On the Chemotherapy of Carcinoma. II.

By

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Chemotherapy of cancer is no doubt a world wide problem. In a preliminary report last year, I concluded that chemotherapy of human cancer would be quite possible, delivering some cases of stomach cancer, which was cured by citronellal and citral intake, both remedies being unsaturated aldehydes of terpene series with C\textsubscript{10}. As I mentioned in the previous report, the hint to this therapy has been gotten from the experiments of Strong.\textsuperscript{2},\textsuperscript{3}

The first case I tried citronellal was a man of 52 years with a child's head large bronchogenic cancer in the chest. After a few months betterment he got fluid in the thoracic cavity and disappointed left the hospital. But the experience in this case gave me a hopeful promise to the chemotherapy of cancer. This case was observed during October 1944-February 1945. Since then I treated many cases of cancer patient with citronellal and later also with citral. The remedies were diluted with cod liver oil and given per os and per rectum. Since last year I succeeded to make emulsion of the remedy which was injected intramuscularly. The emulsion can be prepared by the aid of some emulsifying chemicals. But we use at present NA type magnetostriction vibration (Nukiyama-Aoyagi), which is practiced by favour of the Tohoku University Electrical Communication Laboratory. Following cases were treated with success.


No malignant tumor in the family history. 6 years ago hyperacidity. Otherwise no remarkable disease. Moderately in tobacco and in vacco.

Present disease: Since last spring belching and pain in the stomach without direct connection with meal.

Abdomen flat. Abdominal wall soft. A tumor smaller than a hen’s egg was palpated in the left epigastrium, hard, uneven. Not so well movable. Liver, spleen, kidney not palpable. Extremities thin.

Urine: normal. Faeces: no parasite eggs. Occult blood reaction positive.

Stomach juice, normal acidity. Blood: erythrocytes 4.05 million. Hb 60%. (Sahli’s method).

X-ray examination of the stomach revealed a disk like niche of about 5.5 cm length diameter (Fig. 1 c.). The tumor was palpated coincided with this niche.

Therapy was started on Febr. 9, 1945 and continued till his leaving the hospital on Jul. 2. citronellal-cod-liver-oil āā 3.0 cc. per os and 8 cc. per anum. The condition of the patient was improved rapidly. After 2 months the tumor and niche were disappeared thoroughly. He gained 4½ kg of weight in 3 months and a half. Blood count 3.60 million erythrocytes and 58% Hb at the start of the therapy on February 11 and 4.84 million erythrocytes and 85% Hb. at discharge from the hospital. Since then about 4 years. Always healthy. (Fig. 1. a. b. c. d.)


Family history: no cancer. He was hitherto very healthy. Malaria like fever in 13th and 25th ages. He drinks occasionally and smokes moderately. 7 months ago dull pain in the epigastrium 2–3 hours after meal, which lasted for some weeks. Since 2 weeks again the pain and heartburn. He lost rapidly the weight.


Thorax: normal. Abdomen: flat. A tumor as large as a hen’s egg in the epigastrium, hard, uneven.


X-ray examination revealed a niche as large as a sparrow’s egg in the epigastrum, around which the tumour was palpated.

Therapy: Citronellal-cod-liver-oil āā with 1% citral, 3 cc per os and 8 cc per anum. After a month tumor and niche disappeared.

Blood count 3.71 erythrocytes and Hb. 71%. in admission and the same at discharge. During 10 months be continued to be healthy. Re-examination in March 1949, good health. X-ray finding of the stomach almost normal. (Fig. 2. a. b. c.)

In his family no cancer. Bronchitis in 17th year. Otherwise always healthy. Since end of last year he felt heavy in the epigastrium, had dull pain in the stomach and became rapidly thin.


Thorax: normal.

Abdomen: flat. A tumor as large as a hen's egg in the epigastrium a little on the left from the median line, hard and uneven, moderately movable.

Urine: normal.

Faeces: no parasites eggs. Occult blood reaction positive.

Stomach juice: slight hyperacidity.

X-ray revealed a large shadow defect in the lesser curvature of the stomach, where the tumor was palpated. No pain on palpation.

Therapy. Citronellal-cod-liver-oil 2% citral, 3 cc per os and 8 cc per anum, later combined with injection of emulsion of citral (5%).

Tumor has rapidly diminished in its size. After a months treatment it was no more palpable. X-ray revealed slight stiffness of the lesser curvature. After 3 months the stomach mould was almost normal. Stomach juice hyperacidity. Blood examination

<table>
<thead>
<tr>
<th>Date</th>
<th>Erythrocytes</th>
<th>Hb.</th>
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<tbody>
<tr>
<td>July 6</td>
<td>4.15 mill.</td>
<td>90%</td>
</tr>
<tr>
<td>Sept. 29</td>
<td>5.17 mill.</td>
<td>102%</td>
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6 months after discharge reexamined. He gained 3 1/2 kg in weight. All the examination revealed good health. (Fig. 3. a. b. c.)


No malignant tumour in his family. Hitherto very healthy. Drinks and smokes moderately.

Since last July he had heaviness in the epigastrium and diarrhoea occasionally. Since March of this year he had pain in the stomach, lassitude and rapid loss of body weight.

Status praesens: Good constitution. Somewhat meagre. Anemic. A few lymph glands of the size of soya bean on the left axilla.

Thorax: normal.


Urin: normal.

Stool: parasites eggs not found. Occult blood positive.
Gastric juice: Achylia.

X-ray revealed shadow defect in the pyloric part where the tumour was palpated.

Treatment. Citronellal-cod-liver-oil αα + 2% citral per os 3 cc, per annum 8 cc, later combined with injection of citral (5%) emulsion 3–8 cc.

Tumor diminished rapidly in the size and after three months only resistance in its place. Body weight and blood count about the same in admittance and at the discharge. A half year after discharge reexamination, the stomach almost normal.

These are the cases, whose diagnosis were we think mostly exact. But following cases are examples of uncertain diagnosis. K. S. 61 years old man, who had a skirrus of the stomach in the X-ray examination, achylia and moderate cachexy, was cured by citronellal. A man of 52 year (A. Ch.) admitted in the hospital under diagnosis of primary hepatic cancer, whose liver being enlarged to the navel, had his liver diminished day by day under the action of citronellal. He was discharged after 3 months and was in good condition, when be visited us one year later. Cases which was improved transitorily by this therapy are numerous. Two cases of bronchogenic carcinoma, lost their cancer cells in the sputum and in the pleural fluid by this treatment. (Fig. 4. a. b. c.). In one case of stomach cancer with abdominal fluid and a case of a very large retroperitoneal sarcoma with peritoneal fluid the tumor cells of the fluid disappeared in the course of this therapy. (Fig. 5. a. b. c. d.). Abdominal fluid in the latter case was no more to get after repeated puncture. But we could not save them to our great regret.

Some cases of esophageal carcinoma, cardia carcinoma and pyloric carcinoma, which were quite advanced and the cancer tissue infiltrated almost all the circumference of the wall and destroyed the tissue so far as to the tunica muscularis, were quite improved, but in the course of few months, again increased stenosis, very probably owing to the shrinkage of the scar tissue which might have replased the cancer tissue. Only not much advanced cases gave good results.

From all these we can conclude that most of the stomach cancer would be cured by this therapy, if we could begin with proper stage.

It would be better to consider in this place surgical treatment of cancer in connection with the chemotherapy. I don't think this therapy should prevent the cancer patient from surgical operation. On the contrary it would widen indication of operation of cancer patients. I report here a case of a stomach cancer inoperable at first because of its extent and adhesion, but which was operated with good result after a period of this therapy.

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In 1948 in the clinic and then operated. Diagnosis: Stomach cancer. Since 10 years he had stomach pain and heartburning. These 2 months he became rapidly thin. Vomited almost every evening. Status praesens: Very thin and cachectic. Diffuse resistance in the epigastrium and a rugged irregular shaped tumor as large as a goose egg was palpated, immovable. X-ray revealed shadow defect in the pyloric part extending on both curvatures, corresponding the tumor.

Gastric juice: achylia. Citronellal-cod-liver-oil with 2% citral per os (3 cc) and per anum (8 cc).

Tumor has diminished and appetite increased but transitorily.

The second X-ray showed a shadow defect localised in the pyloric part and tumor became movable but passage of the pylorus became worse. Operation by Prof. Muto. The tumor was resected. But the surgeon noted that recidiv would be inevitable. On reexamination after 10 months, he was found in a very good condition. Recurrence was not detected. (Fig. 6 a. b. c. d.)

The following case of cancer in the S Romanum was first operated and anastomosis was set and then chemotherapy.

S. H. 49 T. House-wife. Admitted on Nov. 5, 1948, operated on Nov. 9, 1948. Father died from rectum cancer. She had habitual constipation because of hemorrhoid from which she suffered and used to apply laxativa. Before 3 months she had pain in the abdomen and diarrhoea after sea-bathing. Since then she had often diarrhoea and following constipation by slight nutritional disturbance. Lately she had obstinate constipation. Laxative and klysma were of no use. She had heaviness in abdomen and borborygma. She became very thin. Extensive tympany in abdomen. Digital palpation in rectum and romanoscopy examination gave nothing. X-ray following barium meal and klysma revealed a high sitted stenosis in the S romanum. Operation showed a skirrhus of colon sigmoideum about 50 cm from anus. As the tumor infiltrated retroperitoneal tissue, radical operation was impossible. An antastomosis of colon sygmoidea of upper and lower part of the stenosis was made. Then she was treated by us with citral and citronellal. She gained rapidly in weight, $11\frac{1}{2}$ kg in 2½ months. No complaint in abdomen. After discharge on March 18, 1949 she continued to get fatter. Now 6 months after begin of chemotherapy she gained more than 16 kg. (Fig. 7. a. b. c.).

Recently I have known that Boyland and associates resumed the work of Strong. They treated the spontaneous mamma carcinoma of mouse and grafted Crocker sarcoma with many sorts of aldehydes. Among those aldehydes Boyland mentioned citral was quite efficacious. So far as I could read I don’t know whether there are reports in which human cancer was treated with aldehydes.
So far as our experiments on chemotherapy of the grafted "Yoshida sarcoma" with aldehydes concerns, which is now only malignant tumour of laboratory animal available in Japan, good effect of citral, citronellal and oenanthol is obvious. A part of these experiments was reported in the Japanese Cancer Society at Osaka on April 6, 1948.

**Summary.**

In this paper I have reported four cases of stomach cancer, who had been cured with chemotherapy and on reexamination after 6 months to 4 years were found free from relapse. Some other cases, in whom chemotherapy was efficacious, are given briefly. Two cancer cases, who were treated with chemotherapy under cooperation of surgery, are mentioned.

**References.**

(2) Handbuch der Erbbiologie. IV/2 p. 1095.
Explanation of figures:

Fig. 1. Y.M. 51 Y. male. Stomach cancer.
   d. May 29. 1945. After treatment. (X-ray photo.)

Fig. 2. D.M. 52 Y. male. Stomach cancer.
   b. Jan. 27. 1948. During treatment. (X-ray photo.)

Fig. 3. E.S. 55 Y. male. Stomach cancer.
   b. July 30. 1948. During treatment. (X-ray photo.)

Fig. 4. T.O. 52 Y. male. Bronchogenic cancer with pleural effusion.
   c. June 3. 1948. After 2 months' treatment. (Micro-photo.)

Fig. 5. D.S. 23 Y. male. Retroperitonealsarcoma with peritoneal fluid.
   d. Sept. 22. 1948. No tumor cell was seen. (Micro-photo.)

Fig. 6. T.S. 50 Y. male. Stomach cancer.
   b. March 9. 1949. 10 Months after operation.
   d. March 26. After 2½ months' chemotherapy. (X-ray photo.)

Fig. 7: S.H. 49 Y. female. Cancer of S romanum.
   c. Sight of operation.