RESTRICTED

7 January 1946

From: Chief, Naval Technical Mission to Japan.
To: Chief of Naval Operations.

Subject: Target Report - Pharmacology and Malariology in Japan - Civilian and Naval.

Reference: (a) "Intelligence Targets Japan" (DNI) of 4 Sept. 1945.

1. Subject report, covering Target M-12 of Fascicle M-1 of reference (a), is submitted herewith.


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Captain, USN
PHARMACOLOGY AND MALARIOLGY IN JAPAN
CIVILIAN AND NAVAL

"INTELLIGENCE TARGETS JAPAN" (DNI) OF 4 SEPT. 1945
FASCICLE M-1, TARGET M-12

JANUARY 1946

U.S. NAVAL TECHNICAL MISSION TO JAPAN
SUMMARY

MEDICAL TARGETS

PHARMACOLOGY AND MALARIOLOGY IN JAPAN

CIVILIAN AND NAVAL

The results of the exploitation of this target have been very uneven. Certain civilian research and reports are included as worthy of careful attention, although the drugs developed, namely "Shiko" and "Koha", were not used in naval medicine.

Naval pharmacology was fairly well standardized, and vaccines and serums employed have been listed. Those produced by the naval medical laboratories have been referenced in Enclosure (E) of "Preventive Medicine and Public Health Organization and Facilities", NavTechJap Report, Index No. M-09. Samples of drugs collected as unfamiliar are listed. Investigation of the largest chemical company producing drugs for the Navy yielded the information in Enclosure (E) of this report.

Field exploitation of naval pharmacology was relatively sterile, but as a sampling of drug stocks, the inventory (drugs only) of the Yokosuka Naval Medical Supply Depot is included as Enclosure (F).

The custom of allowing individual medical officers in the various naval hospitals to order and use a multitude of proprietary drug preparations resulted in a variety of stock in the various naval pharmacies bordering on confusion. The pertinent and interesting information on naval pharmacology is presented in the body of the report as fully as it could be obtained. To exploit civilian pharmacology would require more personnel and time than were available.
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REFERENCES

A. Location of Targets:

The exact locations where the various drugs samples and documents were obtained are indicated in the enclosures to this report.

B. Japanese Personnel Who Assisted in Gathering or Locating Equipment and Documents:

1. Dr. E. OCHIAI - Medical Dept., Tokyo Imperial University, TOKYO, Japan.
2. Dr. T. OGATA - Institute of Physical and Chemical Research, Hongo Ku, TOKYO, Japan.
3. Dr. H. TAMIA - Science Dept., Tokyo Imperial University, TOKYO, Japan.
4. Dr. K. SHIMADA - Surgery Dept., School of Medicine, Keio University, TOKYO, Japan.
5. Dr. H. IMANAGA - Kumamoto Medical School, KUMAMOTO, Kyushu, Japan.
6. Dr. M. MIYAZAKI - Kumamoto Leprosarium, Kumamoto Medical School, KUMAMOTO, Kyushu, Japan.
7. Dr. C. OKA - Nakano Tuberculosis Sanitarium, KHEBA Prefecture, Japan.
8. Dr. S. HATANO - Kumamoto Medical School, KUMAMOTO, Kyushu, Japan.
9. Dr. T. SO - Kitasato Research Institute, TOKYO, Japan.
10. Dr. Y. KOBAYASHI - Pharmacologist, Tokyo Imperial University, TOKYO, Japan.
11. Dr. K. IWASAKI - Kanazawa Medical School, KANAZAWA, Japan.
12. Vice Admiral I. HOMMA - C.O. Ureshino Naval Hospital, URESHINO, Kyushu, Japan.
13. Mr. TAKEDA - Takoda Chemical Co., OSAKA, Japan.
14. Vice Admiral KANAI - Yokosuka Naval Hospital, YOKOSUKA, Japan.

C. Japanese Personnel Interrogated:

1. The personnel listed under reference B of this report were all interrogated and were very helpful.
2. All personnel listed in reference B, NavTechJap Report, "Data Relative to Life in the Jungle and On Sea Islands, and Data on Composition of Insecticides," Index No. M-01, were also interrogated.

D. Reports of Other Investigating Committees Pertinent to the Subject:

INTRODUCTION

The development and progress of pharmacology during the war years was stimulated by the urgent necessity for new or improved drugs. New requirements arose from meeting new diseases, new medical problems, and new or different demands upon the Medical Corps which was charged with the care and treatment of a vast number of sick and wounded. The same problems, varying with the theatre of operations, faced all combatant nations and were met with varying degrees of success by the respective nations.

Our forces encountered the Japanese Navy chiefly in tropical and semi-tropical areas and our interest in this target was activated by a desire to compare the solutions arrived at by the Japanese Medical Corps with our methods for handling the same problems.
THE REPORT

A. NAVY PHARMACOLOGY

1. Penicillin - As reported, research experiments were underway in the Naval Medical School Laboratory in TOKYO, under the direction of Commander HASHTOMOTO, in an attempt to produce penicillin, but only a small amount of crude extract had been prepared. This was hardly sufficient for experimental therapeutic trial.

2. Sulfa-drugs - The use of the sulfa-drugs has been noted in "Preventive Medicine and Public Health Organization and Facilities," NavTechJap Report, Index No. M-09. The question of sulfa-resistant pathogens had not arisen. As noted, owing to the absence of blood concentration determinations, "in vitro" experiments did not have much relation to "in vivo" results. Sulfa-blood concentrations were carried out in NIIGATA at the Medical College. This school apparently was the authority on the usage and dosage of the sulfa-drugs. Recommendations emanating from the results of researches carried out there were adopted by the Navy Medical Bureau and disseminated to medical officers for their information.

3. Benzedrine was used by the Navy only for the prevention of drowsiness, and to stimulate and maintain mental alertness in air corps flight personnel during flight. Its use in general medicine was desultory, and the drug was not stocked routinely in the naval pharmacies.

4. Flash burn protection was effected by enforcing the regulation that all exposed naval personnel wear an adequate amount of clothing at all critical times. The order stated that the body should be completely covered "down to the wrists and ankles". No protective cream had been developed or was in use, nor was the clothing specially designed or impregnated to make it fire-resistant.

5. Pharmacopeia - The Japanese Navy used the Regulation Japanese Pharmacopeia, approved by the national medical governing body. This is a subsection in the Public Health Bureau, charged with the control of drug licensing, standards of purity, etc. Drugs were purchased wholesale from the various manufacturers and put up in tablet or ampoule form at the Ryo-hin-sho (The Central Medical Supply Depot in NAGURO Ku, Tokyo). Some vaccines were prepared there, as was dried human plasma. The pharmacological activities of the depot, (apart from the biological output) consisted chiefly of tablet making, bottling, labelling, packaging, and shipping.

This depot was the central supply depot, in that all orders for drugs and pharmaceuticals from the Navy, ashore and afloat, cleared through it. The orders were authenticated and forwarded to the private commercial houses concerned, from where shipment was made to the requesting activity.

6. Water Purification - Water (in small quantities) for troops in combat was usually carried from the ship landing them. Where any protracted action was expected, chlorination with sodium hypochlorite to an excess of 1-2 parts per million was ordered, but frequently not carried out.

7. Chemotherapy in therapeutics is reported not to have been employed for any helminthic or protozoan disease in the Navy. As such diseases were of rare occurrence and standard treatment was employed, no research on therapy had been done.
B. CIVILIAN AND ARMY PHARMACOLOGY

1. Neocyanine Derivatives.

Enclosures (A), (B), (C), and (D) of this report refer to the synthesis and effects of two new drugs which are considered of extreme interest. The results of the clinical experiments, if confirmed, will undoubtedly justify the adoption and use of these drugs for the treatment of certain diseases and traumatic conditions.

The drugs, derived from neocyanine, were produced in an effort to find some therapeutic agent resembling chlorophyll, with its power of converting sunlight into energy. Since the research workers were unable to obtain active chlorophyll, this light-sensitive agent was selected for trial. The initial experiments with the earlier lots of the drugs were clinically most promising. As the chemical synthetic process was improved, a more refined product was obtained which has not proved as effective as the original unrefined drug. It is believed that the "chemical impurities" either activated the preparations or were themselves active. At present an attempt is being made to follow the original method of preparation and to repeat the clinical work, using the original unrefined product.

From clinical records, laboratory findings, and histo-pathological specimens, it seems that the drugs stimulated the reticulo-endothelial system, increased the phagocytic index as much as 60%, stimulated the regeneration of tissue, improved general body resistance, and increased the viability and survival of damaged tissue cells. The drug, in venereal pyogenic infections, had a more stimulating effect than against the less venilent organisms. For example, streptococcal infection was more rapidly overcome when the hemolytic strains were involved than when the viridans were the pathogen.

In chronic diseases, remarkable effects were demonstrated, particularly in the improvement shown by lepers, from whose lesions the bacillus count became progressively lower, with corresponding healing. Burns and frost bite, when thermal tissue damage is involved, responded with a gratifying acceleration in the healing process.

It is believed that this drug is worth full and careful investigation.

2. Drugs for Improvement of Night Vision.

Since the improvement of "night vision" was a priority requirement, the development of adequate drugs was part of the program. The following drugs were developed and used:

a. By the Navy:

"Melanophore Hormone" - This was an extract of posterior pituitary of cattle (sheep and shark also being used as a source), in normal saline. It was put up in ampoule form, tested for potency by its dilation of the melanophore of the loach (0.1 mg. being injected intraperitoneally). Its potency was expected to last six months, and the dosage was one ampoule by parenteral injection. The effect was to dilate the pupil. Maximum effect was observed two hours after injection, and the injection was given prior to take-off, so as to reach its peak effect when the objective was reached (see reference D).

b. By the Army:

(1) A drug preparation named "Migozai" was developed (see Enclosure G).
(2) "Dehydrogallic Acid", derived from cow's bile, was reported as "best for night blindness of a congenital nature".

3. **Civilian Drugs.**

a. "Cepharanthin" - a preparation of wisteria root alkaloid, was reported, (see Reference D, Army Committee on Investigation of Japanese Medical Science), as useful in the treatment of tuberculosis (pulmonary) There existed such a diversity of opinion as to its value that it is merely noted in passing.

b. The use of various colloidal metals in the treatment of "tropical diseases" was reported as more effective than the present therapeutic agents (see Reference D).

c. The preparation of various metal colloids (reference D) by spraying on glucose crystals in vacuum was reported. This procedure was said to give a potential colloid of stable characteristics, easy to dissolve and administer parenterally when required.

d. The preparation of vaccines and sera for preservation at room temper-atures for tropical shipment, etc., was another technique worthy of comment. Prepared vaccine solutions, typing sera, etc. were dehydrated by vacuum suction at relatively low dehydrating temperatures, the resultant solids retaining their antigenic properties up to approximately 80°F temperatures for one hour.

Note: Detailed reports on the articles and techniques noted in Reference D are to be found in the Reports of the Army Committee for the Investigation of Japanese Medical Sciences, Chief Surgeons Office, GHQ, SCAP, and will be available from the Army Surgeon General's Office, Washington, D. C.

C. **MALARIOLOGY**

1. Several articles on life-cycle research are noted in reference D of this report. The Naval Medical Corps research worker in malaria was aLt. Comdr. KAWAI. His statements were as follows:

"No prophylactic routine is followed in the Navy against malaria. Diagnosis is by microscopic examination of the blood. Henry's reaction also may be used. (If ground cow retina is added to the patient's serum, a whitish precipitation in the area of contact is considered diagnostic.) Treatment - two grams of quinine divided in three daily doses is given for five days. Three days rest period is then given. The course, treatment and rest period, is repeated three times. Plasmochin and atabrine are used on recurrent cases, but when these drugs became scarce provocative measures were substituted. Adrenalin, hot and cold baths, severe muscular exercise, typhoid injection and deep X-ray therapy to the splenic area were followed by the routine quinine course. The results of these procedures were satisfactory."

2. The following methods of malarial therapy, translated from various naval directives and texts, comprise the latest routines adopted. (A - Atabrine; P - Plasmochin; C - Quinine; E - Epirenamin Chloride - a liquid.)
### Navy A P Method

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily Quantity</th>
<th>Period of Treatment</th>
<th>Full Quantity and Number of Days for 1 Cure</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthetic Malaria Drug A</td>
<td>0.3 taken internally 3 times a day after meals</td>
<td>7 days</td>
<td>Synthetic Malaria Drug A 2.1</td>
<td>Depending on conditions, one day’s dosage may be taken at one time</td>
</tr>
<tr>
<td>Abstain from Medicine</td>
<td></td>
<td>2 days</td>
<td>Synthetic Malaria Drug B 0.15</td>
<td></td>
</tr>
<tr>
<td>Synthetic Malaria Drug B</td>
<td>0.03 taken internally 3 times a day after meals</td>
<td>5 days</td>
<td>Number of days of treatment - 14 days</td>
<td></td>
</tr>
</tbody>
</table>

### Navy C P Method

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Daily Quantity</th>
<th>Period of Dosage</th>
<th>Full Quantity and Number of Days for 1 Cure</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enki (Nitrate of Quinine)</td>
<td>1.0 (1.1) taken 3 times a day after meals</td>
<td>10 days</td>
<td>Nitrate of Quinine 10.0 (Sulphate of Quinine 11.0)</td>
<td>One day’s dosage may be taken at one time, depending on conditions</td>
</tr>
<tr>
<td>Ryuki (Sulphate of Quinine)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abstain from Medicine</td>
<td></td>
<td>2 days</td>
<td>Synthetic Malaria Drug B 0.15</td>
<td></td>
</tr>
<tr>
<td>Synthetic Malaria Drug</td>
<td>0.03 taken 3 times daily after meals</td>
<td>5 days</td>
<td>17 days of treatment</td>
<td></td>
</tr>
</tbody>
</table>

### Navy C Method

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Daily Quantity</th>
<th>Period of Dosage</th>
<th>Full Quantity and Number of Days for 1 Cure</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrate of Quinine (Sulphate of Quinine)</td>
<td></td>
<td>10 days</td>
<td>Nitrate of Quinine 17.0 (Sulphate of Quinine 18.7)</td>
<td></td>
</tr>
<tr>
<td>Abstain from Medicine</td>
<td></td>
<td>2 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrate of Quinine (Sulphate of Quinine)</td>
<td></td>
<td>7 days</td>
<td>19 days of treatment</td>
<td></td>
</tr>
</tbody>
</table>

**Remarks:**

a. In general, follow Navy A P Method
b. When there is no synthetic malaria drug A, Follow Navy C P Method.
c. When both synthetic malaria drugs A and B are missing, follow Navy C Method.
### 3. Method of Treatment for Old Malaria

#### Navy A P E Method

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Daily Quantity</th>
<th>Period of Dosage</th>
<th>Full Quantity and Number of days for 1 Cure</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthetic Malaria Drug A</td>
<td>0.3 taken 3 times daily after meals</td>
<td>7 days</td>
<td>Synthetic Malaria Drug A 2.1</td>
<td>Depending on conditions, synthetic malaria drug may be taken at one time</td>
</tr>
<tr>
<td>Abstain From Medicine</td>
<td></td>
<td>2 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synthetic Malaria Drug B</td>
<td>0.03 taken 3 times daily after meals</td>
<td>5 days</td>
<td>Synthetic Malaria Drug B 0.15</td>
<td></td>
</tr>
<tr>
<td>Epirenamin Chloride (liquid)</td>
<td>0.5 - 0.7 cc subcutaneous injection. First, try 0.3 cc, and according to strength of reaction and bodily weight, increase or decrease succeeding injections.</td>
<td>alternate days throughout whole period</td>
<td>Epirenamin Chloride (liquid) - 3.3 - 4.5 cc</td>
<td>14 days period of treatment</td>
</tr>
</tbody>
</table>

#### Navy C P E Method

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Daily Quantity</th>
<th>Period of Dosage</th>
<th>Full Quantity and Number of days for 1 Cure</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muriaate of Quinine (Sulphate of Quinine)</td>
<td>1.0(1.1) taken 3 times daily after meals</td>
<td>10 days</td>
<td>Muriaate of Quinine 17.0 (Sulphate of Quinine 18.7)</td>
<td>Depending on conditions, synthetic malaria drug may be taken at one time</td>
</tr>
<tr>
<td>Abstain From Medicine</td>
<td></td>
<td>2 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synthetic Malaria Drug B</td>
<td>0.03 taken 3 times daily after meals</td>
<td>5 days</td>
<td>Synthetic Malaria Drug B 0.15</td>
<td></td>
</tr>
<tr>
<td>Epirenamin Chloride (liquid)</td>
<td>0.5 - 0.7 cc subcutaneous injection. First, try 0.3 cc, and according to strength of reaction and bodily weight, increase or decrease succeeding injections.</td>
<td>alternate days throughout whole period</td>
<td>Epirenamin Chloride injection liquid 3.8 - 5.2 cc</td>
<td>17 days period of treatment</td>
</tr>
</tbody>
</table>
### Navy C E Method

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Daily Quantity</th>
<th>Period of Treatment</th>
<th>Full Quantity and Number of days for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enki (Ryuki)</td>
<td>1.0(1.1) taken 3 times daily after meals</td>
<td>10 days</td>
<td>1 Cure Enki 17.0 (Ryuki 18.7)</td>
</tr>
<tr>
<td>Abstain from Medicine</td>
<td></td>
<td>2 days</td>
<td></td>
</tr>
<tr>
<td>Enki (Ryuki)</td>
<td>1.0(1.1) taken 3 times daily after meals</td>
<td>7 days</td>
<td></td>
</tr>
<tr>
<td>Epirenamin Chloride (liquid)</td>
<td>0.5 - 0.7 cc subcutaneous injection. First, try 0.3 cc, then according to strength of reaction increase or decrease succeeding injections.</td>
<td>alternate days throughout whole period</td>
<td>Epirenamin Chloride (liquid) 4.3 - 5.9 cc</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Period of treatment 19 days</td>
</tr>
</tbody>
</table>

**Remarks:**

a. As a rule, follow Navy A P E Method.
b. When Synthetic Malaria Drug A is lacking, follow Navy C P E Method.
c. When Synthetic Malaria Drug A and B are lacking, follow Navy C E Method.
d. On days of abstinence from medicine, do not use Epirenamin Chloride (liquid) injection.
e. When Epirenamin Chloride liquid is lacking, it is necessary to make use of other methods (cold water baths, cold and warm baths alternating, X-ray spleen application, etc.)

4. Method for Treating Persons Having Protozoa ("field insect")

Follow the treatment for old malaria. However, in combat areas where it is difficult to carry out such treatment, the epirenamin chloride injections may be omitted.
5. Method of Treating Clinical Malaria

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Daily Quantity</th>
<th>Period of Treatment</th>
<th>Full Quantity and Number of days for 1 Cure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthetic Malaria Drug A - as an injection</td>
<td>0.3 once a day, injection into musculus glutaeus</td>
<td>7 days</td>
<td>Synthetic Malaria Drug A - 2.1</td>
</tr>
<tr>
<td>Abstain from Medicine</td>
<td></td>
<td>2 days</td>
<td></td>
</tr>
<tr>
<td>Synthetic Malaria Drug B - as an injection</td>
<td>0.03 once a day, injection into the musculus glutaeus</td>
<td>5 days</td>
<td>Synthetic Malaria Drug B - 0.15</td>
</tr>
<tr>
<td>Epirenamin Chloride (liquid)</td>
<td>0.5 - 0.7 cc subcutaneous injection. First, try 0.3 cc and then according to strength of reaction and bodily weight increase or decrease succeeding injections.</td>
<td>alternate days throughout whole period</td>
<td>Epirenamin Chloride (liquid) 3.3 - 4.5 cc 14 days of treatment</td>
</tr>
</tbody>
</table>

Remarks:
When there is no synthetic malaria drug for injection, make an injection into the muscle of quinine injection liquid or add 25% of the above to 20 cc of dextrose and very slowly make an injection intravenously. According to the symptoms and bodily constitution, do this once or twice. When no results can be quickly discerned from Navy A P E method, make use at the same time of quinine injection.

D. PARASITOLOGY

The work done in Japan on parasitology, with the exception of that pertaining to malaria, has apparently been outside the Naval Medical Corps. It was repeatedly reported by clinicians that the Navy had no problem with parasitic infection, and that save for a few cases of pin and round-worm infestation, naval personnel had no parasitic disease. The findings in hospital patients returned from over-seas, including the South Pacific, were negative for such pathology. The problem of filariasis was non-existent or unrecognized, and no concern was expressed over the possibility of the introduction of parasitic disease into the homeland, as it was felt the numbers of such patients would be negligible.

Hence, no new treatments had been developed, no new drugs produced, and no research undertaken in this field. Other investigating committees, (see reference D) have made allusion to evidences of some activity in this field, chiefly by Japanese civilian agencies.
ENCLOSURE (A)

CHEMICAL FORMULAE OF "KOHA" AND "SHIKO"

Both "Koha" ("rainbow wave") and "Shiko" ("violet light") are sensitive coloring matter, neocyanine, the former being a derivative of lepidine methiodide and the latter of 2,4-dimethylthiazole methiodide. The reason for giving both these compounds names relating to light is that the first idea for applying these chemicals on a living body was to use the energy of light in obtaining therapeutic effect.

Chemical Formulae - Chemical formulae for these compounds have not been proved decisively. To use Hamer's neocyanine formula (F. M. Hamer: J. Chem. Soc., London, 1928, 1472-3) they can be represented as follows:

KOHA (Formula A) - 1,1,1'-triethyl-10-lepidyl-4,4'-trimethine-quinocyanine-1,1'-diiodide.

SHIKO (Formula B) - 3,3',3'',4,4',4''-hexamethyl-7(2''-methyl-thiazolyl)-2,2'-trimethinethiazolocyanine-3,3''-diiodide.

\[
\text{(A)}
\]

\[
\text{(B)}
\]
ENCLOSURE (A), continued

From analysis values and synthetic processes, other formulae are possible, but they also lack positive proof. The following formulae (II and III) represent some of the possibilities with Hamer's formula (I) drawn schematically.
Properties - "Koha" is copper colored crystals with metallic lustre, is almost insoluble to most solvents but when dissolved, the solution is green. The decomposition point is not sharp and wavers between 275-281°C according to the way of heating. The picrate is copper colored prisms melting at 274-6°C.

"Shiko" contains needle crystals of bluish-violet color and its solubility in water, alcohol, etc., is much greater than that of "Koha". The decomposition point is 283°C.

Synthesis - Lepidine methiodide, 2,4-dimethylthiazole methiodide and ethyl-orthoformate are heated and condensed under the presence of organic bases, such as pyridine, or organic acids. Other cyanine pigments that formulate at the same time are removed by way of repeated recrystallization and refined.

Characteristics - The structural characteristics of these neo-cyanine dyestuffs is that the oxidoreduction system of the aromatic heterocyclic ring is bound inside the molecule by conjugated double bond. That is, instead of having separate molecules of oxidizing and reducing systems, as in codehydrase, these are bound by a conjugated system inside the same molecule. This point may have some meaning physiologically.

About 300 such dyestuffs with chemical structure as in "Koha" were synthesized, and those that were examined most biologically were "Koha No. 1" and "Shiko No. 12".
ENCLOSURE (B)

OUTLINE OF THE RESULTS ON THE STUDY OF "KOHA"
IN THE SURGICAL FIELD

The results of the treatment herein explained were obtained by giving "Koha" per os or intravenously, in addition to local and general treatment. (Sulfamin preparation, penicillin, etc., were not used).

1. Wounds

Twenty-five cases of hard-healing unspecific ulcer: Studies on the healing curves, mostly on ulcer of the leg, show that 11 cases in which "Koha No. 1" was used per os progressed favourably, with curves descending in a straighter line than before taking the preparation, and with marked improvement in the healing index.

"Koha" used as a local dressing is not effective. 0.25 - 1.0 milligrams per os is the suitable dose. An experimental skin wound was made on the back of a rabbit, and surveys were made from time to time during the epithelization process. From this we came to know that the degree of expansion of the epithelization when taking "Koha No. 1" per os was the most effective. The histologic variation of the wound of the animal appears three days after the start of the experiment; in cases that have taken "Koha No. 1" per os the production of the young tissue cells and fibers is very obvious. Six days later the new forming of capillaries can also be clearly seen. Nine days later the same case shows the third layer of the skin clearly. The pathologic histologic variation of the ulcer of the leg on the human being is that the production of connective tissues and fibers is not so obvious as in the animal experiments, but the new forming of capillaries can clearly be seen, and instead of leukocytes, plasma cells can be seen.

2. Acute Suppurative Surgical Diseases

By using "Koha No. 1" (0.25-1.0 milligrams per day per os or intravenously), the suppurative process was clearly localized.

(a) In nine cases of carbuncle, "Koha No. 1" taken per os localized the inflammation in two to seven days.

(b) In eight cases of erysipelas, fever was removed in two to three days and cured in five to ten days. In these cases results were similar to those of sulfamid preparations.

(c) In 11 cases of surgical pyemia, one case of pneumococcus died, and eight cases of staphylococcus, one case of streptococcus haemolyticus were cured.

The effect of "Koha" in pyemia is not as prompt as penicillin, but works gradually.

In an experiment to study the effect of "Koha No. 1" and "No. 12" on phagocytose, 0.2 milligram per day per os were used for five days, on eight healthy boys. Phagocytose was studied before and after the experiment, and it was noted that phagocytose was very active against staphylococcus aureus, streptococcus haemolyticus, and pyococcus for three to nine days after administration of the preparation, but against streptococcus viridans, pneumococcus (III Type), and collicommons it is less active.

In three cases of surgical pyemia, phagocytose has become active after taking "Koha" per os.
3. Combustion

In 25 cases observed carefully, 0.25 - 1.0 milligrams "Koha No. 1" was given per os or intravenously, with the following results:

(a) Progress of epithelization is prompted.
(b) The contraction of the skin is mild (Sores treated by "Koha" are thin).
(c) Bacterial infection is slight.
(d) Demarcation comes earlier.
(e) A skin transplantation operation can be made earlier.

(For local dressings, only wet dressings of 1-2% boric acid or physiologic solutions were used.)

Next are the results of treatment with "Koha" on third-degree combustion on the skin of the back of a rabbit made by placing a red-hot iron plate five centimeters in diameter on the skin for seven seconds:

(a) The granulation of the wound treated with "Koha No. 1" and "No. 12" (0.1 milligrams per day per os) is generally better than the untreated. "Koha No. 1" per os gave especially good results.

(b) Ten days after the burn, microscopic inspection of the subcutaneous tissues of the spot of the burn shows that in cases treated by "Koha" new formation of capillaries and connective tissues is much more active, and dropy and cell infiltration relatively lighter than in the untreated cases.

4. Paralysis of the Peripheral Nerves

In eight cases treated with "Koha No. 1" or "No. 12" (0.1 - 0.25 milligrams per day per os) two cases not caused by accident were treated within two weeks after the peripheral nerves were paralyzed and were cured in a month without any other treatment. The six cases caused by accident were treated within three weeks of injury, not all were cured, but the paralysis was lightened.

In experiments performed on dogs, after amputation of the nerves ischiadicus of 10 days at the height of the thigh, nerve connecting operations were made. After treatment with 0.01 - 0.5 milligrams "Koha No. 1", and 0.01 - 0.1 milligrams "Koha No. 12", per os for a certain period of time, studies were made on how the dog walked and microscopic variations of the operated nerve. An ulcer formed on the back of the foot of the untreated control dog about nine days after the operation; but the treated dog did not form an ulcer so easily.

The untreated dog's muscle atrophy became quite obvious 14 days after the operation, but in the case of the treated it was rather light.

Even after 110 days the untreated dog walked on the back of the foot, but the treated, especially the dog treated with "Koha No. 1", walked mostly on the footsole after 46 days (in each case the sense of pain seemed not to return).

There was no outstanding variation in pathologic histology of the operated nerve, but 34 days after the amputation a secondary degeneration (Waller's degeneration) and cell infiltration could be seen quite clearly. On the contrary, those treated with "Koha No. 1" (0.25 milligrams per day per os) showed
only a light Waller's degeneration 36 days after the amputation. Cell infiltration is also light.

5. Lymphadenitis Tuberculosa

Of 159 cases of tuberculosis lymphadenitis treated with "Koha" 69 cases (43.4%) were cured; 56 cases (35.2%) improved; 34 cases (21.4%) remained unchanged.

"Koha" is effective on the early, the hard and the ulcer types of tuberculous lymphadenitis, but less effective on the abscess type.

This treatment shows results as satisfactory as the X-ray treatment for tuberculous lymphadenitis, and the treatment is much simpler.

Method of the Treatment:

Dose: "Koha No. 1", 0.01 mg. per day or every two or three days per os. Special care should be taken in using this preparation when the condition of the patient is serious, especially in the case of active tuberculosis of the lung.

6. Congelation

Two-hundred and twenty-six grammar school pupils with frost bite were divided into two groups, the first group treated with "Koha No. 1", the second group with "Koha No. 12". The results obtained after 18 days observation showed that "Koha No. 12", used 0.01 milligrams per day per os, was the better. Of the 51 cases treated with "Koha No. 12", 26 cases were cured; 20 were improved; three were unchanged, and two became worse.

Of 456 frostbitten factory workers treated with "Koha No. 12", 0.01 - 0.03 mgr. per day per os, 74% were cured or improved. "Koha" can be used for frostbite, but cannot prevent it.
ENCLOSURE (C)

SYNTHETIC PROCESS FOR "SHIKO"

1. Thioacetamide

Process - 20gms (5 moles) of acetamide, 15gms powdered phosphorus pentasulphide (1 mole) and 100cc benzene are boiled for 20 to 30 minutes, filtered while hot, and left to cool when the crystals precipitate. The insoluble substances are digested with benzene three times more, benzene solution condensed and left to cool when more crystals are precipitated. These rhombo-prism crystals are filtered. Yield is 8gms (30% of theory) of crystals melting at 107-8°C.

2. 2,4-Dimethylthiazole


Process - To the mixture of 16cc chloraceton and 20cc water are added 15gms of thioacetamide in small portions, heated for one hour at 75°, one hour at 100°, and then left to cool. To this is added about 50cc 5% hydrochloric acid and the insoluble oil is removed by ether. The aqueous layer is alkalinified with sodium hydroxide; the base that separates is extracted with ether, dried with potassium hydroxide, the solvent distilled off, and the residue distilled under reduced pressure. Yield is 10gms (46% of theory) of distillate boiling out at 78-81°C. The picrate melts at 138°C.

3. 2,4-Dimethylthiazole Methiodide

Process - 10gms 2,4-dimethylthiazole and 13gms methyliodide are sealed in a tube, heated for three hours at 90°, the content washed out with acetone and recrystallized from acetone. Yield is 20gms (89% of theory) of crystals melting at 225° (decomp.)

4. 2,3',2'',4',4''-Hexamethyl-7(-2''-Methylthiazolyl)-Trimethine-Thiazolocyamine-3,3''-diiodide


Process - 1.04gms 2,4-dimethylthiazole methiodide, 1.6cc orthoformic ethyl ester and 0.64cc acetic anhydride are heated for 30 minutes at 165°C under agitation. After the content has cooled, it is washed out with ether and then with water until the water acquires bluish-purple tint. This is recrystallized from methanol to greenish-purple fine needle crystals melting at 283° (decomp.). Yield 0.37gms (42% of theory).

PROPERTIES OF "SHIKO"

"Shiko" is formed in greenish-purple fine needle crystals. decomposition point is 283°C, and more constant than that of "K-ha". The solubility is also comparatively greater, so it can be recrystallized from water.

Absorption maximum: 5955 Å (O₂H₂O)H
Sensitivity maximum: 6400 Å
ENCLOSURE (D)

SYNTHETIC PROCESS FOR "KOHA"

1. Acetoacetic Acid Anilide


Process - In a four-necked flask provided with stirrer, thermometer, cooler and separatory funnel, 156gms (1.2 moles) acetoacetic ester, 250cc commercial xylene, and three drops pyridine are put. From the funnel a solution containing 93gms (1 mole) aniline, 250cc xylene and three drops pyridine\(^1\) is added in drops while keeping the content of the flask at 135\(^0\)C and stirring all the time, the whole process taking about two hours. Alcohol formed in the process is distilled out through the cooler. After the aniline addition is complete, the flask is heated for two hours at 135\(^0\)C. The light reddish-yellow content is left to cool; crystals thus precipitated are filtered and washed with a small amount of xylene. Yield 111gms\(^3\) of crystals melting at 82\(^0\)C\(^4\) (63% against aniline, 52% against acetoacetic ester).

2. 2-Oxylepideine


Process - 50gms Acetoacetic anilide (dried at 50\(^0\)C in vacuum) is added gradually in concentrated sulphuric acid (d 1.84), kept at 90-95\(^0\)C and completely dissolved. Heat generates at this stage, so temperature control is necessary. After heating for 30 minutes, the content is cooled to about 60\(^0\)C, poured in 3 l. of water and the precipitate is filtered off. The filtered precipitate is washed with water, dried at about 50\(^0\)C, and recrystallized from alcohol. Yield is 41gms (91% of theory) of crystals melting at 218-220\(^0\)C. When recrystallized, the melting point becomes 221\(^0\)C.

3. 2-Chlorolepideine

Bibliography - Knorr, Annalen, 236, 97.

Process - 12gms oxylepine, 18gms phosphorus pentachloride and 8cc phosphorus oxychloride are refluxed at 90 to 100\(^0\)C in a flask provided with reflux condenser and calcium chloride tube. When the generation of hydrochloric acid gas has terminated, the content is cooled, decomposed by about 100cc of water, neutralized with sodium hydroxide, and the crystals that precipitate are filtered off. The crystals are washed with water, dissolved in ether, dried with sodium sulphate, and distilled under reduced pressure. Yield is 13gms (97.5% of theory) of distillate boiling out at 164\(^0\)C, melting point 59\(^0\)C.

The original report provides for steam distillation after neutralizing with sodium hydroxide. This method would be suitable for a large amount.

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\(^1\) Yield drops if pyridine is not added.

\(^2\) Yield drops either above or below this temperature.

\(^3\) Yield in the original report is given as 85-88% against aniline.

\(^4\) Bibliography gives the melting point as 85\(^0\)C. Those melting at 82\(^0\)C will do for the next process.

\(^5\) Above 90-95\(^0\)C, bubbling becomes vigorous and the yield drops.
If this material dissolved in 10% HC\textsubscript{1} and shaken with ether, the resinous matter will dissolve in ether, and when the hydrochloric solution is diluted with water, white needle crystals will precipitate. Melting point is 59°. This can be carried on to the next process as it is.

4. Lepidine

**Process:**

a. 30cc 1% solution of \textsubscript{2}CH\textsubscript{2}, 0.5gms activated charcoal and 3cc 10% hydrochloric acid are shaken in hydrogen stream and saturated. To this 0.1gms of alcohoholic solution of 42gms 2-chlorolepidine and catalytically reduced in hydrogen stream. About 53000cc hydrogen is absorbed and saturated. The catalyst is removed by filtration, alcohol distilled off from the filtrate and alkanified with sodium hydroxide. The base that precipitates is extracted with ether, dried with potassium hydroxide, ether distilled, and the residue distilled under reduced pressure. 3gms of lepidine (99% of theory\textsuperscript{6} boiling out at 130-130° are obtained. The piorate melts at 108-110°C.

b. 47gms 2-chlorolepidine, 90cc of a mixed solution of 38% hydrochloric acid and water in 1:5-2 proportion, and 4.5gms tin sponge are mixed together and heated for six hours at 70-80°. After cooling, a double salt, melting at 135°, is precipitated, filtered, decomposed with sodium hydroxide, and extracted with ether. Three grams raw lepidine are obtained; it is distilled at reduced pressure, and 2.5gms (about 66% of theory) of lepidine boiling out at 128-130° are obtained.

5. Lepidine Iodoethylate

**Process** - 10gms lepidine and 25gms ethyl iodide are sealed in a tube and heated for three hours in a water bath kept at the boiling point. The yellow crystals thus precipitated are washed out with acetone, the acetone distilled off and recrystallized from alcohol. 18gms (86% of theory) of crystals melting at 139-140° are obtained.

6. 1,1',1''-Triethyl-10-Lepidyl-4,4'-Trimethinequinocyanine-1,1'-Diiodide


**Process** - 3gms lepidine ethiodide and 2cc acetic anhydride are put in a distillation flask and immersed in a glycerine bath (kept at 115-150°) so as to bring the surface of the content and the bath in a line, and under stirring, 3gms (3.0cc) orthoformic ethyl ester are added in five minutes and heated, while stirring constantly, for 15-20 minutes at the same temperature. Then the flask is immersed deeper in the bath for about five minutes or until the distillate reaches about 450°. The content is then washed out with alcohol and 1.5 to 1.6gms copper-red crystals are obtained. This is recrystallized from 2 l. of alcohol\textsuperscript{7} and 0.8gms of crystals melting at 287° (decomp.) is obtained.

\textsuperscript{6} 45.5% against acetoacetic ester.

\textsuperscript{7} This substance is slightly soluble in alcohol. When processing in large quantity, it should be dissolved in aniline in high concentration, precipitated with benzene, and the crystals washed with ether. For example, 100gms of crystals can be dissolved in 7000cc aniline, 4000cc benzene added and precipitated.
PROPERTIES OF "KOHA"

Decomposition Point - Decomposition point varies according to manner of heating, being generally in the range of 275-281°C. When the crystals are put in the bath at 220-225°C, heated to 270°C in about four minutes, and then brought gradually towards the decomposition point, the decomposition is lowered to 271-2°C.

Crystals - "Kohä" crystals are copper-colored powder that dissolves in alcohol to give green solution. It dissolves very slightly in benzene, forming a colorless solution. It is colorless in acidic solution, but turns green on being alkalized.

Absorption maximum: 7750 Å, 6337 Å, 4400 Å, 4050 Å, 3100 Å.

Derivatives

Hydrochloride: Copper colored fine needle crystals, Fp 263°C (decomp.).
Picrate: Copper colored fine prisms, Fp 224°C (decomp.).
Styphnate: Copper colored needles, Fp 216°C (decomp.).
Picroclonate: Copper colored prisms, Fp 205°C (decomp.).
ENCLOSURE (E)

SURVEY OF TAKEDA YAKUHIN KOGYO K. K., MANUFACTURERS OF PHARMACEUTICALS,
27 DOSHO MACHI, OSAKA, JAPAN

PART I

General Information

1. The primary functions of the Takeda Company, Ltd., were:
   a. The manufacture of civilian pharmaceuticals.
   b. The manufacture of industrial chemicals.

2. The company had no direct affiliation with the Imperial Japanese Navy.
   a. The Navy sent a request to the Ryohinsho at TOKYO. The Ryohinsho in turn sent a request to the firm. The firm made an estimate and, if approved, received a contract. (Note: The Ryohinsho was the central Navy drug supply depot.)
   b. See Part III for list of drugs supplied to the Navy by Takeda.

3. No biologicals of any nature were manufactured.

4. Catalogues
   a. "Takeda's New Drug Catalogue" (Dec. 1943)
      (1) In Japanese.
      (2) Contains the chemical formula of each medicine.
      (3) Latest issue available.
   b. "Compendium of Pharmaceutical Specialities" (no date)
      (1) In English.
      (2) Advertising organ - no formulae given.
   c. "Compendium of New Drugs" (1938)
      (1) Same as "b", except in Japanese.
   d. There was no special Navy catalogue at any time.

5. New Drugs or Previously Unheard of Drugs
   a. "Apellagrin" - Vitamin P.
   b. "Abotest" for testing blood types.

PART II

Inspection and Reports of the Research Laboratory Attached to Takeda Co.
No. 24 Suso Mishino-Gcho 4-Chome, Higashiyodogawaku, OSAKA
Mr. KUBOTA, Director of Takeda, as Guide

1. The research laboratory is a modern building of three stories and given entirely to research on all phases of medicine. It was, however, almost entirely made up of dark, poorly-ventilated laboratories staffed by young college graduates.
ENCLOSURE (B), continued

2. Special Research Ordered by the Navy Through the Ryohinsho
   a. Sedative - Similar to "Eviapen".

   \[
   \begin{array}{c}
   \text{CH}_2\text{-CH} \quad \text{C} - \text{C} \quad \text{CO-N-C}_3 \\
   \text{CH}_2\text{-CH} \quad \text{CO-NH} \quad \text{C}_2\text{H}_5
   \end{array}
   \]

   (1) Formula:

   (2) Approved June, 1945.

   b. Non-Crystalizing Sulfa - "Pannidin".

   \[
   \begin{array}{c}
   \text{NH}_2 \quad \text{SO}_2\text{-NH} \quad \text{C}-\text{CH} \\
   \text{N} - \text{C}-\text{CH} \quad \text{N} \quad \text{CH}_2
   \end{array}
   \]

   (1) Formula:

   (2) One approved sample - not yet produced on commercial scale.

   c. Advice on Special Herbs to Be Grown by Navy Personnel on Isolated Islands.

   Plants were being used, as food and medicine, at such places as SAIPAN, RABAUL, etc.

3. Miscellaneous Notes

   a. The Takeda Company has a branch office at TOKYO: Takeda Yakuhin Kogyo K. K. Tokyo Branch, Dai San Kokubu Bldg. (4th floor), Gofukubashi, Nihonbashiku.

   b. Biologicals are manufactured at the following places in OSAKA:

   (1) Bussei Butsu Kenkyujo - Osaka Imperial University Medical School.
   (2) Kessei Yakuhin, Osaka.
   (3) Osaka Saikin Kenkyujo.

PART III

Articles Delivered to the Navy By the Takeda Company

The sales value in aggregate is as follows:

¥3,300,000 (from April, 1944 to March, 1945)
¥1,530,000 (from April, 1945 to August 15, 1945)

The articles listed are those delivered to the Navy from April 1944 to August 1945. All the books and contracts were destroyed by air-raids; therefore quantities are not indicated. The articles marked with asterisks are the important items delivered.

Acriflavin powder  Biofermin
Acriflavin injection  Borragnol suppositories
*Acrinol powder  Bromvalerylurea
Acrinol injection  *Castor oil
Alsolin  Chinonjodin
Aminopyrin  Cruculon liquid
Amolisin  *Cruculon tablets
Barbital  Erstsin
ENCLOSURE (E), continued

Euvestin tablets
Gelatin injection
Glacial acetic Acid
Glucose
Igrosin
Malphanyl
Melysin
Migrainin
Neo evanin powder
*Neo evanin liquid
Normosan
Periphermin
Polytamin liquid
Quinine ethylcarbonate
Quinine hydrochloride tablets
*Quinine injection
Quinine sulfate
*Quinine sulfate tablets
Rodealin liquid
Rodealin injection
*Sodium bicarbonate
Sodium salicylate
*Synthetic antimalarial A
(Chinobrin tablets)
*Synthetic antimalarial B
(Tropoquin tannate tablets)
Ubanin
*Vitacampher
*Vitamin B₁
Vitamin B₁ injection
Vitamin B₁ tablets
Vitamin C
Vitamin C injection
*Vitamins B₁ & C tablets
Vitamin P injection
Vitamin K injection

PART IV
Reports on Researches
(Translations)

NAME OF LABORATORY:
Research Laboratory Attached to Takeda Pharmaceutical Industries, Ltd.

LOCATION:
No. 54, Juso Nishino-Cho 4-Chome, Higashi-Yodogawaku, OSAKA.

A.

1. SUBJECT: Study of the Manufacture of Vitamin B₁.

2. EXPERTS IN CHARGE: Sajuro KURODA, Keinosuke TARUI, Chiyoko KIMURA.

3. STATE OF RESEARCH: Studying the combination of 2-methyl-4-amino-5- bromomethyl-pyrimidine-hydrobromide with 4-methyl-5-oxethyl-thiazole, the last step in the manufacture of vitamin B₁ preparation.

4. REMARKS: None.

B.

1. SUBJECT: Study of Ergotalkaloids.

2. EXPERTS IN CHARGE: Yoshio SASAGAWA, Takiko YAMAMOTO

3. STATE OF RESEARCH:
   a. Research for the products made by the partial catalytic reduction of agroclavine.
   b. Manufacture of lysergic acid preparation.

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c. Research for literature of oxydation of agroclavin records and study of separation of a-picolin from the picolin mixtures.

4. REMARKS: None.

C.

1. SUBJECT: Extraction of emetin from leaves of ipecacuanha.

2. EXPERTS IN CHARGE: Shizuo YOSHIKI, Hiroshi HITOMI, Yasushi MIKI, Haeko NAKAMURA.

3. STATE OF RESEARCH: For the extraction of emetin from leaves of ipecacuanha, we make the leaves into powder and wet the powder with tartaric solutions, then take off the chorophyll from the material with benzol and make the extractions of benzol on the condition of ammonia wet in room temperature.

We get the hydrobromic salts of emetin from the solution of extraction. But the product is not satisfactory, and barely equal to 0.07 percent of raw material.

4. REMARKS: None.

D.

1. SUBJECT: Research for effective component of "Hange".

2. EXPERTS IN CHARGE: Shizuo YOSHIKI, Hiroshi HITOMI, Yasushi MIKI, Yaeko NAKAMURA.

3. STATE OF RESEARCH: Studies on the components of "Hange", have been very few and are in a report by Hichitaro NAKAYAMA (1924 A.D.) only.

He finds palmitic acid, glycerine and iso-oleic acid from ether extract of "Hange" and also the substance of alkaloid from the alcohol extract, and gets the same carbon-hydroxide from its aqua extract. Re ashes, he only had found the silicates which were not soluble in hydrochloride, magnesium and calcium.

Then we have been proceeding with the research accordingly, on inorganic substance, slycose and starch to study the effective component of "Hange".

4. REMARKS: None.

E.

1. SUBJECT: Study of Penicillin.

2. EXPERTS IN CHARGE: Minoru KAWASHIMA, Jiro ESAKI, Hisako TAKEDA.

3. STATE OF RESEARCH: We have been making efforts to recover the potentiality of decreased culture fluid of penicillin and also attempting separation of its ca-salts.

4. REMARKS: None.
ENCLOSURE (E), continued

F.

1. SUBJECT: Research for absorption and elution of alkaloids with various kinds of Japanese acid earth.

2. EXPERTS IN CHARGE: Taunaharu KUSAKA, Kiyoji MATSUURA, Takako NAGAOKA, Kazuo KONDO.

3. STATE OF RESEARCH: We have performed elution and determination of lycorin in absorbed material of alkaloid which is obtained from Lycors radiata by Japanese acid earth.

4. REMARKS: None.

G.

1. SUBJECT: Study of absorbing power of Japanese acid earth.

2. EXPERTS IN CHARGE: Jusaburo ISHIKAWA, Kikuko OKAMOTO.

3. STATE OF RESEARCH:
   a. Relation between volume and time in alkaloid absorption by Japanese acid earth.

      We have examined the ratio between volume and time in absorption experiments in alkaloid solution through the medium of Japanese acid earth, activated earth, etc.


      We have made experiments to examine the relation between temperature and volume in absorption.

4. REMARKS: None.

H.

1. SUBJECT: Research in manufacture of anthelmintics.

2. EXPERTS IN CHARGE: Chuji HARUKAWA, Toru MASUDA, Yasuo NAKAGAWA, Hisashi ISHIKAWA.

3. STATE OF RESEARCH:
   a. We are making sulfuric ester salts of various carbohydrates.

   b. We continue the study of synthesis of santonin derivatives and 3-nitrotetralin as the raw material.

4. REMARKS: None.

I.

1. SUBJECT: Study of Synthetic Vitamin B1 and its Homologs.

2. EXPERTS IN CHARGE: Osamu TANI, Yoshiko MORITA.
ENCLOSURE (E), continued

3. STATE OF RESEARCH: We are studying a new method of Vitamin B₁ synthesis. At first we prepared 4-methyl-5-6-oxyethyl-thiazol by a different method from the previous report, but could not obtain the substance. We obtained an unknown crystal. There is also the method that prepares the nitroamino-compound by the nitration of 2-amino-compound, reduces it to hydrazin-compound and decomposes it by copper-sulphate or another reagent to thiazol-compound, which has not the substitution radical at the Z-position. Previously we tried this method about 2-amino-4-methyl-5-carbethoxy-thiazol, but the nitroamino-compound has not been obtained.

4. REMARKS: None.

J.

1. SUBJECT: Study of synthetic vitacamphor.

2. EXPERTS IN CHARGE: Sueo TATSUOKA, Jisaburo UEYANAGI, Akira MORIMOTO, Masuo MIYAMOTO, Mitsuko NISHIMURA, Shiu RIN, Kaneko SONE.

3. STATE OF RESEARCH:
   a. When we studied the synthesis of \(-\)trans-oxo-camphor we tried to separate the pure components from camferol to get the standard preparation of \(-\)oxycamphor.
   b. Synthesis of \(-\)trans-oxo-camphor by chlorine-method: \(-\)a-chloro-camphor was prepared by chlorination of camphor.
   c. Synthesis of \(-\)trans-oxo-camphor by bromine-method: \(-\)a-bromo-camphor was prepared by bromination of camphor.

4. REMARKS: None.

K.

1. SUBJECT: Biological Study on the Antiemetic Action of the Sedative, which Contain Rhizoma Pinellial and Fellen.

2. EXPERTS IN CHARGE: Ichiro ISHIKAWA.

3. STATE OF RESEARCH: With dogs we observed antiemetic action of the sedative, which contains rhizoma pinellial and fellen. Our experiments have been so few that we cannot confirm the antiemetic action as satisfactory, but the test is being carried on.

4. REMARKS: None.

L.

1. SUBJECT: Researches for the urgent manufacture of various medical preparations from drugs.

2. EXPERTS IN CHARGE: Susumu KAMEOKA, Takeshi WATANABE, Shunka SHIA.
ENCLOSURE (E), continued

3. STATE OF RESEARCH: Using drugs which grow or will probably cultivated in future in our land, we are attempting to replenish the stock of compounded preparations and to manufacture our own remedies, by making pharmaceuticals from the familiar Sino-Japanese drugs of olden times. As the first subject we have completed the experimental manufacture of cataplasm, haemostatic, medicines for fatigue, antifebric, diuretic, antidiarrhoeic, stomachic, antiemetic, ointment, medicine for gynaecological use, and ointment for skin diseases.

4. REMARKS: None.
# INVENTORY OF DRUGS - YOKOSUKA NAVAL MEDICAL SUPPLY DEPOT

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<th>Unit</th>
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### Name of Drug | Unit | Quantity | Name of Drug | Unit | Quantity
--- | --- | --- | --- | --- | ---
Extractatum Secalii cornuti | grams | 100 | sterilsatius | piece | 700
Postilii Vitamin B1 | piece | 80,000 | Sterilized salt water | piece | 2,015
Emplastrum saponatum salicylatum | piece | 32 | Oleum Jodatum | piece | 300
Injection of Multin | piece | 450 | Injection made with the stop eluding medicine for vessels | piece | 2,600
Injection of Salsoliate | piece | 520 | Strychninum nitricum | piece | 11,030
Injection of Digitabis | piece | 1,000 | Sticknin | piece | 3,965
Injection of sugar | piece | 146 | Strophanthinum | piece | 3,700
Thick solution of salt | piece | 15 | Injection of gelatine | piece | 330
Injection of Nupercaine | piece | 1,330 | Injection of Minglin | piece | 70
Favonol | piece | 1,500 | No. 1 roll of bandages | piece | 2,686
Atropine | piece | 4,000 | Medical papers | sheet | 17,000
Papaverin atropine | piece | 230 | Printing papers for X-rays | doz. | 340
Examining liquor for Syphilis | piece | 36,800 | Liquid measurer | piece | 3
Injection of Vitamin B1 | piece | 554 | Package for emergency medicine | piece | 26
Injection of Hormone | piece | 153 | Ovoviglass | piece | 500
Injection of Ringersloke | piece | 950 | Gauze | roll | 2,260
Injection of Lumitropine | piece | 200 | Small roll of gauze | piece | 532
Injection of Lobeline | piece | 5,700 | Mosquito stick | piece | 716
Injection of Vitamin C | piece | 29,500 | Dry cell | piece | 510
Sulphanilamide | piece | 189 | Ophthalmic bandage | piece | 70
Secoramine | piece | 2,140 | Small roll of absorbent cotton | piece | 35
String | piece | 301 | Intestinal string | piece | 6,970
Silk thread | bundle | 12,000 | Pipe of Injector | piece | 9,742
Binder twine | bundle | 642 | Fine of Injector | piece | 15,844
Flask | piece | 21 | Eye Cup | piece | 25
Beaker | piece | 2 | Soap | piece | 25
Case for Flasters | piece | 39 | Eyewash bottle | piece | 26
Medical papers | bundle | 100 | Eye-washer | piece | 10
No. 3 Roll of bandage | piece | 50 | No. 2 roll of bandages | piece | 35
Sharley | piece | 160 | Sticking plaster | roll | 230
Three cornered bandage | sheet | 660 | Ice bag | piece | 120
Absorbent cotton | package | 383 | Bosom-warmer | piece | 10
Brush | piece | 2 | Enema-syringe | piece | 7
No. 3 Roll of bandage | piece | 383 | Metal spoon | piece | 1,000
Absorbent cotton | piece | 2 | Sterilizer for apparatus | piece | 4
Kettle | piece | 10 | Blood sink meter | piece | 6
Rubber blower | piece | 1 | Oxygen inhaler | piece | 4
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<td>Mirror for examining nose</td>
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ENCLOSURE (G)

LIST OF DOCUMENTS FORWARDED TO NMRI, BETHESDA, MD.

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<td>ND-10-7501.3 (M12)</td>
<td>11 July 1945, Medical Affairs II Annex #1, &quot;Prevention of Malaria through Internal Medicine&quot;</td>
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ENCLOSURE (H)

LIST OF DRUGS AND PHARMACEUTICALS FORWARDED TO NMRI, BETHESDA, MD.

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ENCLOSURE (1)

LIST OF DOCUMENTS FORWARDED TO WASHINGTON DOCUMENT CENTER THROUGH ATIS

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<td>Catalogue of New Drugs for 1938</td>
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ENCLOSURE (J)

TRANSLATION OF JAPANESE MEDICAL DOCUMENTS

No. 2 - On the New Method of Malaria Treatment (T. SUGITA, M. TAGUCHI, H. MURATA).

Object: Chronic malaria shows a high rate of relapse when treated by the usual medical methods. We attempted to reduce the rate.

Results: By the usual medical treatment with provocative method of injecting Epirenamin-HCl every day or every other day we obtained the following good results:

<table>
<thead>
<tr>
<th></th>
<th>Usual Treatment</th>
<th>Our Treatment</th>
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<tbody>
<tr>
<td>Clinical relapse rate</td>
<td>25-36.4%</td>
<td>5.9-0%</td>
</tr>
<tr>
<td>Protozoan relapse rate</td>
<td>72.7-100%</td>
<td>17.6-0%</td>
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</table>

No. 3 - On the Studies of New Methods for Prevention and Treatments of Conge-
lation. (Y. NAKAUCHI, S. YOKOBARI, G. SASSA).

Results:

1. The subcutaneous injection of the 1% 2-benzylimidazoline hydro-
chloride 1-2cc is effectual for incipient congestion.

2. The internal use of 2-benzylimidazoline dionolate 0.075gms
three times a day has the same effect.

No. 4 - On the Study of the Prophylactic Vaccine of Dengue Fever.

Results:

1. The prevention of dengue fever was not achieved without weaken-
ed virulent virus.

2. The urtrutone-wave method was used to weaken the virus.

No. 6 - On the Prevention of Malaria (M. SASSA).

Result: We conclude that since it is very difficult to eliminate mosqui-
tos completely, it is better to subject patients to mass examination,
such as blood tests and liver and spleen measurements.

No. 7 - On the Biological Examination of Medicine for Cure and Prevention of
Malaria (I. MIYAO, M. SASSA, H. ROSOYA).

Results:

1. Experiment on bactericide against sickle-form and extra-red-
form - We injected the breast emulsion of sick Hitossiji-shimaka
(in JAPAN) into young, healthy, domestic fowl, treated these fowl
for 4-5 days, and observed the growth of plasmodiae and extra-red
plasmodiae in blood and brain capillaries. This method is excellent
for determining medical effect.

2. Experiment on bactericide against reproduction form - Fowls in-
fected by plasmodiae were injected with test chemicals. After 15
minutes the blood of these animals was sucked by healthy mosquitoes;
the mosquitos were dissected after seven days, and fallicle production was observed in stomach wall. This method is considered excellent.

No. 8 - On the Immunological Simple Method of Cholera Diagnosis. (K. Kariya, S. Azuma, H. Komatsu).

Results:

1. We can determine the pathogene and their type by the "factor serum" of cholera.

2. This method is easy to manipulate, so we can save about two-thirds of the time and materials.

3. By this method, it is easy to determine the bacterial type and to differentiate the resemblances.

4. This factor serum, frozen and dried in vacuum, is suitable for long-time reserve and for transport in tropic zones, unlike previous serums.

No. 10 - On the Mass Examination of Tuberculosis (N. Shindo, K. Watanabe, M. Ikeda, T. Yokoo, H. Murata, T. Mori).

Results:

1. In mass examination for tuberculosis the combination method of cultivation and indirect photography is necessary.

2. Family and individual recollection is a useful and easily accessible adjunct to examination.

3. Selection by the tuberculin-reaction missed 10.7% of the cases.

4. By one measurement of the red blood cell sinking only 45.7% were detected.

No. 11 - The Study on the Prophylactic Vaccination of Dengue-Fever.

Results: The author injected the virus into white rats, marmots, and incubated eggs, and prepared the vaccine. With this vaccine we obtained a constant result, but must continue attempts to improve its efficiency.


Results: The following method is adopted: Immerse the Gibbs in 1% warm Na-CO₃ solution in order to unfasten the bandage and put them in sea water for one or two days. Afterwards wash off the salt and boil in 10% NaHCO₃ or 20% Na₂CO₃ solvent for half an hour. After one day thoroughly wash and dry.

No. 14 B - Experiment on the Medicinal Value of the Trison (S. Ariga and M. Kashimura).
Object: The authors examined the medicinal value of the Trimon, oxyanthrilacid, which is described as excellent for accelerating the functions of the liver.

Results: Its effectiveness was found to be slight.

No. 14 C - On the Effect of Oxyanthrilacid in Failure of the Liver Function (Y. KAWAKUBO).

Results: Liver function is examined by measuring the azorubin-S excretion in the urine. Oxyanthrilacid (0.6mg per kg daily) is effective in the case of rabbits suffering from failure of liver-function owing to combustion from high-temperature thermite.


Object: Potency of the standard serum of the Japanese Navy deteriorated from preservation at high temperature and often could not be used in the tropics. We investigated the variation of potency of the standard serum originated by FUKAO and KOHINO.

Results: According to our investigations, power of standard serum to determine blood type, originated by FUKAO and KOHINO, was scarcely damaged by preservation for six months at a temperature of 37°C.

No. 15 - On the Preparation of Drinking Water from Sea Water (R. HAYASHI).

Results: By utilization of electric charge of synthetic resin "Orgacid" we absorbed ionen in sea-water and could prepare pure water. To prepare drinking-water half weight of Orgacid is needed.

No. 17 - Indirect Photography (S. YOKOKURA).

Size of Fluorescent Screen in Mass Health Examination.

In mass health examinations, 35mm standard film, 170cm long, is used, for the sake of speed and standardization, and in order that chests of all naval and military personnel can be photographed. Fluorescent screen 36x36cm is used, or 34x36cm screen with 24x25.5mm film.

(Note: The original translation, made by a Japanese, is unintelligible; but it is believed that the above text expresses the intended sense of the author.)

"Mittelform" Indirect Photography

In comparison of methods, it is considered that f2.0, focal distance eight and 10cm, 50x55mm mittelform indirect photograph is better than the f1.5, focal distance 5cm, using 35mm standard film; but in practice the exposure time is so much longer that we cannot say which is actually better in use.

Quantitative Difference of X-Ray in Langsbild

Object: The light of the fluorescent screen is different in each part, so the degree of blackness of each part of the film differs. The question is whether, considering the above factors, a diagnosis can be made.
Examination: Using Kustner's measuring apparatus, the quantity of light reaching the fluorescent screen is measurable.

Result: Center part is covered by the heart and the difference of using that part is so slight that it is possible by using the X-ray tube lengthwise.

No. 18 - On the Sterilizing Power of the test preparation "Positivion Soap" (S. Kawai).

Results: It was concluded that the effectual limit of this preparation is 0.005%.

No. 19 - On the Utilization of a Luminous Fungus (S. Kawai).

Results: The light emitted from the flat fungus with 10cm diameter cannot be recognized distinctly from 100m distance or more.

No. 20 A - On the Study of the Oil-Sprinkler (H. Hosoya).

Object: Design of oil-sprinklers for destruction of the mosquito larva.

Results: The author designed "watergunstyle" and "sprinkler with blower", which are very handy for use.

No. 20 B - Investigation on the Necessary Quantity of V-C (R. Hayashi).

The author measured the quantity of V-C excreted in the urine of 35 students, and at the same time measured the quantity in their food. The latter result indicated 57mg as an average. According to the standard, this dose is enough for Japanese laborers; but their excretive curve is equal almost to that of men deficient in V-C. The curve shows 4.6% deficient in V-C, 16.6% saturated.

No. 20 C - On the Effect of Acridine Coloring Matter (S. ARA).

Results:

1. The acridine disinfectants are less effectual in blood than in bouillon.

2. The most effectual disinfectants against several pathogenes in bloods are as follows: isarvin, panseptine and rivancol.

No. 20 D - On the Value of Human Urine as a Material of Bacillus Culture Fluid. (H. Sakurai).

Object: Investigation of the possibility of using human urine as a substitute for meat juice or meat extract in the preparation of bacillus culture fluid.

Results: Human urine is poorer than horseflesh or meat extract as a material of bacillus culture fluid; however, under the pressure of war conditions, we found that it could be used.

No. 21 - On the Manufacture of Metilen Blan (R. Hayashi, K. Takeda).

Results: The authors devised a method for producing relatively pure metilen blan, which can be used not only as a material for Agua I and II, but as a medicine after refining.
ENCLOSURE (K)

ILLUSTRATED DISEASE VECTORS

Figure (K)1
CHOLERA VIBRIO

Figure (K)2
TYPHUS RICKETTSIAE

Figure (K)3
DYSENTERY BACILLI

Figure (K)4
WHIP-WORM

Figure (K)5
WHIP-WORM

Figure (K)6
DYSENTERIC AMOEBA
ENCLOSURE (E), continued

Figure (E)7
SAND-FLY

Figure (E)8
KALA-AZAR

Figure (E)9
TROMBICULA AKANUSHI

Figure (E)10
RICKETTSIA ORIENTALIS
ENCLOSURE (K), continued

Figure (K)11
RECURRENT FEVER

Figure (K)12
TREPONEMA PALLIDA

Figure (K)13
LIFE CYCLE OF THE MALARIA PROTOZOA
Figure (El) 14
LIFE CYCLE OF THE MALARIAL MOSQUITO
Figure (K) 25
SHITUNERU'S METHOD OF MEASURING THE SPLEEN
ENCLOSURE (L)

HISTOLOGICAL COMPARISONS, SHOWING EFFECTS OF TREATMENT WITH "KOHA".

LEGEND

A - First Layer, Cellular Exudation.

B1 - Closed Cell Structure.

E - Severed Edge Of Healthy Epidermis.

K - New Capillaries.

M - Subcutaneous Muscular Cell Structure.

Nb - Some Closed Cell Structure and Fiber.

NE - New Epidermis.

P - Sudden Appearance Of Epidermis Papilla.

Zf - White Cell Saturation.
ENCLOSURE (L)

0.01 mg "Kohla" Mk 1 given internally.

No treatment.

0.1 mg "Kohla" Mk 12 given internally.

COMPARISON (L) 1
On Third Day
ENCLOSURE (L), continued

No treatment.

0.1 mg "Koha" No 1 given internally.

0.1 mg "Koha" No 12 given internally.

COMPARISON (L) 1 (continued)
On Sixth Day
ENCLOSURE (L), continued

0.02 mg "Koja" Me 1 given internally.

0.01 mg "Koja" Me 12 given internally.

COMPARISON (L): 1
(continued)
On Ninth Day

50
ENCLOSURE (L), continued

Comparation (L)a
Treatment: 0.01 mg "Zoha" No. 12

30 days after treatment.

Before treatment.
ENCLOSURE (L), continued

Before treatment.

COMPARISON (L)3
Treatment: 1.0 mg "Koha" Mk 1

10 days after treatment.
34th day after severance. Secondary, i.e. Waller's degeneration is comparatively clear. Round cells, though saturated, can be seen clearly.

56th day after severance. Traces of Waller's degeneration greatly diminished and only few saturated cells remain.

COMPARISON (L)4
Dog Pelvic Nerve
Treatment: 0.2 mg "Koha" Hg
1 given internally daily.
ENCLOSURE (M)

PHOTOGRAPHS SHOWING EFFECTS OF "KOHA" ON FIBULAR NERVES

Four days after outbreak and before treatment.

95 days after beginning treatment. Complete recovery.

CASE (M) 1
Neuro-Paralysis of Fibular Nerve
Age 27 - Male
Treatment: 0.1 mg "Koha"
Hr 1 given internally daily.
ENCLOSURE (H), continued

47 days after receiving wound.  
No treatment.

110 days after beginning treatment. Flexion of left foot impossible. No other abnormality.

CASE (N)2  
Aneurism From Knife Wound in the Thigh  
(Also Neuro-Paralysis in Left Fibula)  
Age 27 - Male  
Treatment: 0.1 mg "Koha"  
Mg 1 given internally daily.
ENCLOSURE (N)

PHOTOGRAPHS SHOWING EFFECTS OF TREATMENT OF BURN VICTIMS WITH "KOHA"

Before treatment.
Day after burn.

Same as above.

CASE (N) 1
Second Degree Burns From Boiling Water
Age 25 - Female
Treatement: 0.25 mg of "KoHa" Mk 1 given internally every day. Ichthyol applied locally.
ENCLOSURE (N), continued

After 15 days.
Full treatment.

Same as above.
CASE (W'1)
(continued)
ENCLOSURE (N), continued

CASE (N) 2
Second Degree Burns From Boiling Water
Age 2
Treatment: 0.1 mg "Koha" Nk 1 given internally daily. Ichthyl applied locally.

Before treatment. Day after burn.

After six days of treatment.
ENCLOSURE (N), continued

Before treatment.
Day after burn.

Same as above.

CASE 1793
Second and Third Degree Burns From Boiling Water
Age 3
Treatment: 0.2 mg "Koh" Nk 1 given internally daily. Ichthyol applied locally.
After 17 days of treatment only small ulcer in central region of first phalanx of foot remains.

Same as above.

CASE (N)3
(continued)
ENCLOSURE (N), continued

Before treatment.
Same day as burn.

After 17 days of treatment.
No fear of death after 10 days. Seven days thereafter Thiersch's grafting technique used.

CASE (11).4
Third degree burns from boiling water
Age 19 - Female
(Patient is traumatic epileptic)
Treatment: 0.25 mg "Kohla" Wk 1 given internally daily. Ichthyol applied locally.
After 45 days of treatment.
12 days after grafting.

22 days after grafting was begun. All instances, epithelium began to form

CASE (H) 4
(continued)
ENCLOSURE (N), continued

CASE (N) 5
Burns from Burning Oil
Age 32
For 68 days patient received treatment with ointment. A bacillus infection had developed and there were large ulcers in the hypodermis. Patient was hospitalized, and on eight day of treatment secretions suddenly decreased, and granulations formed. After twentieth day, Thiersch's grafting technique was used with immediate success.
Condition after about 5⁄4 months of treatment. Ulcers have completely healed. Hypodermis has recovered its elasticity. 0.1 mg of "Koha" No 1 given internally daily. Ichthyol applied locally.

Nervature of articulating gense is normal, and its functioning has not been impaired in the least.

CASE (No) 5.
(continued)
ENCLOSURE (N), continued

Before treatment.
Seven days after being burned.

CASE (N) 6
Benzene Burns
Age 25

Treatment: 0.25 mg "Kohu" Mk 1 given internally daily. Ichthyol - boric acid - water preparation applied locally.
ENCLOSURE (N), continued

After eight days of treatment.

CASE (N)6
(continued)
Same as
front view.
ENCLOSURE (N), continued

After 45 days of treatment, only light wound scars remain.

CASE (N)6
(continued)
Same as front view.

CASE (N)16
(continued)
ENCLOSURE (O)

PHOTOGRAPHS SHOWING EFFECTS OF TREATMENT OF ULCERS OF THE LEG WITH "KOHAI".

Before treatment.

20 days after appearance of ulcer.

Out patient after 31 days.
Full course of treatment.

CASE (O) 1
Age 38 - Female
Treatment: 1.0 mg "Kohai" Mk 1 administered internally once a day. Boric acid ointment applied locally.
Before treatment.
15 months after appearance of ulcer.

After 51 days of treatment.
Full course. Hospitalized.

CASE (0:2)
Age 45 - Female
Treatment: 0.01 mg "Zola" No. 12 administered internally once a day.
Rivanol gauze and boric acid-water-schthyl preparation applied locally.
Before treatment.
20 days after appearance of ulcer.

Out patient after 33 days of treatment.
Full course.

CASE (0)3
Age 27 - Female
Treatment: "Koha" gauze applied locally. Improvement slight.
ENCLOSURE (P)

PHOTOGRAPHS SHOWING EFFECTS OF "KOHA" TREATMENT ON TUBERCULAR LYMPHADENITIS

Before Treatment

37 Days After Treatment

CASE (P) 1
ENCLOSURE (P), continued

Before Treatment

103 Days After Treatment

CASE (pl2)
ENCLOSURE (P), continued

Before Treatment

66 Days After Treatment. 
After 15 Intravenous Injections

After Treatment

CASE (P) 4

76
ENCLOSURE (P), continued

Ulcer Before Treatment

77 Days After Treatment

CASE (P)5
ENCLOSURE (P), continued

Before Treatment

440 Days After Treatment

CASE (P) 6

78
ENCLOSURE (P), continued

Before Treatment

420 Days After Treatment

CASE (P) 7

79
ENCLOSURE (P), continued

Before Treatment

After 45 Days of Giving 0.1 mg
of "Koha" Mk 1 Internally

CASE (p) 8

Treatment: "Koha" Mk 1 given in
following doses: 1.0 mg internally,
five doses on alternate days; 0.1 mg
internally, 12 doses on alternate days;
0.1 mg internally, 14 doses daily.

80
ENCLOSURE (P), continued

315 Days After Treatment Was Begun

315 Days After Treatment Was Begun

CASE (P) 8
(continued)
ENCLOSURE (P), continued

Ulcus Before Treatment

126 Days After Treatment Was Began

CASE (plq)

82
ENCLOSURE (P), continued

Before Treatment

210 Days After Treatment was begun

CASE (p) 80
CASE (P)11

Treatment: 0.25 mg of "Koha" Mh 1 given internally every day.
ENCLOSURE (P), continued

Before Treatment

After Treatment

CASE (p. 12)
Treatment: Following doses of "Koha"
Mark 1 given internally: 20 doses of
0.1 mg every other day; then 50 doses
of 0.1 mg daily; 43 doses of 0.01 mg
daily.
ENCLOSURE (P), continued

Before Treatment

During Treatment

CASE (P) 13

86
ENCLOSURE (P), continued

During Treatment

After Treatment

CASE (P) 19
ENCLOSURE (P), continued

Before Treatment

335 Days After Beginning Treatment

CASE (P) 14
ENCLOSURE (Q)

PHOTOGRAPHS SHOWING EFFECTS OF "Koha Treatment on Tubercular Leprosy

CASE (Q): 1
Tubercular Macular Leprosy
Age 30 - Male

Treatment: Following doses of "Koha" Mk 1 six times a week: 3.0 mg by nasal suppository; 1.0 mg internally; 2.0 mg intramuscularly - twice a week; 3.0 mg nasal suppository. Full course: 54 doses, totaling 151.0 mg of "Koha", given over period of 103 days.
ENCLOSURE (Q), continued

CASE (Q)/2
Primary Tubercular Leprosy
Age 18 - Male

Treatment: 3.0 mg "Koha" Mk 1 administered by anal suppository from three to six times a week. Full Course: 53 applications, totaling 159.0 mg of "Koha", given over a period of 130 days.
CASE (Q)3
Primary Tubercular Leprosy
Age 21 - Male
Treatment: 3.0 mg "Koha" Mk 1 given by anal suppository three to six times a week. Full course: 50 applications, totaling 150.0 mg of "Koha", given over period of 112 days.
ENCLOSURE (Q), continued

Before Treatment

CASE (Q4)
Primary Tubercular Leprosy
Age 29 - Male
Treatment: "Koha" Mt. 1 administered internally three to six times a week. Full
course: 41 doses, totaling 41.0 mg of "Koha", given over period of 243 days.
ENCLOSURE (Q), continued

CASE (Q)5
Primary Tubercular Leprosy
Age 37 - Male

Treatment: 1.0 mg "Koha" Mk 1 by urethral injection three times a week. Full course: 25 injections, totaling 12.5 mg of "Koha", given over a period of 25 days.
CASE (Q) 6
Primary Tubercular Leprosy
Age 23 - Male

Treatment: 3.0 mg "Koha" Nk. 1 by anal suppository three to six times a week. Full course: 63 applications, totaling 189.0 mg of "Koha", given over a period of 154 days.
ENCLOSURE (Q), continued

CASE (Q)
Secondary Tubercular Leprosy
Age 18 - Female

Treatment: 1.0 mg "Koha" Mk 1 administered internally three to six times a week. Full course: 89 doses, totaling 89.0 mg of "Koha", given over a period of 211 days.
ENCLOSURE (Q), continued

Before Treatment

After Treatment

CASE 1018
Secondary Tubercular Leprosy
Age 32 - Male

Treatment: 0.1 mg "Koha" M/12 administered internally three times a week. Ten doses, totaling 1.0 mg of "Koha", given over a period of 30 days.
ENCLOSURE (Q), continued

CASE (Q) 9
Secondary Tubercular Leprosy
Age 18 - Female

Treatment: 2.0 mg "Koha" Mk 1 injected intramuscularly six times a week, and 0.1 mg of "Koha" Mk 1 administered internally three times a week. Full course: 58 doses, totaling 97.0 mg of "Koha", given over period of 140 days.
ENCLOSURE (Q), continued

Before Treatment

After Treatment

CASE (Q) 10
Secondary Tubercular Leprosy
Age 44 - Male
Treatment: 1.0 mg "Koha" Hk 1 injected intravenously three to six times a week. Full course: 76 injections, totaling 76.0 mg of "Koha", given over period of 144 days.
ENCLOSURE (9), continued

CASE (Q) 11
Secondary Tubercular Leprosy
Age 40 - Male

Treatment: 0.3 mg "Koha" Mk 1 injected intravenously three times a week. Full course: 35 injections, totaling 10.5 mg of "Koha", given over period of 120 days.
ENCLOSURE (Q), continued

CASE (Q) 12
Secondary Tubercular Leprosy
Age 27 - Male

Treatment: 1.0 mg "Koha" Mk 1 injected subcutaneously three to six times a week. Full course: 67 injections, totaling 67.0 mg of "Koha", given over period of 118 days.
ENCLOSURE (Q), continued

CASE (Q) 13
Secondary Tubercular Leprosy
Age 21 - Male

Treatment: 1.0 mg "Koha" Mk 1 by urethral injection three times a week. Full course: 6 injections, totaling 6.0 mg of "Koha", given over period of 15 days.
CASE (Q) 14
Secondary Tubercular Leprosy
Age 44 - Male

Treatment: "Koha" Mh 1 given in following doses: 2.0 mg intravenous injection six times a week; 2.0 mg intramuscular injection six times a week; 3.0 mg by anal suppository six times a week; 3.0 mg internally six times a week; 1.0 mg internally three times a week; 1.0 mg internally six times a week; 3.0 mg by inhalation three times a week. Full course: 39 doses, totaling 202.0 mg of "Koha", given over period of 124 days.
CASE 1015
Secondary Tubercular Leprosy
Age 38 - Male

Treatment: 0.1 mg "Koha" Nk 12 administered internally twice a week. Full course: 10 doses, totaling 1.0 mg of "Koha", given over period of 32 days.
ENCLOSURE (2), continued

CASE (Q) 16
Secondary Tubercular Leprosy
Age 18 - Male

Treatment: 0.1 mg "Koha" Mkt 1 given internally twice a week, and 0.1 mg "Koha" Mkt 12 given internally twice a week. Full course: 27 doses, totaling 1.8 mg of "Koha" Mkt 1 and 0.9 mg of "Koha" Mkt 12, given over period of 164 days.
ENCLOSURE (Q), continued

CASE (Q) 17
Secondary Tubercular Leprosy
Age 31 - Male

Treatment: 1.0 mg "Koha" Mh 1 given in spinal injection. 1.0 mg of "Koha" Mh 1 was injected intravenously three times a week, and 0.1 mg of "Koha" Mh 12 was administered three times a week. Full course: 17 doses, totaling 19.0 mg of "Koha" Mh 1 and 0.6 mg of "Koha" Mh 12, given over period of 121 days.
ENCLOSURE (Q), continued

Before Treatment

CASE (Q):8
Secondary Tubercular Leprosy
Age 21 - Male

Treatment: Following doses of "Koha" Hk 1 six times a week: 3.0 mg by anal suppository; 5.0 mg internally; 2.0 mg intravenously; 2.0 mg intramuscularly. 2.0 mg of "Koha" Hk 1 internally six times a day each day. 0.1 mg of "Koha" internally two times a week. Full course: 51 doses, totaling 510.7 mg of "Koha", given over period of 112 days.

After Treatment
CASE (W) 10
Secondary Tubercular Leprosy
Age 38 - Male

Treatment: 0.1 mg "Koha" daily internally three times a week. Full course: 28 doses, totaling 1.8 mg of "Koha", given over period of 41 days.
ENCLOSURE (Q), continued

Before Treatment

CASE (Q) 20
Advanced Tubercular Leprosy
Age 20 - Female

Treatment: 0.2 mg "Koha" Mk 1 internally twice a week. Full course: 20 doses, totaling 4.0 mg of "Koha", given over period of 48 days.

After Treatment
ENCLOSURE (Q), continued

CASE (Q) 21
Advanced Tubercular Lepra
Age 34 - Male

Treatment: 3.0 mg "Koha" Mk 1 by external application three to six times a week.
Full course: 74 applications, totaling 222.0 mg of "Koha", over period of 182 days.
ENCLOSURE (Q), continued

Before Treatment

After Treatment

CASE (Q) 22
Advanced Tubercular Leprosy
Age 29 - Female

Treatment: 1.0 mg "Koha" Mk 1 administered externally three to six times a week.
Full course: 75 doses, totaling 75.0 mg of "Koha", over period of 171 days.
CASE (Q) 23
Advanced Tubercular Leprosy
Age 34 - Male
Treatment: 0.9 mg "Koha" Mk 12 internally each day. Full course:
15 doses, totaling 4.5 mg of "Koha", given over period of 15 days.
CASE (Q) 24
Advanced Tubercular Leprosy
Age 32 - Male
Treatment: 0.2 mg "Koha" Hk 1 internally twice a week. Full course: 24 doses, totaling 4.8 mg of "Koha", given over period of 106 days.
ENCLOSURE (Q), continued

CASE (Q) 25
Advanced Tubercular Leprosy
Age 22 - Male

Treatment: 0.2 mg "Kohne" Hb 1a internally three times a week. Full course: 14 doses, totaling 2.8 mg of "kohne", given over period of 92 days.
CASE (Q) 26
Advanced Tubercular Leprosy
Age 43 - Female
Treatment: 2.0 mg "Koha" Mk 1 injected intravenously three to six times a week. Full course: 54 injections totaling 108.0 mg of "Koha", given over period of 124 days.
ENCLOSURE (2), continued

CASE (Q) 27
Advanced Tubercular Leprosy
Age 35 - Male

Treatment: 1.0 mg "Koha" Wk 1 injected three times a week. Full course: 12 injections, totaling 12 mg of "Koha", was given over period of 31 days.
CASE (Q) 46
Advance Tubercular Leprosy
Age 33 - Female
Treatment: 1.0 mg "Koha" M. 1 administered internally three to six times a week. Full course: 50 doses, totaling 52.0 mg of "Koha", given over period of 172 days.
ENCLOSURE (Q), continued

CASE (Q) 20
Advanced Tubercular Leprosy
Age 33 - Female
Treatment: "Koha" Mk 1 administered internally three times a week, injected intravenously three times a week. Full course: 53 doses, totaling 34.1 mg of "Koha", over period of 204 days.
ENCLOSURE (Q), continued

CASE (Q) 30
Advanced Tubercular Leprosy
Age 42 - Female

Treatment: "Koha" No. 1 in following doses: 1.0 mg internally three times a week, 2.0 mg internally six times a day every day; 3.0 mg by inhalation six times a week; 1.0 mg intravenously three times a week; 3.0 mg by inhalation three times a week. Full course: 87 doses, totaling 371.0 mg of "Koha", over period of 100 days.
CASE 12:31
Advanced Tubercular Leprosy
Age 32 - Male

Treatment: 1.0 mg "Koha" Mk 1 injected intravenously three times a week. Full course: 60 injections, totaling 60 mg of "Koha", over period of 202 days.
ENCLOSURE (Q), continued

CASE (Q)32
Advanced Tubercular Leprosy
Age 24 - Male

Treatment: 0.3 mg "Koha" Mk 1 injected intravenously two times a week. Full course: 17 injections, totaling 5.1 mg of "Koha", given over period of 78 days.