were picked up among the breast cancer cases, the total months of lactation among this group of subjects was not statistically different from that among the controls, but among the breast cancer cases without experience of mastitis and not less than 45 years old, the total months of lactation were significantly longer than among the controls. Among those 44 years and below, the difference was not significant.

When one of the mammae showed deficient milk secretion, it is overwhelmingly more frequent that this mamma becomes the site of subsequent cancer than otherwise. In Japan, cases with deficiency of milk secretion is more frequent in the left mamma.

With high probability, we may enumerate the custom of lengthy lactation as one of the cause of low frequency of breast cancer in Japan. It was not rare to find cases of atrophied uterus following lactation dragged on for 2 years and more, in rural districts in Japan till quite recently. Now, the Welfare Ministry is striving to disseminate the idea that breast feeding should be limited to one year at the longest.

The standardized mortality ratio for mammary cancer by prefectures in Japan is high in Tokyo and Hokkaido. (Fig. 9) In Tokyo, where the rate of child-births is low and the period of lactation is generally short, the high frequency of this cancer seems natural enough, but why Hokkaido should come next cannot
be explained. Hokkaido shows also a high rate of deaths for pulmonary cancer.

8. Uterine Cancer

The age-adjusted death rate for uterine cancer is the highest except U.S.A. Non-whites, Austria and Denmark among the 24 countries cited here in.

The death rate for uterine cancer in Japan is perceptibly declining, quite as in most other countries. The wide practice of early diagnosis and early treatment of uterine cancer has much contributed in diminishing the death rate in many countries in recent years.

Uterine cancer should be discussed under the separate headings of uterine corporal and cervical cancers, for these have different pathogenesis, and the corporal cancer seems particularly correlated with cancers of the breast and the ovaries in geographical distribution. In England and Wales, the rate of death certificates carrying the specification of cancer of the uterine corpus and cervix is very high, but in Japan, such a specification is forthcoming regrettably too rarely. It must be pointed out, however, that the percentage of carcinoma corporis uteris among all uterine cancers in Japan is at any rate very low, for clinical statistics show that only 3–5% of the total uterine cancer cases are of corporal cancer. I have no accurate data available, but I have the impression that the death rate for uterine cervical cancer only is rapidly falling, while that for corporal cancer remains unchanged or is rather rising in most countries.

In the map of geographical distribution of uterine cancer in Japan\(^8\), mostly uterine cervical cancer as mentioned already, Kyushu is seen to contain many prefectures with particularly high rate of death for uterine cancer (Fig. 10). Why
such prefectures with high death rates are so densely distributed in the southernmost island is not known. This district has been known for the high death rate for syphilis among sucklings. We could not establish a geographical correlation between the rate of child-births and the death rate for uterine cancer. In Japan, deaths for penis cancer are rare, but prefectures with high crude death rates for penis cancer are also found most in southern Japan, and there is a geographical correlation between the crude death rate per prefecture for uterine cancer and that for penis cancer at the level of significance of $5\%$.

The results of our epidemiological survey with 1,849 cases of uterine cervical cancer as objects showed that the percentage of married women was significantly higher among the uterine cancer cases than among the general female population and the percentage of unmarried, divorced and bereaved women was lower among the former. Only two cases of 17 and 18 years of age among the cancer patients was recorded as yet unmarried. Such rare exceptions do not restrain us from thinking of some correlation between sexual intercourse and uterine cancer. The ages of first menstruation, first matrimony and first child-birth were all significantly lower among the patients. We could not obtain any statistical data supporting the idea that uterine cancer is more frequent among women with oft-repeated experience of child-births. These findings are in agreement with those obtained by Wynder in U.S.A. Cases with anamnesis of syphilis are markedly more frequent among the uterine cancer cases. As the control cards in this survey were filled in at a number of the Health Centers at our request, the accuracy of the reported data may have been more or less detracted. No conclusion could be arrived at on the frequency of deaths for uterine cancer versus the social standing of the patients. In Japan, it is difficult to settle a good standard for classifying the subjects by social standing, so that it is hard to obtain systematic data by social classes.

The frequency of deaths for uterine cancer in Japan cannot be blamelessly attributed to any final cause, but we might propose the lower age of first matrimony, once so prevalent in Japan, as one of the probable causes of the frequency.

Malignant cholioepithelioma is believed to be frequent in Japan and other Asian countries. In 1958, the number of deaths for this tumor was 266, indeed markedly larger than in England and Wales, U.S.A. etc. In England and Wales, the number was only less than 36 in 1957. This neoplasm is known to be frequent after delivery of hydatid moles, which, according to our investigation, are apt to result from pregnancy in high age. In Japan, pregnancy in high age had been more frequent than in the Western countries till recently, but the rate of child-births in old age has fallen lower than in most Western countries, but this lowered frequency of child-births is inferred to be due to the high prevalence of artificial abortion among older women rather than to an actual fall in the rate of
pregnancies; this rate is estimated to be still higher than in most Western countries.

9. Ovarian Cancer

Deaths for ovarian cancer account for an important portion of deaths for cancers among the female population in the Western countries, and the number of such deaths shows a tendency of still increasing. Doubts on the accuracy of diagnosis may not be excluded, but it is certain that the death rate in Japan is markedly low. Since gastric cancer is frequent among Japanese women, the number of ovarian cancer cases probably includes a high percentage of cases with Kruckenberg's tumor metastasised from the stomach, so that when these are excluded, the net deaths for primary ovarian cancer in Japan are still further reduced. According to Higuchi,
Fig. 11. Trend of age-adjusted death rates for pulmonary cancer in Japan, England and Wales, and United States (White). (Standard population: 46 countries in 1950)

Fig. 12. Standardized mortality ratios for pulmonary cancer by prefectures, 1954–1956
12. Pulmonary Cancer

The age-adjusted death rate for pulmonary cancer in Japan is far lower than in the Western countries, but is recently rising very steeply and nearly at equal pace among males and females. The trend of the rising rate reminds us of that in England and Wales about 20–25 years ago. (Fig. 11)

According to our computation, the standardized mortality ratios per prefecture in 1954–56 were high in Tokyo, Hokkaido, Fukuoka, Kanagawa, Kyoto, Miyagi and Kumamoto Prefectures among males and in Fukuoka, Tokyo, Kyoto, Kanagawa, Miyagi and Hokkaido Prefectures among females. (Fig. 12)

In Japan, Tokyo, Osaka, Nagoya, Yokohama, Kyoto and Kobe have more than 900,000 population, and in Fukuoka Prefecture in Northern Kyushu, several cities are closely packed side by side, forming in substance a large city area. The name of a prefecture is either identical with the name of the capital city (e.g., Osaka, Fukuoka) or not (e.g., Kanagawa and Miyagi Prefectures, with the gubernatorial residence in Yokohama and Sendai respectively). In Tokyo, the metropolis is the prefecture.

In the above mentioned prefectures, with high death rates for pulmonary cancer among males are included all the prefectures containing the 7 great city areas enumerated above, except Osaka, Aichi (capital: Nagoya) and Hyogo (capital: Kobe), and among females, all the 5 except Osaka and Aichi Prefectures. It is a common feature of the list of the total male-female death rates that the 4 large city areas of Tokyo, Yokohama, Kobe and Fukuoka are included in the prefectures with high rates, all of which contain industrial centers.

We have computed the specific rates for pulmonary cancer of the aggregate deaths among the males and females of all ages divided by the number of populations of the respective sex above 40 years of age in all the 1,027 city and county areas in Japan in 1955. The city and county areas with this specific death rate significantly higher than the average among men counted 41 and among women 18. When areas with high rates, either for males or females, are picked up, we find 19 of them among the urban areas with more than 50,000 population and 38 among the cities with less than 50,000 population and county areas, accounting for 8.0% and 4.8% of the total number of areas of each group, respectively. These figures show a tendency of the distribution of deaths for this cancer to be inclined toward the side of major cities.

In Japan, administrative divisions with populations of above 30,000 are incorporated as cities as a rule, but some county areas have more than 30,000 residents. If these areas are classified into the cities with less than 50,000 population and county areas, medium-sized cities with populations of 50,000 to 900,000 and the metropoles with more than 900,000 residents, the specific death rate per 100,000 population over 40 years of age is found the higher, the larger
There are four major industrial areas in Japan (Tokyo plus Kanagawa Prefecture containing Yokohama, Aichi Prefecture containing Nagoya, Osaka plus Hyogo Prefectures containing Kobe and Northern Kyushu with Fukuoka as the center). Of these, the death rate for pulmonary cancer is not particularly high in Osaka District and Aichi Prefecture. The lowness of the rate below the national average in Aichi is a wondrous phenomenon.

The rate of deaths for pulmonary cancer is high in Hokkaido, Kyoto and Miyagi Prefectures. Kyoto city, the ancient capital of Japan, is now not an industrial center, but merely a tourists' resort. But it may be noted that it lies at the bottom of a basin surrounded by hills—a feature not shared by any other major city in Japan. Miyagi Prefecture is rather poor in industrial facilities, and we cannot account for the high rate of pulmonary cancer from this angle, but we may cite here as a cause of the apparent high rate the activity of Dr. Suzuki of Tohoku University (in Sendai, the capital city of this prefecture) who is ever alert for detection of pulmonary cancer in the X-ray pictures taken at mass-examinations for tuberculosis.

The frequency of pulmonary cancer in Hokkaido, (standing in the second place in the list of death rates among males) is rather noteworthy. In our search for city and county areas showing death rates for pulmonary cancers significantly rising above the nation-wide mean in Japan, we found that the north-western maritime district of Hokkaido, facing the Japan Sea was densely packed with such high-rated areas.

In Japan, we have two major coal-producing centers—the one in Northern Kyushu and the other in Hokkaido. Kyushu produces 54% and Hokkaido produces 31% of the total coal supply in Japan (1960). Fukuoka Prefecture, wherein the majority of the Kyushu collieries are situated, has well-developed industrial activity, and the death rate for pulmonary cancer among males ranks the fourth, while that among females is the highest in Japan.

In Hokkaido, however, no large industry is thriving, and in the above-mentioned district of high death rate for pulmonary cancer, there is no large city to speak of.

In the other parts of Japan, coal has been scarcely used for space-heating in ordinary homesteads, except in Hokkaido. It is known that the air in winter at Sapporo is as much polluted as in the heavy industrial centers in the other districts.

Another point to be mentioned in this connection is the rather wide difference of climatic conditions obtaining in Hokkaido from those in the other districts of Japan.

In Japan, a north-western wind from Siberia prevails in winter. This cold wind is humid and causes great snow-fall in the parts of Honshu lying to the
north-west of the mountain chain forming the backbone of the island, but on passing over this mountain range, the air loses humidity, so that fair weather prevails in winter in the regions facing the Pacific Ocean. The heavy industrial areas and most of the major cities, except those in Northern Kyushu, are situated in the Pacific side of Japan. The cycle of alternately passing migratory high and low atmospheric pressure increases in frequency in the end of February through March, and serene fair days alternate with windy days. In the former half of June, a meteorological front comes to stay over mid-Japan, and a rainy season begins, to continue to mid-July. Then, a sultry south-easterner becomes the prevalent wind, inaugurating the unpleasantly humid Japanese summer. In September again front-lines pass over, accompanying frequent wet weather, and typhoon often comes up along such a front line to attack Honshu. In October, the front-lines go downwards to South Sea and all Japan is favored by long spells of fair fall weather.

Except in autumn and winter in some parts, the weather condition in Japan is characterized by larger rainfall and more frequent windy days than in Western Countries.

Rain Fall in Some Cities in Japan
Mean annual precipitation of 30 years (1921-1950)

<table>
<thead>
<tr>
<th>City</th>
<th>Precipitation (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sapporo (Hokkaido)</td>
<td>1119</td>
</tr>
<tr>
<td>Sendai (Miyagi Prefecture)</td>
<td>1216</td>
</tr>
<tr>
<td>Tokyo</td>
<td>1568</td>
</tr>
<tr>
<td>Niigata</td>
<td>1743</td>
</tr>
<tr>
<td>Nagoya (Aichi Prefecture)</td>
<td>1513</td>
</tr>
<tr>
<td>Kyoto</td>
<td>1488</td>
</tr>
<tr>
<td>Osaka</td>
<td>1274</td>
</tr>
<tr>
<td>Fukuoka</td>
<td>1596</td>
</tr>
</tbody>
</table>

Such seasonal changes of weather conditions do not prevail in Hokkaido. In this district, the rainy season in June-July is not known, and typhoon rarely come up so far, move often landing somewhere in the southern half of Japan and glancing off eastwards into the Pacific. In winter, snowy days are frequent and sunny weather is a rare occurrence in Hokkaido, especially in the area facing the Japan Sea, where pulmonary cancer is prevalent. Though snow is copious in winter, the absence of rainy season in summer keeps down the total precipitation throughout the year below the general standard in Japan. These climatic conditions somewhat resemble those prevailing in England and Wales.

We have inquired for the possible correlation between the precipitation recorded at the weather stations in Japan in 1921-50 and the standardized mortality ratios for pulmonary cancer in 1954 through 1956 in the prefectures where the stations are located, and found a negative correlation of $r=-0.288$, which is, however, below significance at the level of 5%.
The above observations of the present lower frequency of pulmonary cancer in Japan than in the Western countries and the comparatively high frequency of pulmonary cancer in Hokkaido which is rather poor in industrial enterprises give the impression that the frequency of pulmonary cancer at least partly depends on the climatic conditions described above as well as the prevalence of coal stoves. Our survey\(^{11}\) for the relation between smoking and pulmonary cancer revealed that patients of this disease smoked 19.3 and 17.9 cigarettes and the control cases consumed 13.8 and 13.2 cigarettes in daily average, in the urban and the rural areas, respectively, showing a significant difference at the level of 1\%, as already reported.

We searched through the records concerning pulmonary cancer cases in the

| TABLE I. Number of Cases of Lung Cancer under Investigation by Sex, Age-group and Histological Classification |
|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
|                                             | Male                                             | Female                                           |                                             | Male                                             | Female                                           |                                             | Male                                             | Female                                           |                                             | Male                                             | Female                                           |                                             |                                             |                                             |                                             |                                             |
|                                             | Total     Epidermoid     Adenocarcinoma    Undifferentiated    Total     Epidermoid     Adenocarcinoma    Undifferentiated    Total     Epidermoid     Adenocarcinoma    Undifferentiated    Total     Epidermoid     Adenocarcinoma    Undifferentiated    Total     Epidermoid     Adenocarcinoma    Undifferentiated |
| All ages                                   | 314       143           63                      108               85        20            40                      25               85        20            40                      25               85        20            40                      25               85        20            40                      25               85        20            40                      25         |
| 20–29 years                                | 2         —             1                        1                2         —             1                       1                2         —             1                       1                2         —             1                       1                2         —             1                       1                2         —             1                       1                2         —             1                       1                2         —             1                       1         |
| 30–39                                      | 10        1             3                        6                10        1             6                       3                10        1             6                       3                10        1             6                       3                10        1             6                       3                10        1             6                       3                10        1             6                       3         |
| 40–49                                      | 32        9             8                        15               19        4             9                       6                19        4             9                       6                19        4             9                       6                19        4             9                       6                19        4             9                       6                19        4             9                       6         |
| 50–59                                      | 144       69            24                       51               31        9             14                      8                31        9             14                      8                31        9             14                      8                31        9             14                      8                31        9             14                      8                31        9             14                      8         |
| 60–69                                      | 111       57            22                       32               19        6             8                       5                19        6             8                       5                19        6             8                       5                19        6             8                       5                19        6             8                       5                19        6             8                       5         |
| 70–79                                      | 15        7             5                        3                3         —             2                       1                3         —             2                       1                3         —             2                       1                3         —             2                       1                3         —             2                       1                3         —             2                       1         |
| 80 and over                                | —         —             —                        —                1         —             —                       —                1         —             —                       —                1         —             —                       —                1         —             —                       —                1         —             —                       —                1         —             —                       —                1         —             —                       —         |

TABLE II. Frequency of Smokers by Sex and Histological Classification, and Number of Cases with Habit of Smoking by Daily Quantity of Tobacco Consumption, among Lung Cancer Patients

|                                             | Male                                             | Female                                           |                                             | Male                                             | Female                                           |                                             | Male                                             | Female                                           |                                             | Male                                             | Female                                           |                                             |                                             |                                             |                                             |                                             |                                             |
|                                             | Total     Epidermoid     Adenocarcinoma    Undifferentiated    Total     Epidermoid     Adenocarcinoma    Undifferentiated    Total     Epidermoid     Adenocarcinoma    Undifferentiated    Total     Epidermoid     Adenocar
| No smoking                                  | 19        4             7                        8                60        14            32                      14               60        14            32                      14               60        14            32                      14               60        14            32                      14               60        14            32                      14                60        14            32                      14                60        14            32                      14                60        14            32                      14                60        14            32                      14         |
| Smoking                                     | 295       139           56                       100               25        6             8                       11               25        6             8                       11               25        6             8                       11               25        6             8                       11                25        6             8                       11                25        6             8                       11                25        6             8                       11                25        6             8                       11                25        6             8                       11                25        6             8                       11         |
| 1–9 (pieces day)                           | 32        12            5                        16               15        2             6                       7                15        2             6                       7                15        2             6                       7                15        2             6                       7                15        2             6                       7                15        2             6                       7                15        2             6                       7                15        2             6                       7                15        2             6                       7         |
| 10–19                                      | 111       40            25                       37               4         3             —                       —                4         3             —                       —                4         3             —                       —                4         3             —                       —                4         3             —                       —                4         3             —                       —                4         3             —                       —                4         3             —                       —                4         3             —                       —         |
| 20–29                                      | 87        45            18                       24               5         1             2                       2                5         1             2                       2                5         1             2                       2                5         1             2                       2                5         1             2                       2                5         1             2                       2                5         1             2                       2                5         1             2                       2         |
| 30–39                                      | 26        15            2                        9                1         —             —                       —                1         —             —                       —                1         —             —                       —                1         —             —                       —                1         —             —                       —                1         —             —                       —                1         —             —                       —                1         —             —                       —                1         —             —                       —                1         —             —                       —         |
| 40–49                                      | 20        9             3                        8                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —         |
| 50–59                                      | 8         4             1                        3                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —         |
| 60 and over                                 | 10        5             2                        3                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —                —         —             —                       —         |

Note: 1 gr. of cut tobacco ("Kizami") has been counted as equivalent to 1 piece of cigarette.
TABLE III. Frequency Distribution of Daily Consumption of Tobacco by Age-classes and Histological Classification and the Average Quantity of Consumed Tobacco of Habitual Smokers, among Male Patients with Lung Cancer

<table>
<thead>
<tr>
<th></th>
<th>Epidermoid carcinoma</th>
<th>Adenocarcinoma</th>
<th>Undifferentiated ca.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20-49 years</td>
<td>50-59 years</td>
<td>60-69 years</td>
</tr>
<tr>
<td>Total (pieces)</td>
<td>10 66(3)</td>
<td>49(8)</td>
<td>7</td>
</tr>
<tr>
<td>0 (pieces/day)</td>
<td>-</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>(1)</td>
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<tr>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>1</td>
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<tr>
<td>6</td>
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<td>7</td>
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<td>9</td>
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<td>2</td>
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<tr>
<td>10</td>
<td>2</td>
<td>13</td>
<td>6(2)</td>
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<tr>
<td>12</td>
<td>-</td>
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<td>1</td>
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<td>6</td>
<td>7(2)</td>
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<tr>
<td>18</td>
<td>-</td>
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<tr>
<td>20</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>23</td>
<td>-</td>
<td>1</td>
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<tr>
<td>29</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>35</td>
<td>1</td>
<td>2</td>
<td>5(1)</td>
</tr>
<tr>
<td>40</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>50</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>55</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>60</td>
<td>1</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>70</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>90</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>100</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Average quantity (in numbers of cigarettes) | 21.80 | 21.10 | 22.24 | 10.15 | 18.64 | 18.71 | 22.00 | 9.25 | 16.50 | 22.42 | 17.26 | 21.67

Average quantity (all ages) | 21.05 | 17.41 | 19.73

Note: 1. Classes with negative frequency have been omitted.
2. The figures in parentheses denote the number of smokers of cut tobacco ("Kizami") only and those outside the parentheses that of smokers of cigarettes plus smokers of cut tobacco.
3. 1 gr. of cut tobacco ("Kizami") has been counted as equivalent to 1 piece of cigarette.

recent years on file at the four hospital clinics noted for treatment of pulmonary cancer cases par excellence in Japan—Keio University Hospital (Dr. S. Ishikawa), Tokyo Medical College Hospital (Dr. K. Shinoi), Chiba University Hospital (Dr. Kawai and Dr. Watanuki) and Tohoku University Hospital (Dr. C. Suzuki) and obtained data leading to the following conclusions. (Tab. I-III)

The percentage of smokers is higher among the lung cancer cases with epidermoid carcinoma than among those with the cancer of other types.

The percentage of non-smokers plus light smokers of less than 5 cigarettes
or their equivalent a day was smaller, but the percentage of heavy smokers consuming more than 15 cigarettes or their equivalent in tobacco was higher among the cases with lung cancer of the epidermoid type than the others. When only cigarette smokers are counted in exclusion of the smokers of cut tobacco, the tendency is more perceptible. The mean quantity of consumed tobacco per day was generally the highest among the cases with epidermoid cancer and the lowest among the adenoid cancer cases.

A significant positive correlation at the level of significance of 1% was observed between the quantity of cigarettes sold in the 46 prefectures in Japan in 1957 per male population above 20 years inclusive and the standardized mortality ratio for pulmonary cancer among males in 1954 through 1956.

A significant negative correlation at the significance level of 5% was found between the population per number of motor vehicle of exhaust capacity of 200 cc and above of each prefecture and the standardized mortality ratio for pulmonary cancer among males in 1954 through 1956.

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