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U. S. NAVAL TECHNICAL MISSION TO JAPAN
CARE OF FLEET POST OFFICE
SAN FRANCISCO, CALIFORNIA

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7 January 1946

RESTRICTED

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.

2. The investigation of the target and the target report were accomplished by Lt. W.W. Woodworth, USNR, Lt.(jg) F.J. Gilbert, USNR, Lt.(jg) R.M. Hendrickson, USNR, Lieut. P.E. Arioli, (MC) USNR, and Comdr. P.B. Ayers, (MC) USNR.

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30630

RESTRICTED M-12

PHARMACOLOGY AND MALARIOLOGY 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 (B) 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.

TABLE OF CONTENTS

LIST OF ENCLOSURES

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. N. 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, CHEBA 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 - Takeda 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:

1. "Periodic Reports on the Activities of the Committee for the Technical and Scientific Investigation of Japanese Activities in Medical Science" - GHQ, AFPAC, Office of the Chief Surgeon (Advance Echelon).
2. Reports of the U.S. Typhus Commission in Japan. Files of the U.S. Typhus Commission.
3. Army Commission for the Study of Schistosomiasis, GHQ, AFPAC, Office of the Chief Surgeon (Advance Echelon).

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 HASHIMOTO, 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 MEGURO 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 theropeusis 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 venilent 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:

"Malanophore 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 intrapentoneally). 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 temperatures for tropical shipment, etc., was another technique worthy of comment. Prepared vaccine solutions, typing sera, etc. were dehydrated by vacumm suction at relatively low dehydrating temperatures, the resultant solids retaining their antigenic properties up to approximately 800F 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 a Lt. 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

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

Navy C P Method

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

Navy C Method

Medicine	Daily Quantity	Period of Dosage	Full Quantity and Number of Days for 1 Cure	Remarks
Nitrate of Quinine (Sulphate of Quinine)		10 days	Nitrate of Quinine 17.0 (Sulphate of Quinine 18.7)	
Abstain from Medicine		2 days		
Nitrate of Quinine (Sulphate of Quinine)		7 days	19 days of treatment	

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

Medicine	Daily Quantity	Period of Dosage	Full Quantity and Number of days for 1 Cure	Remarks
Synthetic Malaria Drug A	0.3 taken 3 times daily after meals	7 days	Synthetic Malaria Drug A 2.1	Depending on conditions, synthetic malaria drug may be taken at one time
Abstain from Medicine		2 days		
Synthetic Malaria Drug B	0.03 taken 3 times daily after meals	5 days	Synthetic Malaria Drug B 0.15	
Epirenamin Chloride (liquid)	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.	alternate days throughout whole period	Epirenamin Chloride (liquid) - 3.3 - 4.5 cc 14 days period of treatment	

Navy C P E Method

Medicine	Daily Quantity	Period of Dosage	Full Quantity and Number of days for 1 Cure	Remarks
Muriate of Quinine (Sulphate of Quinine)	1.0(1.1) taken 3 times daily after meals	10 days	Muriate of Quinine 17.0 (Sulphate of Quinine 18.7)	Depending on conditions, synthetic malaria drug may be taken at one time
Abstain from Medicine		2 days		
Synthetic Malaria Drug B	0.03 taken 3 times daily after meals	5 days	Synthetic Malaria Drug B 0.15	
Epirenamin Chloride (liquid)	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.	alternate days throughout whole period	Epirenamin Chloride injection liquid 3.8 - 5.2 cc 17 days period of treatment	

Navy C E Method

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

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

Medicine	Daily Quantity	Period of Treatment	Full Quantity and Number of days for 1 Cure
Synthetic Malaria Drug A - as an injection	0.3 once a day, injection into musculus glutaeus	7 days	Synthetic Malaria Drug A - 2.1
Abstain from Medicine		2 days	
Synthetic Malaria Drug B - as an injection	0.03 once a day, injection into the musculus glutaeus	5 days	Synthetic Malaria Drug B - 0.15
Epirenamin Chloride (liquid)	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.	alternate days throughout whole period	Epirenamin Chloride (liquid) 3.3 - 4.5 cc 14 days of treatment

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)

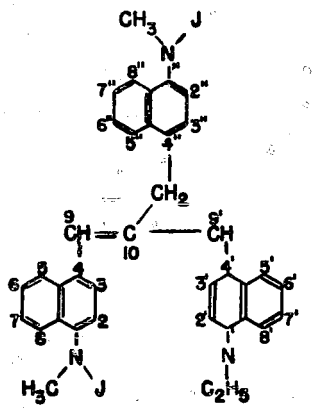
CHEMICAL FORMULAE OF "KOHA" AND "SHIKO"

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.

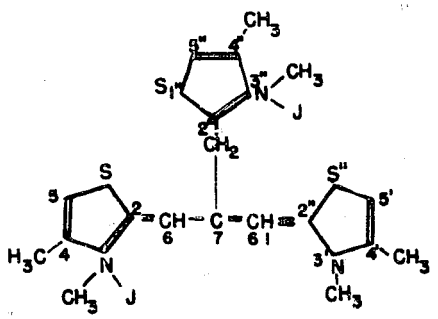
Chemical Formulae - Chemical formulae for these compounds have not been proved decisively. To use Hamer's neocyanine formula (F. M. Hamer: J. Chem. Soc., London, 1928, 1472-8) they can be represented as follows:

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.



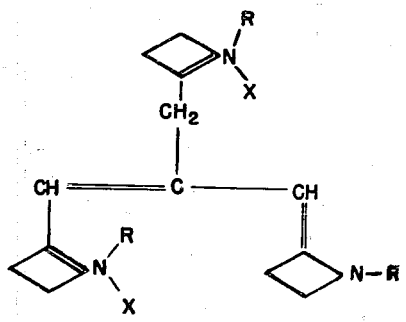
(A)



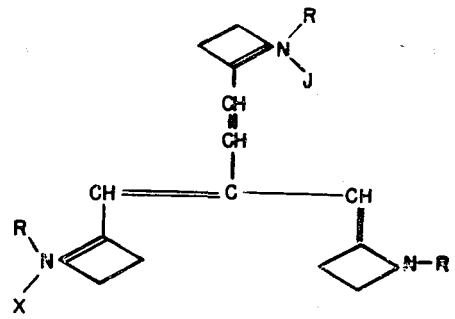
(B)

ENCLOSURE (A), continued

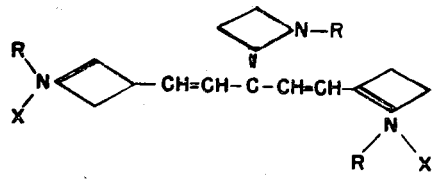
From analysis values and synthetic processes, other formulae are possible, but they also lack positive proof. The following formulae (II and III) represent some of the possibilities with Hamer's formula (I) drawn schematically.



(I)



(II)



(III)

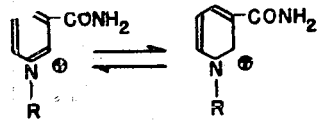
ENCLOSURE (A), continued

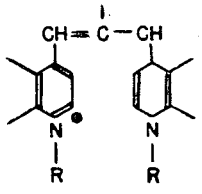
Properties - "Koha" is copper colored crystals with metallic lustre, is almost insoluble to most solvents but when dissolved, the solution is green. The decomposition point is not sharp and wavers between 275-281°C according to the way of heating. The picrate is copper colored prisms melting at 274-6°C.

"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 ethylorthoformate 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 neocyanine dyestuffs is that the oxydoreduction system of the aromatic heterocyclic ring is bound inside the molecule by conjugated double bond. That is, instead of having separate molecules of oxidizine 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 pyocaneus for three to nine days after administration of the preparation, but against streptococcus viridans, pneumococcus (III Type), and collicommunis it is less active.

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

ENCLOSURE (B), continued

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 dropsy 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 atrophia 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

ENCLOSURE (B), continued

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 lymphadentitis, 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 .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) 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

Bibliography - Hantsch: Ann. 250, 262.

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. 3,3',3'',4,4',4''-Hexamethyl-7(-2''-Methylthiazolyl)-Trimethine-Thiazolocyanine-3,3''-Diiodide

Bibliography - Terutaro OGATA: J. Inst. Physic. Chem. Research, (13), 6, 497-500.

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 "Kōha". The solubility is also comparatively greater, so it can be recrystallized from water.

Absorption maximum: 5955 Å (C_2H_5OH)

Sensitivity maximum: 6400 Å

ENCLOSURE (D)

SYNTHETIC PROCESS FOR "KOHA"

1. Acetoacetic Acid Anilide

Bibliography - Eduards, David, Ziegler: Helv. XI, 779 (1928).

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°[2] 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°. 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°C[4] (63% against aniline, 52% against acetoacetic ester).

2. 2-Oxylepidine

Bibliography - Michailow: Chem. Zentralblt., 1937, I, 1941.

Process - 50gms Acetoacetic anilide (dried at 50° in vacuum) is added gradually in concentrated sulphuric acid (d 1.84), kept at 90-95°[5] 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°, poured in 3 l. of water and the precipitate is filtered off. The filtered precipitate is washed with water, dried at about 50°, and recrystallized from alcohol. Yield is 41gms (91% of theory) of crystals melting at 218-90C. When recrystallized, the melting point becomes 221°.

3. 2-Chlorolepidine

Bibliography - Knorr, Annalen, 236, 97.

Process - 12gms oxylepidine, 18gms phosphorus pentachloride and 8cc phosphorus oxychloride are refluxed at 90 to 100° 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°C, melting point 59°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°C. Those melting at 82° will do for the next process.

[5] Above 90-95°, bubbling becomes vigorous and the yield drops.

ENCLOSURE (D). continued

If this material dissolved in 10% HCl 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 $PdCl_2$, 0.5gms activated charcoal and 3cc 10% hydrochloric acid are shaken in hydrogen stream and saturated. To this is added 100cc alcoholic solution of 42gms 2-chlorolepidine and catalytically reduced in hydrogen stream. About 5300cc hydrogen is absorbed and saturated. The catalyst is removed by filtration, alcohol distilled off from the filtrate and alkalinified with sodium hydroxide. The base that precipitates is extracted with ether, dried with potassium hydroxide, ether distilled, and the residue distilled under reduced pressure. 34gms of lepidine (99% of theory)[6] boiling out at 130-1°C are obtained. The picrate 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.

Bibliography - Terutaro OGATA, Chem. Physic. Research, (13), 6, 491-6.

Process - 3gms lepidine ethoiodide and 2cc acetic anhydride are put in a distillation flask and immersed in a glycerine bath (kept at 145-150°) so as to bring the surface of the content and the bath in a line, and under stirring, 3gms (3.6cc) 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 45cc. 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[7] and 0.8gms of crystals melting at 287° (decomp.) is obtained.

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(6) [6] 45.5% against acetoacetic ester.

(7) [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 700cc aniline, 4000cc benzene added and precipitated.

ENCLOSURE (D), continued

PROPERTIES OF "KOHA"

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

Crystals - "Koha" 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 alkalinized.

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

Derivatives

Hydrochloride:	Copper colored fine needle crystals, Fp 263° (decomp.).
Picrate:	Copper colored fine prisms, Fp 224° (decomp.).
Styphnate:	Copper colored needles, Fp 216° (decomp.).
Picrolonate:	Copper colored prisms, Fp 205° (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) Advertizing 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. 54 Suso Nishino-Cho 4-Chome, Higashi-Yodogawaku, OSAKA Mr. KUBOTA, Director of Takeda, as Guide

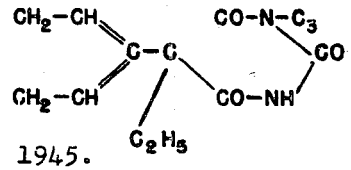
1. The research laboratory is a modern building of three stories and given entirely to research on all phases of medicine. It was, however, almost entirely made up of dark, poorly-ventilated laboratories staffed by young college graduates.

ENCLOSURE (E), continued

2. Special Research Ordered by the Navy Through the Ryohinsho

a. Sedative - Similar to "Eviepan".

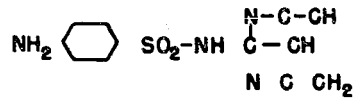
(1) Formula:



(2) Approved June, 1945.

b. Non-Crystalizing Sulfa - "Panmidin".

(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
Acriflavin injection
*Acrinol powder
Acrinol injection
Alsilin
Aminopyrin
Amolisin
Barbital
Biofermin
Borraginol suppositories
Bromvalerylurea
*Castor oil
Chinojodin
Cruculon liquid
*Cruculon tablets
Erstin

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 (Tropochin tannate tablets)
Uabanin
*Vitacampher
*Vitamin B_1
Vitamin B_1 injection
Vitamin B_1 tablets
Vitamin C
Vitamin C injection
*Vitamins B_1 & C tablets
Vitamin P injection
Vitamin K injection

PART IV

Reports on Researches
(Translations)

November 1, 1945

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 B_1.

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

3. STATE OF RESEARCH: Studying the combination of 2-methyl-4-amino-5-brommethyl-pyrimidine-hydrobromide with 4-methyl-5-oxyethyl-thiazole, the last step in the manufacture of vitamin B_1 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.

ENCLOSURE (E), continued

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 chrorophyl 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, slycoside 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.

b. Relation between temperature and volume in alkaloid absorption of Japanese acid earth.

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 B_1 and its Homologes.

2. EXPERTS IN CHARGE: Osamu TANI, Yoshiko MORITA.

ENCLOSURE (E), continued

3. STATE OF RESEARCH: We are studying a new method of Vitamin B_1 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 2-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 Follen.

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, antidiarrhoic, stomachic, antiemetic, ointment, medicine for gynecological use, and ointment for skin diseases.

4. REMARKS: None.

ENCLOSURE (F)

INVENTORY OF DRUGS - YOKOSUKA NAVAL MEDICAL SUPPLY DEPOT

Name of Drug	Unit	Quantity
Zincum Oxydatum	grams	25,000
Aceto-Anilid	grams	1,400
Acrinol	grams	600
Vaselinum Acrinol	grams	3,000
Aseno Benzoldrug	piece	7,800
Pastilli Aspirini	piece	110,000
Asprin	grams	15,000
Adsorbin	grams	1,000
Alcohol	grams	66,500
Coffeinum-Natrium benzoicum	grams	3,375
Liquor Ammonii caustici	grams	1,000
Oxycyano Mercury	grams	2,350
Pastilli Osvanyl	piece	11,250
Liquor Epinaremin hydrochloricum	piece	58
Oxidatum flavum	grams	4,000
Oxydol	grams	10,500
Medicine of liver	grams	500
Kalium permanganicum	grams	30,000
Natrum Causticum	grams	100
Kali Causticum	grams	1,000
Sapo Kalinus	grams	11,000
Hydrargyrum chloratum	grams	37,500
Pepsinum Saccharatum	grams	700
Wax Ointment	grams	17,000
Pastelii Oleum Jecario	piece	6,000
Medicine for scalds & burns	grams	56,500
Camphor	piece	500
Aqua Prum Armeniacae	piece	48,000
Formaldehyde Chinae	piece	375
Quinophene	piece	19,000
Acidum hydrochloricum dilectum	piece	3,000
Tinctura Amara	piece	4,700
Glycerine	piece	3,000
Cloysen	piece	1,500
Alcohol Methylicus	grams	2,500
Salt	grams	7,500
Soda Acidum citricum	grams	1,200
Argentum nitricum	grams	100
Pure alcohol	grams	8,000
Pastilli Natrium Salicylicum	piece	81,600
Medicine of Saponine	grams	12,250
Phenylum Salicylicum	grams	11,025
Salicylicum Acid	grams	14,500
Solutio Kalii Acetici	grams	25,000
Santoninum	grams	1,600
Hydragyrans Salicylicum	grams	2,000
Natrium bicarbonicum	grams	101,100
Syrups	grams	30,000
Hydrargyrum bichloratum	grams	500
Acidum Oxalicum	grams	2,500
Spiritus Ammoniae foeniculatus	grams	1,500
Ammonium Sulfoichthydicum	grams	34,500
Uva Ursi Liquor Extracta	grams	33,000
Ephedoline hydrochlorium	grams	325
Quinine Ethyl carbonate	grams	1,800
Aether pro narcosi	piece	700
Hydrargyrum bichloratum hydrochlorate	piece	1,500
Morphine hydrochloricum	piece	1,400
Procaine hydrochloricum	piece	2,090
Cocaine hydrochloricum	grams	2,100
Tropacocaine hydrochloricum	grams	125
Papaverine hydrochloricum	grams	40
Ethyline	piece	800
Port Wine	grams	124,800
Medicine of Digitalis	grams	19,500
Sodium Thiosulphate	grams	1,500
Diuretin	grams	2,000
Calcium Diuretin	grams	450
Serum for treatment	grams	80

ENCLOSURE (F), continued

Name of Drug	Unit	Quantity
Medicine of Salphamine	grams	63,400
Angentum Hydrargyri cinereum	grams	60,500
Pastilii Cepharanthin	piece	112,000
Sulfur depuratum	grams	9,000
Ungentum Natrium Metallicum	grams	16,500
Liquor Mandle	piece	3,000
Liquor Mastichi	grams	1,500
Alumen	grams	2,700
Natrium carbonicum	grams	2,700
Magnesium carbonicum	grams	1,500
Injection of Igrosin	piece	200
Injection of Isrevin	piece	500
Injection of Interenin	piece	20
Albumen Medicine	piece	3,000
Albumen Calcium Chloride	piece	2,520
Uva Wanine	piece	300
Uva Wanine Ephedeine hydrochloricum	piece	2,470
Uva Wanine Procaine hydrochloricum	piece	3,600
Uva Wanine Procaine Camphor	piece	14,085
Uva Wanine cataflavin	piece	220
Medicine of Bismuth	piece	7,780
Medicine of Natrium Citricum	piece	200
Dovers Salt	grams	1,000
Tinct Iodine	grams	62,000
Iodine	grams	13,500
Pastilii Bismuth Iodine	piece	50,000
Nanpole	piece	725
Calcariae lactirem	grams	14,500
Saccharum Lactis	grams	2,000
Barbital	grams	28,500
Hasethrol	grams	5,550
Halamin	grams	300

Name of Drug	Unit	Quantity
Thiantholum	grams	35,0[illegible]
Diastase	grams	1,0[illegible]
Calcanae phosphoricum praceipitatum	grams	4,400
Thymol	grams	500
Medicine for Ozaena	piece	393
Dermoleitz	grams	15,500
Herba Swertiae	grams	4,000
Standard Class Serum	piece	450
Castor Oil	grams	62,000
Silver protein	grams	29,900
Kalium Cromatum	grams	12,800
Phenovalin	grams	105,000
Brovalin	grams	125
Natrium bro[illegible]um	grams	23,000
Percarb	grams	6,000
Acidum boricum	grams	71,000
Deodorizer	grams	48,000
Antiseptic solution for prevention of epidemics	grams	20,500
Codeinum Phosphoricum	grams	4,600
Magnesium Sulphuricum	grams	13,000
Quinine Sulphuric tablet	piece	12,000
Paraffinum liquidum	grams	500
Atropine sulphate	grams	100
Pastilii Extracti Scopoliae	piece	124,800
Scopolia Extract	grams	10,000
Plaster of paris	grams	10,000
Medical Yeast	grams	4,600
Vaseline	grams	17,000
Injection of Acriflavin	piece	160
Atropine	piece	3,400
Injection of Coffeinum Natrium benzoicum	piece	11,600
Injection of synthetic malaria Drug A	piece	1,100
Injection of synthetic malaria Drug B	piece	6,900
Injection of Cornidin	piece	150
Aqua destillata		

ENCLOSURE (F), continued

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

ENCLOSURE (F), continued

Name of Drug	Unit	Quantity
Splice-piece	piece	80
Bandage	roll	3,121
Water-proof paper	sheet	4,500
Rolled sticking plaster	roll	10
Mask	piece	65
Raw cotton	package	442
Cotton	roll	556
Writing brush	piece	40
No. 4 roll of bandage	piece	6
Gauze of Iodoformium	roll	132
Funnel	piece	2
Eye-washer bottle (Fixtures)	piece	35
No. 1 Medical appliance	bag	10
Gloves for operation	pair	1,600
Cap for operation	piece	1,600
Large glass bottles	piece	3
Clinical thermometer	piece	810
Eye-wash bowl	piece	6
Pus bowl	piece	35
Pin set	piece	370
Mirror for examining nose	piece	5
Formaline sterilizer	piece	2
Foot warmer	piece	5
Blood-transfusing apparatus	piece	1

ENCLOSURE (G)

LIST OF DOCUMENTS FORWARDED TO NMRI, BETHESDA, MD.

NavTechJap No.	Document	ATIS NO.
ND-10-7501.2 (M12)	"Compendium of Navy Prescriptions"	3120
ND-10-7501.3 (M12) Annex #1	11 July 1945, Medical Affairs II Secret #13, "Prevention of Malaria through Internal Medicine"	3120

ENCLOSURE (H)

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

NavTechJap Equipment No.	Item	
JE-21-7507	Pyriform	Sodium Evipan
	Metilon	
JE-21-7525	Lieanalin	Pastill
	Coca Colae	Atonin
	Thorotrast	Dolantin
	Rosol Acid	Miyarisan
	Penargan	The Aifu
	Yuso	Omnin
	Purifying Powder	Thiocalgen
	Purifying Solution	Athinon
	Nissitin	Aparajin Tab.
	Compral	Kinkan
	Disinfectant #2	Mikezol
	Smile	Ritomatsu
	Karubun Keni Salve	Tocamol
	Praehormon	
JE-10-7504	Japanese Drug Samples, Ureshino Naval Hospital .	
JE-10-7505	Pentoral	Ebazol
	Spranchin	Philopon
	Marmor	Nissitin
	Cornidin	Opystan
	Cepharanthin Pills	Opium Alkaloid
	Miniglin	Tincture Opium
	Neomochin	Ovoral
	Nesbosan	Histamine
	Inhaling Chloride	Neo Ehramisol
	Supla Pills	Arsenic Paste
	Kinthiol	Sodium Picrate
JE-21-7526	Koha) Shiko) Neocyanine derivatives	
JE-21-7527	Drug samples from Takeda Pharm. Inst.	
	Apellagrin	Abotest

ENCLOSURE (1)

LIST OF DOCUMENTS FORWARDED TO WASHINGTON DOCUMENT CENTER THROUGH ATIS

NavTechJap No.	Document	ATIS NO.
ND-21-7506.1 (M-12)	Compendium of Pharmaceutical Specialties	3114
ND-21-7506.2 (M-12)	Catalogue of Takeda's New Drugs	3114
ND-21-7506.3 (M-12)	Catalogue of New Drugs for 1938	3114

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:

	Usual Treatment	Our Treatment
Clinical relapse rate	25-36.4%	5.9-0%
Protozoen relapse rate	72.7-100%	17.6-0%

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

Results:

1. The subcutaneous injection of the 1% 2-benzylimidazoline hydrochloride 1-2cc is effectual for incipient congelation.

2. The internal use of 2-benzylimidazoline dionalate 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 weakened 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 mosquitos 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. HOSOYA).

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 infected by plasmodiae were injected with test chemicals. After 15 minutes the blood of these animals was sucked by healthy mosquitos;

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.

No. 13 - Study on the Reproduction Gauze for Gibbs Bandage (K. SUZUKI, M. KIMURA).

Results: The following method is adopted: Immerse the Gibbs in 1% warm $Na-CO_3$ 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% $NaHCO_3$ or 20% Na_2CO_3 solvent for half an hour. After one day thoroughly wash and dry.

No. 14 B - Experiment on the Medicinal Value of the Trimon (S. ARIGA and M. KASHIMURA).

ENCLOSURE (J), continued

Object: The authors examined the medicinal value of the Trimon, oxyanthranylacid, 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 Oxyanthranilacid in Failure of the Liver Function (Y. KAWAKUBO).

Results: Liver function is examined by measuring the azorubin-S excretion in the urine. Oxyanthranilacid (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.

No. 14 D - On the Variation of Potency of Fukao Standard Serum (R. UCHIDA).

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 KOSHINO.

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

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 36x38cm 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.

ENCLOSURE (J), Continued

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 48.6% 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: isravin, panseptine and rivanol.

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

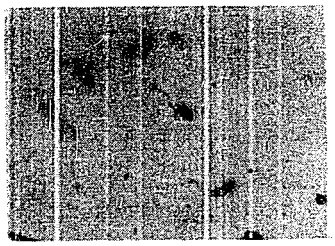


Figure (K)1
CHOLERA VIBRIO

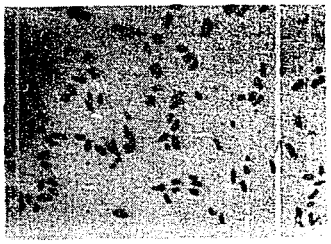


Figure (K)2
TYPHUS RICKETTSIAE

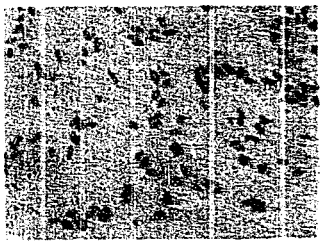


Figure (K)3
DYSENTERY BACILLI

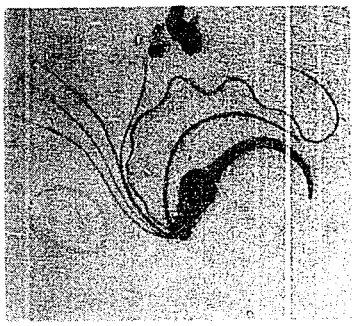


Figure (K)4
WHIP-WORM

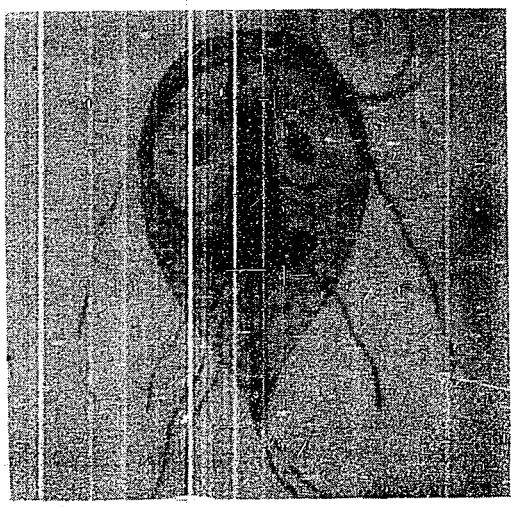


Figure (K)5
WHIP-WORM

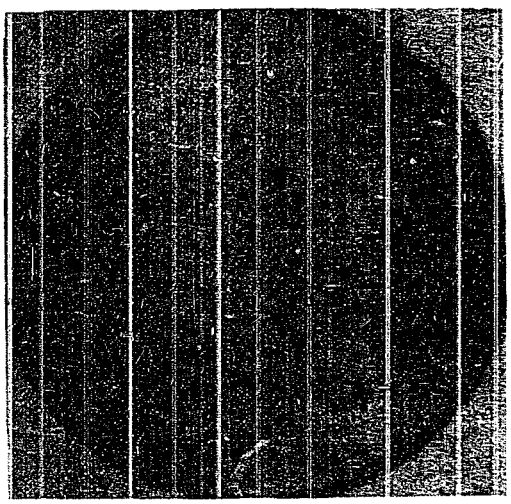


Figure (K)6
DYSENTERIC AMOEBA

ENCLOSURE (K), continued

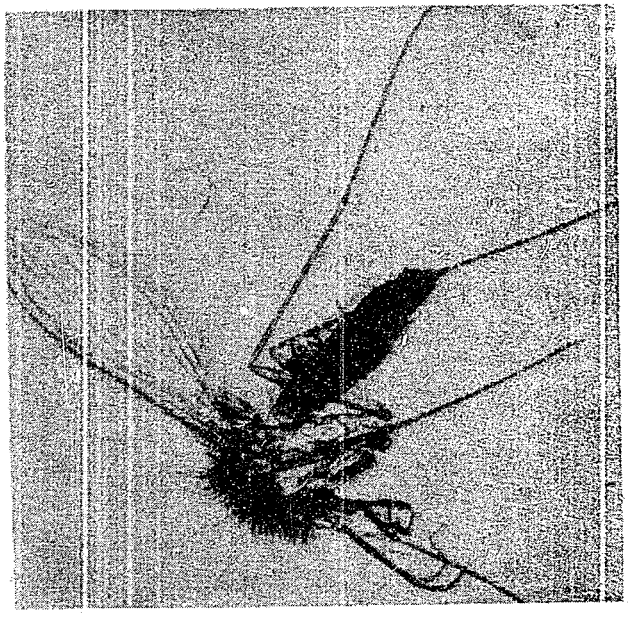


Figure (K)7
SAND-FLY

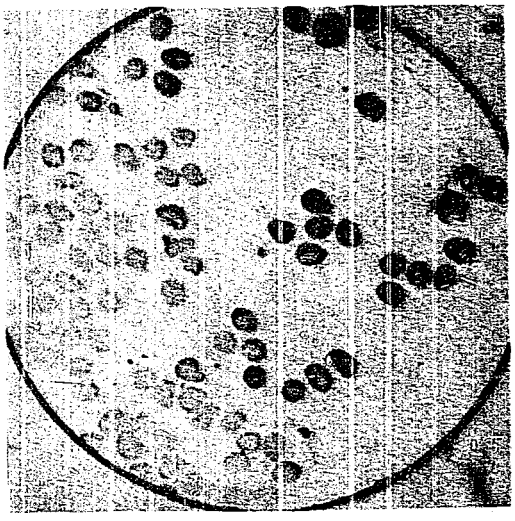


Figure (K)8
KALA-AZAR

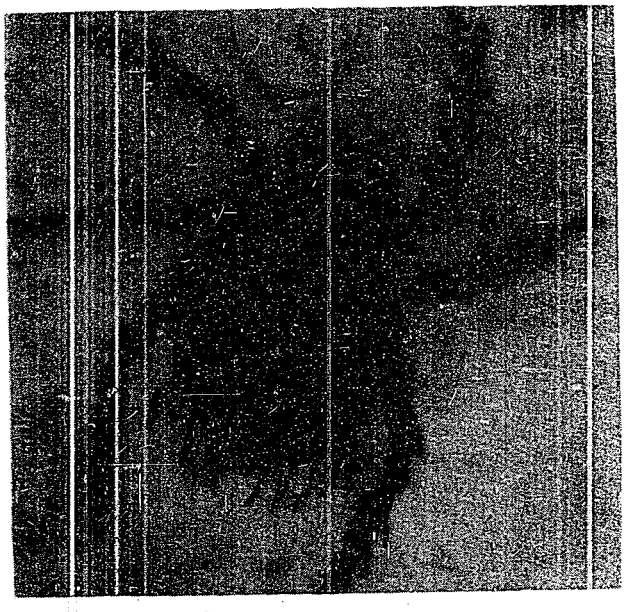


Figure (K)9
TROMBICULA AKAMUSHI

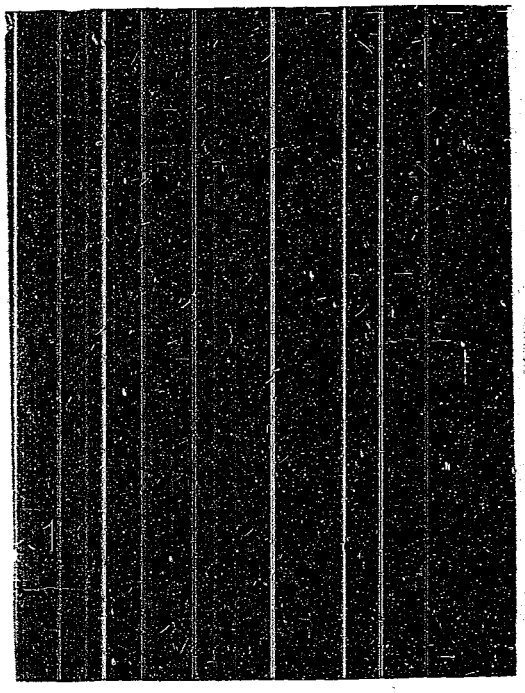


Figure (K)10
RICKETTSIA ORIENTALIS

ENCLOSURE (K), continued

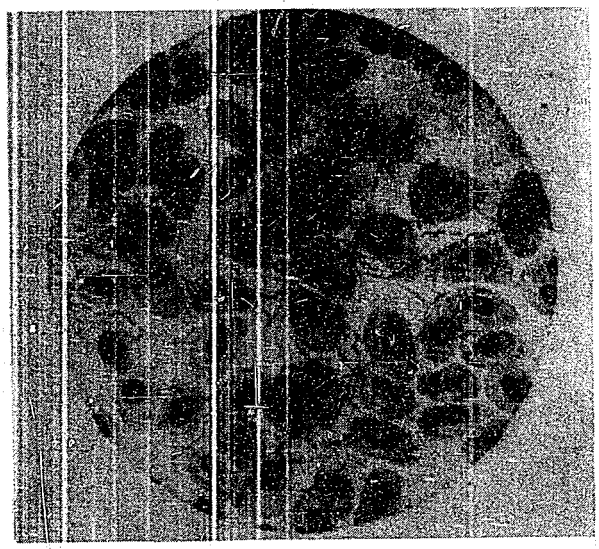


Figure (K)11
RECURRENT FEVER

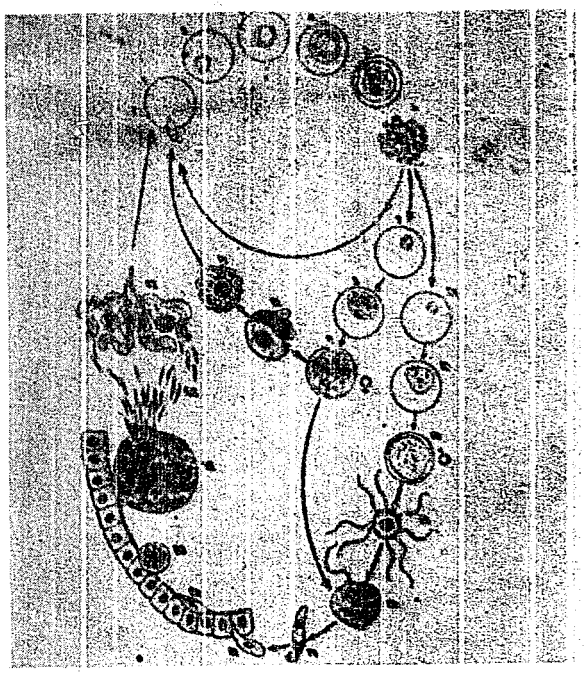
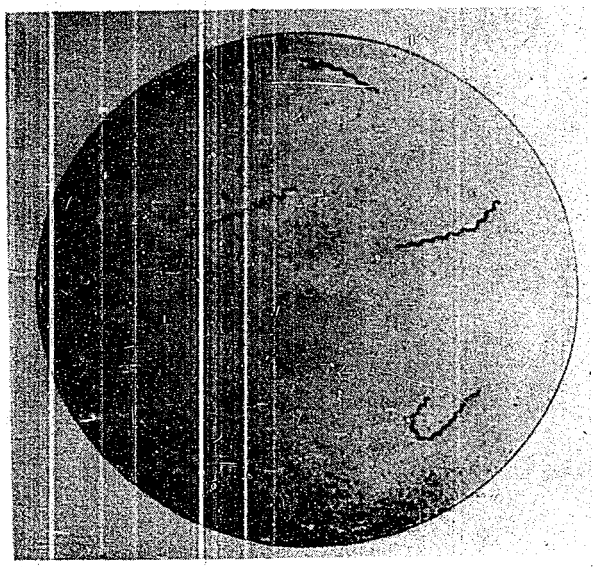


Figure (K)13
LIFE CYCLE OF THE MALARIA PROTOZOA

Figure (K)12
TREPONEMA PALLIDA



ENCLOSURE (K), continued

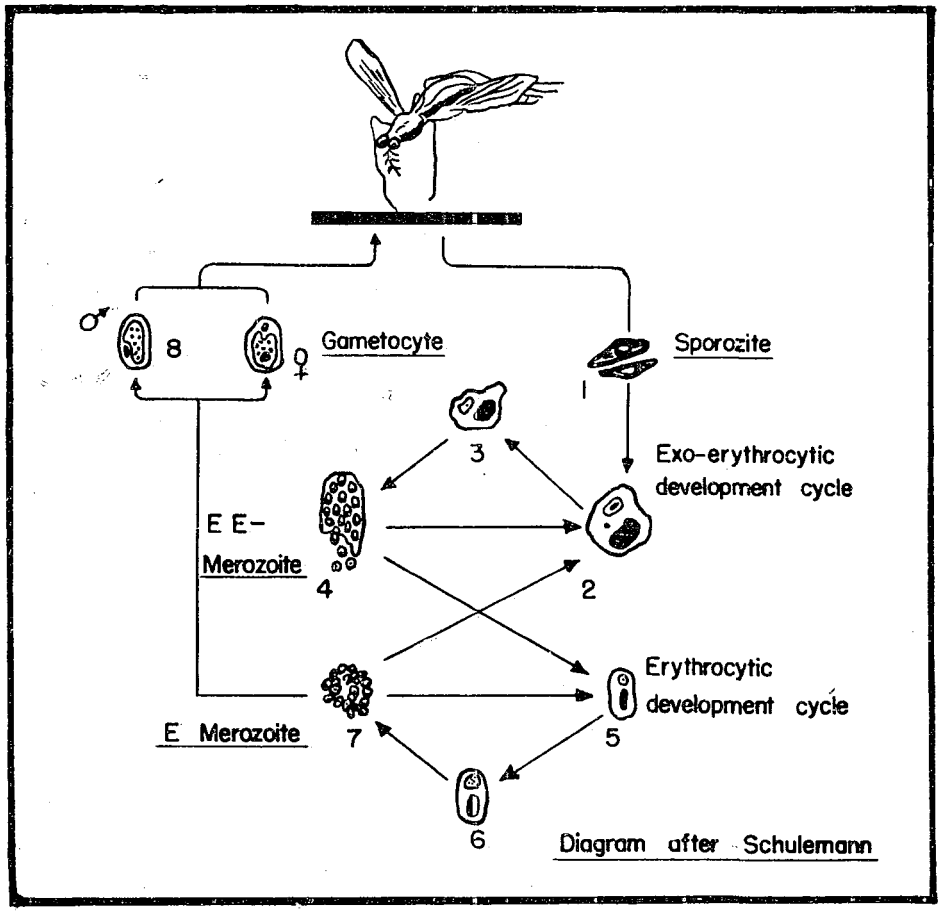


Figure (K)14

LIFE CYCLE OF THE MALARIAL MOSQUITO

ENCLOSURE (K), continued

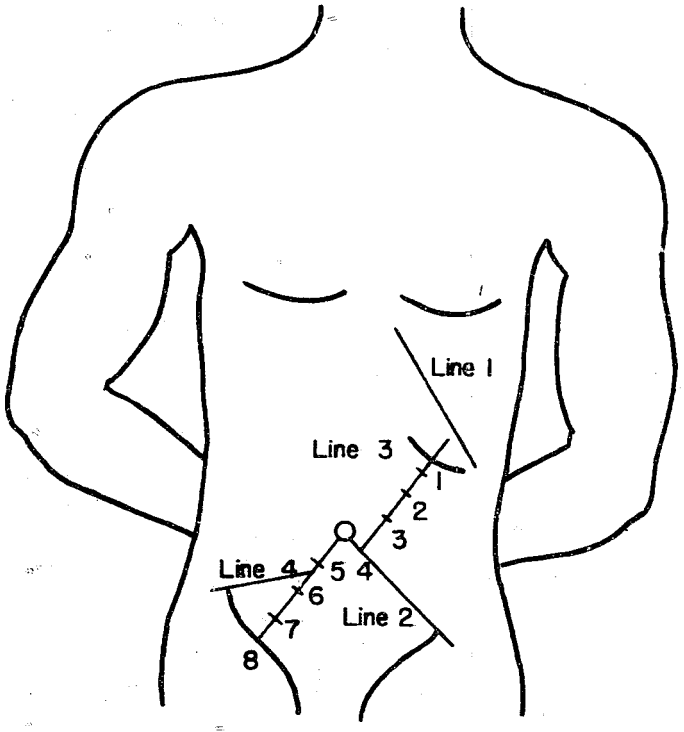


Figure (K) 15

SHIYUNERU'S METHOD OF MEASURING THE SPLEEN

ENCLOSURE (L)

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

L E G E N D

A - *First Layer, Cellular Exudation.*

Bd - *Closed Cell Structure.*

E - *Severed Edge Of Healthy Epidermis.*

K - *New Capillaries.*

M - *Subcutaneous Muscular Cell Structure.*

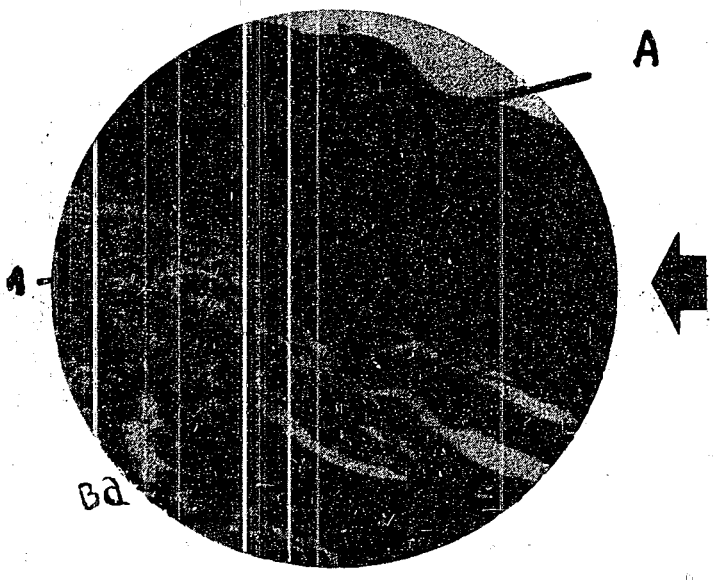
Nb - *Some Closed Cell Structure and Fiber.*

NE - *New Epidermis.*

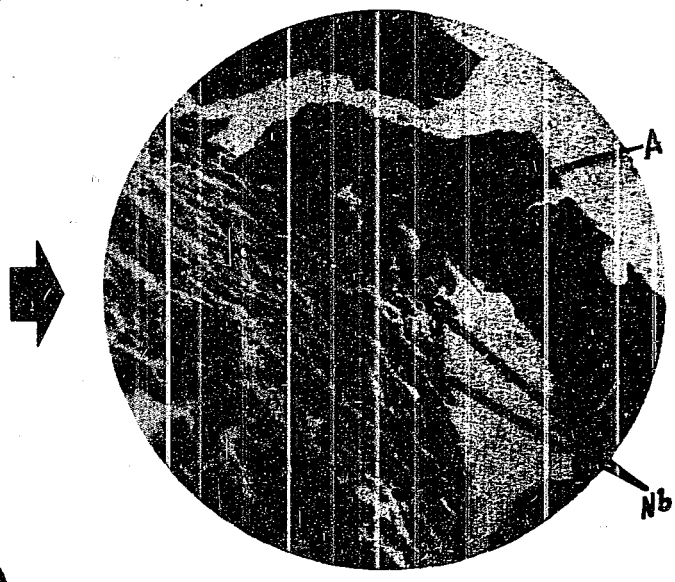
P - *Sudden Appearance Of Epidermis Papilla.*

Zf - *White Cell Saturation.*

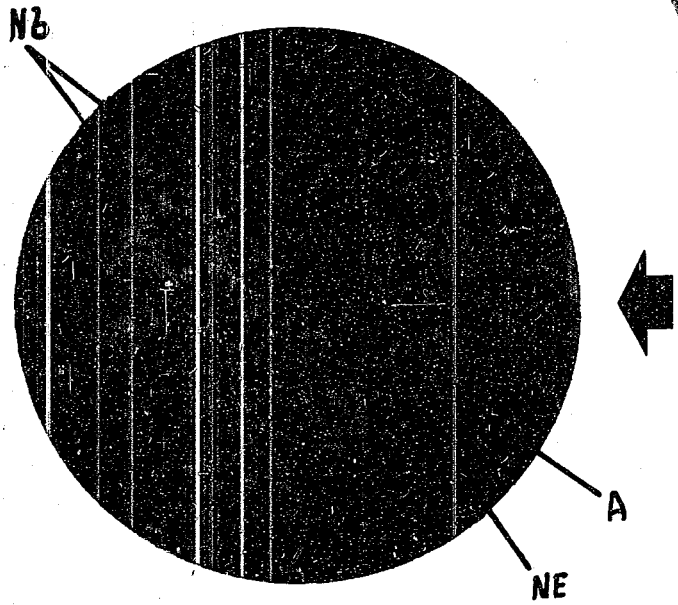
ENCLOSURE (L)



No treatment.



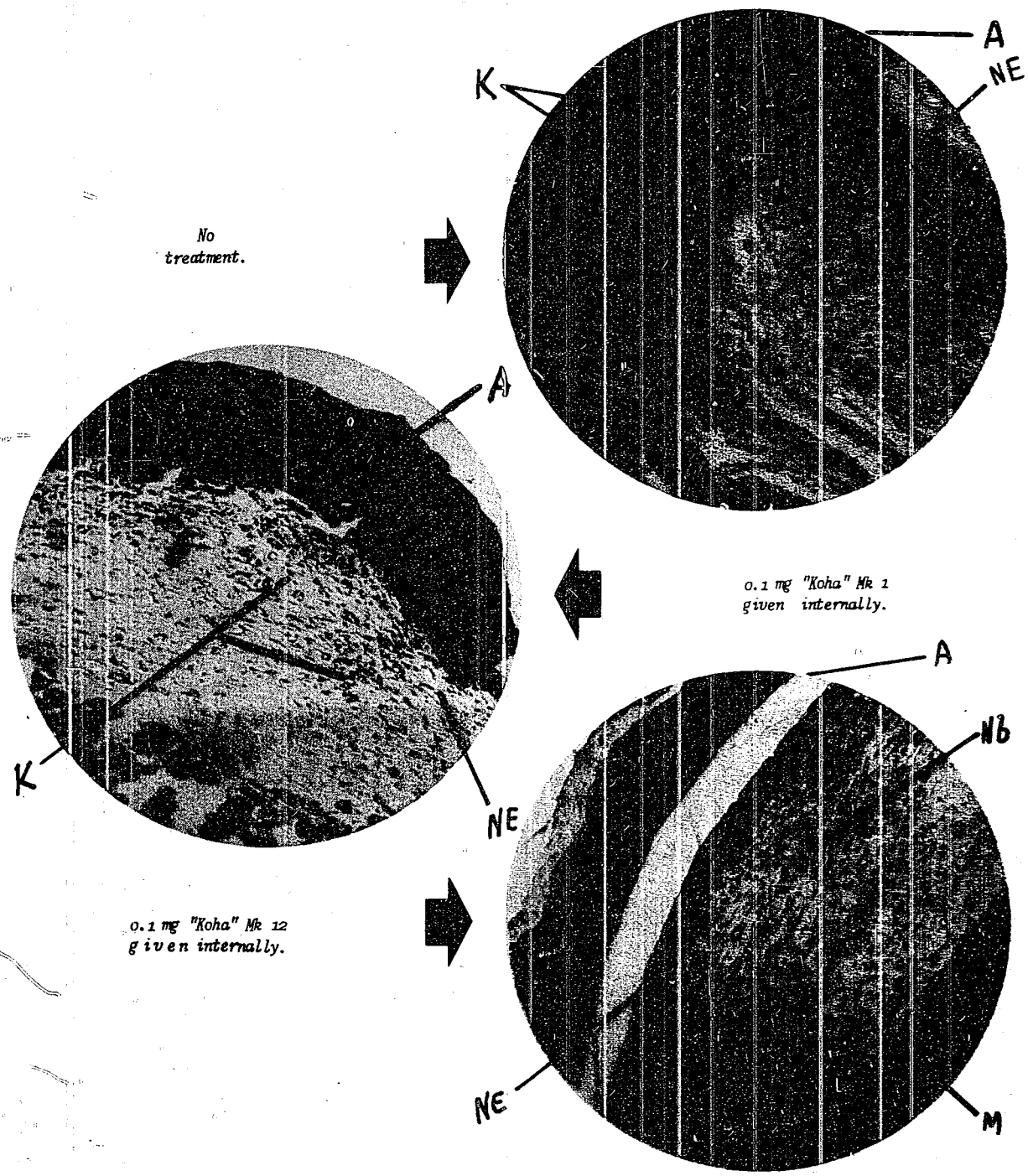
0.01 mg "Koha" Mk 1 given internally.



0.1 mg "Koha" Mk 12 given internally.

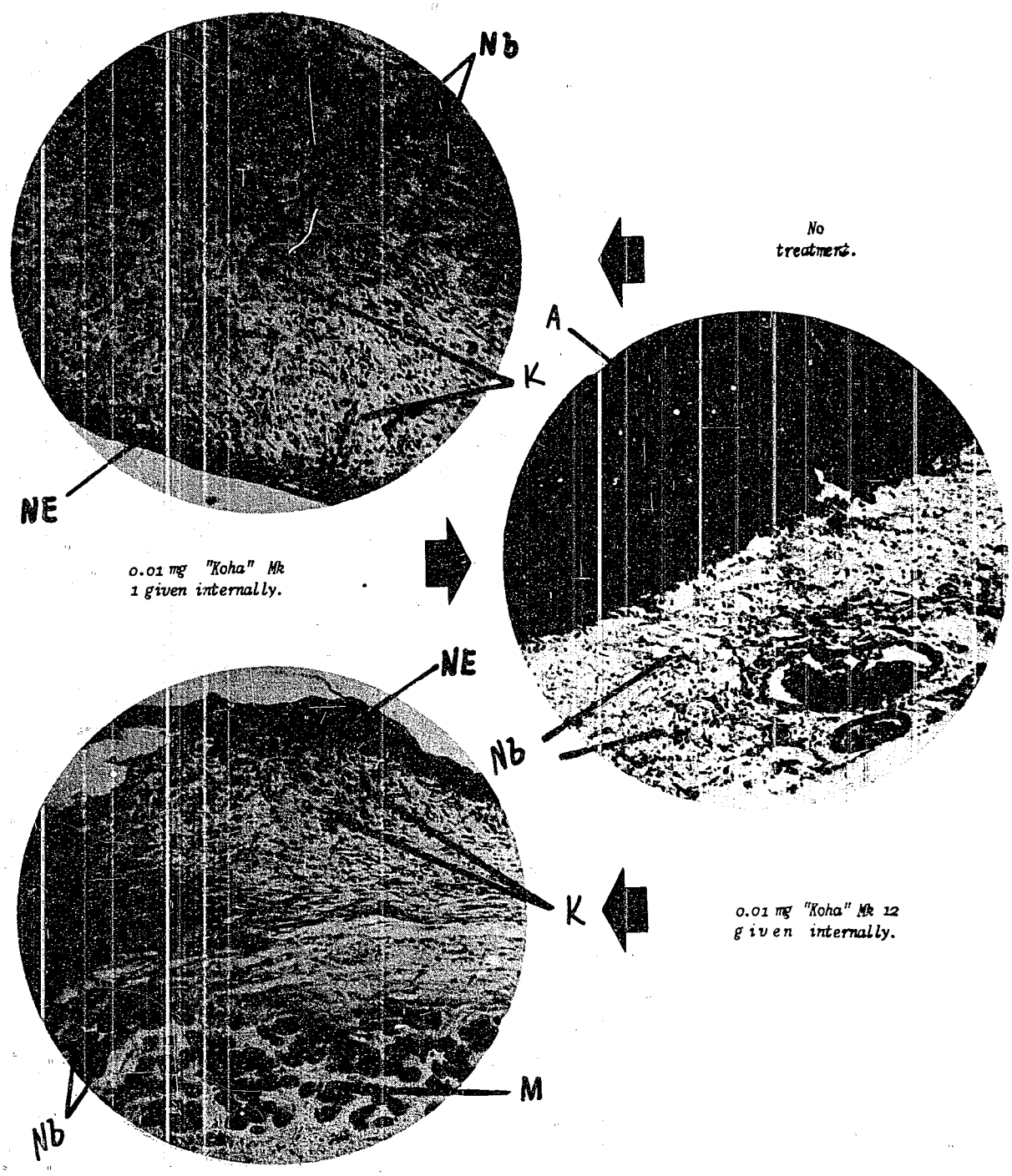
COMPARISON (L) 1
On Third Day

ENCLOSURE (L), continued



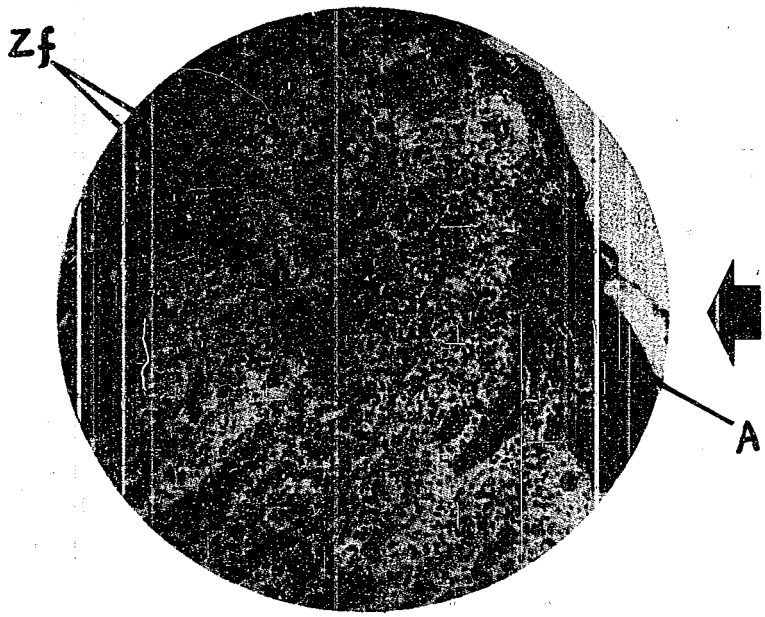
COMPARISON (L)1
(continued)
On Sixth Day

ENCLOSURE (L), continued

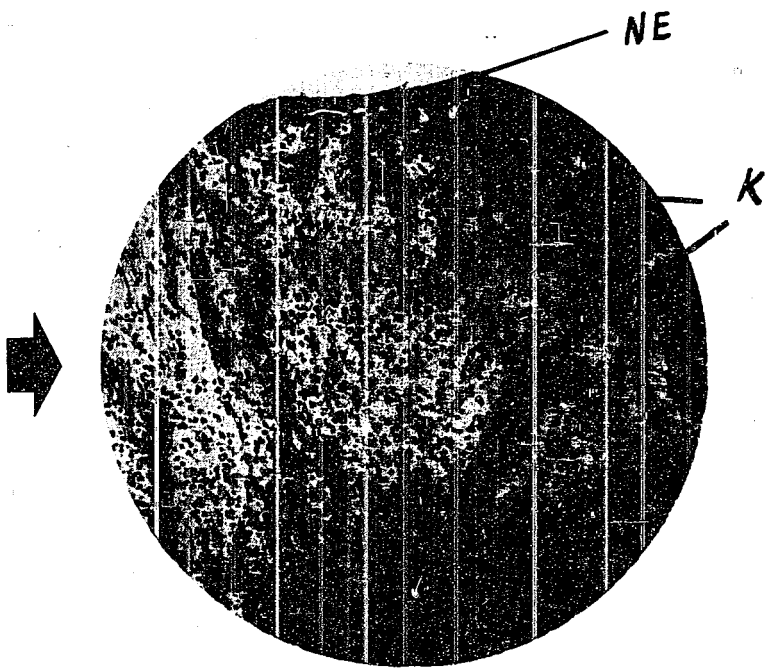


COMPARISON (L) 1
(continued)
On Ninth Day

ENCLOSURE (L), continued



Before treatment.

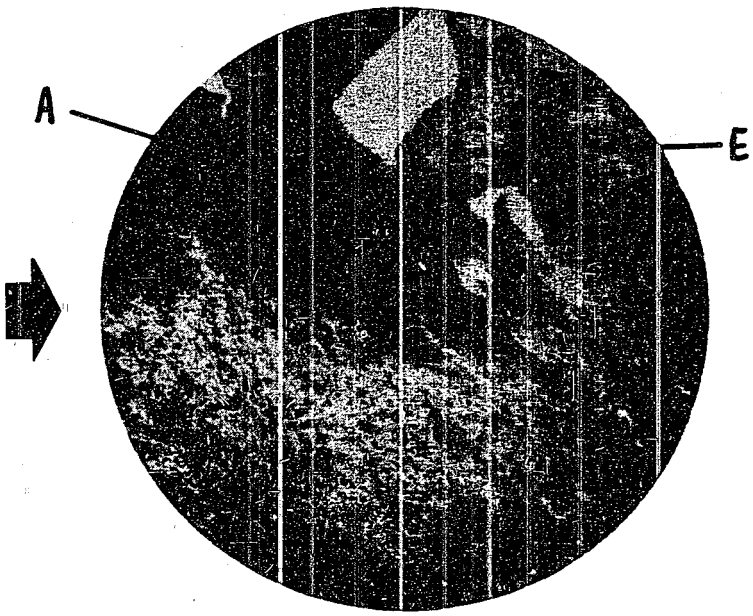


32 days after treatment.

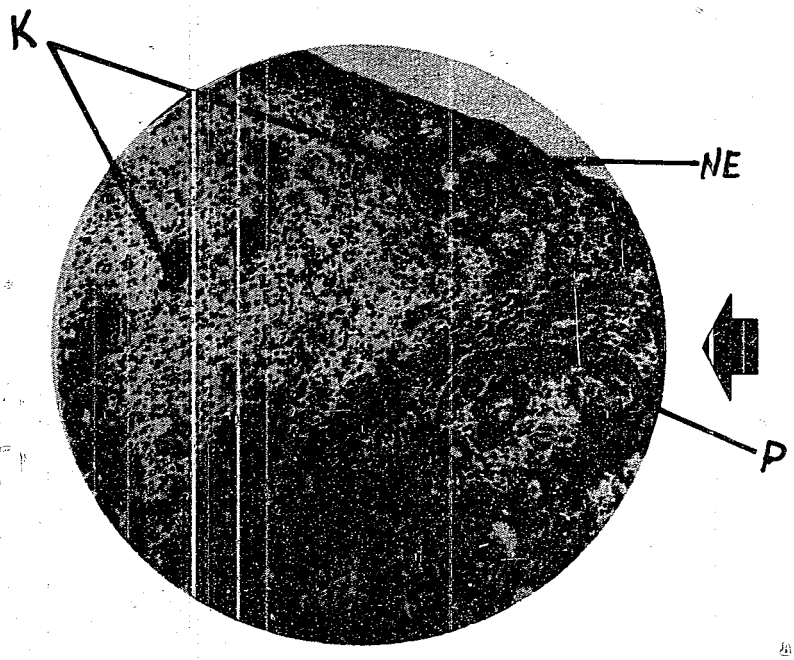
COMPARISON (L)2

Treatment: 0.01 mg "Koha" Nº 12

ENCLOSURE (L), continued



Before treatment.

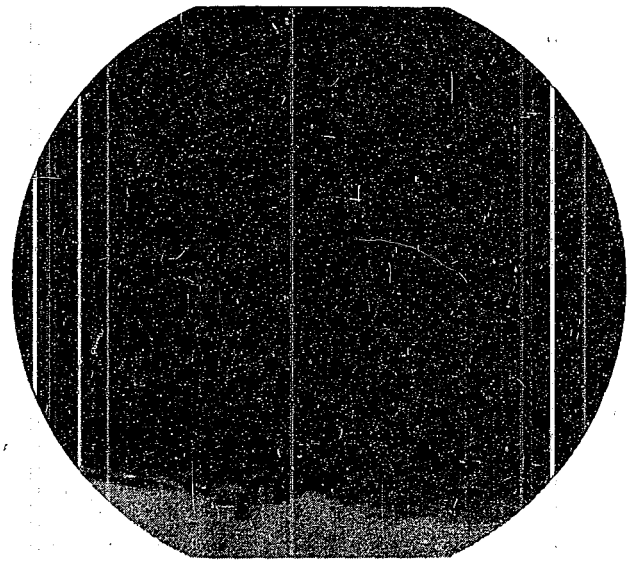


10 days after treatment.

COMPARISON (L)3

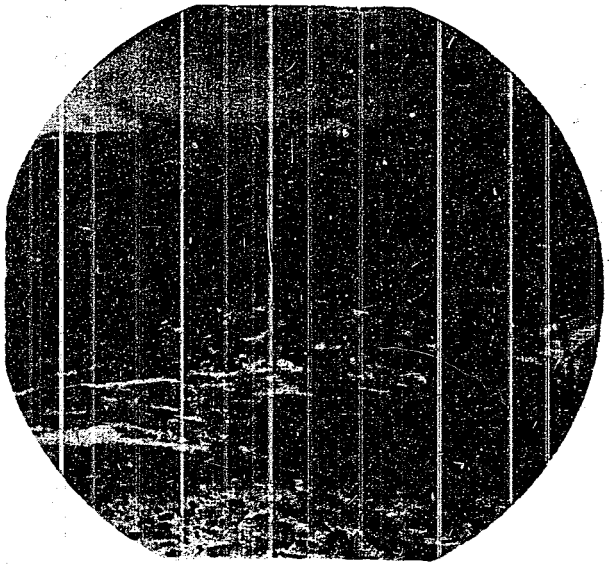
Treatment: 1.0 mg "Koha" Mk 1

ENCLOSURE (L), continued



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

36th day after severance. Traces of Waller's degeneration greatly diminished and only few saturated cells remain.



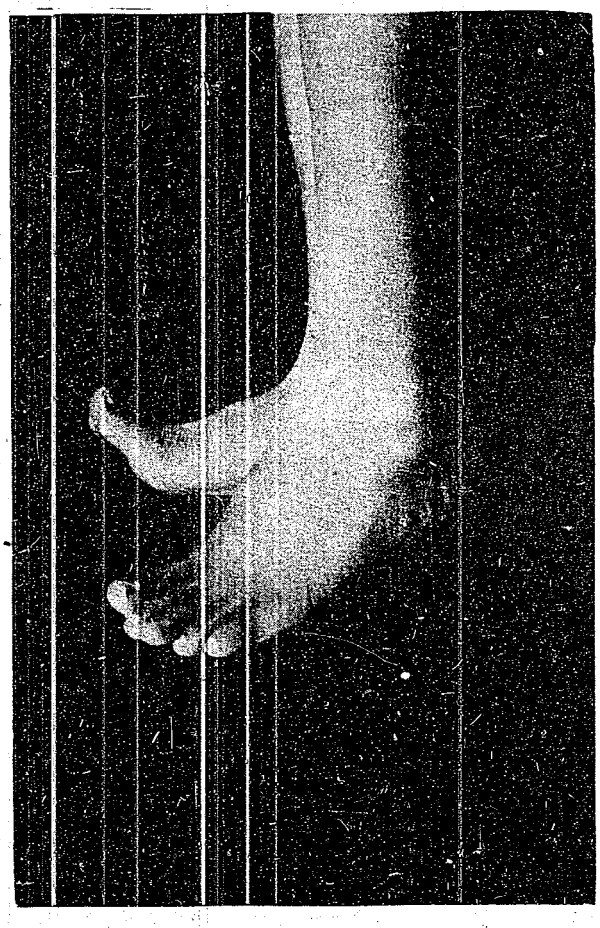
COMPARISON (L)4

Dog Pelvic Nerve

Treatment: 0.2 mg "Koha" Mk 1 given internally daily.

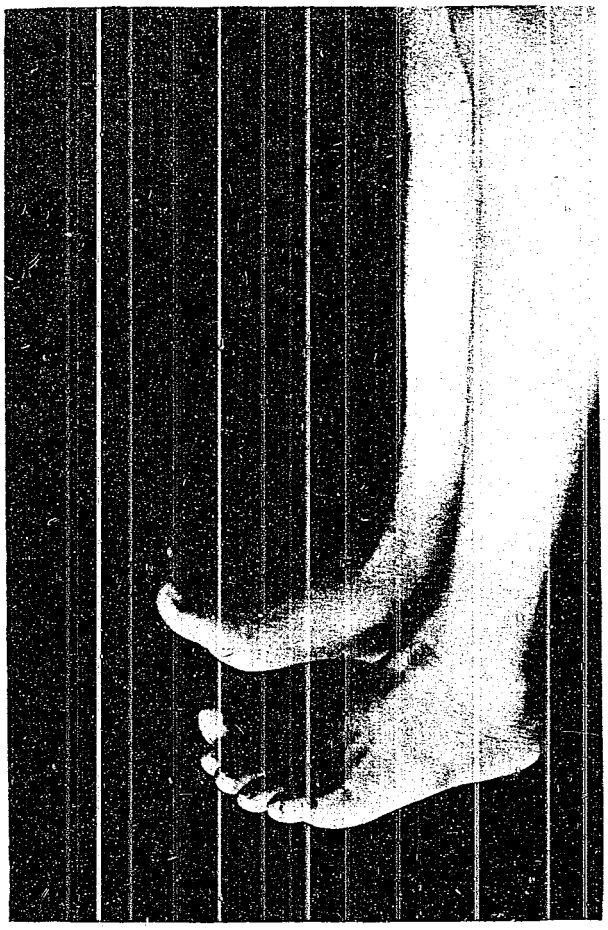
ENCLOSURE (M)

PHOTOGRAPHS SHOWING EFFECTS OF "KOHA" ON FIBULAR NERVES



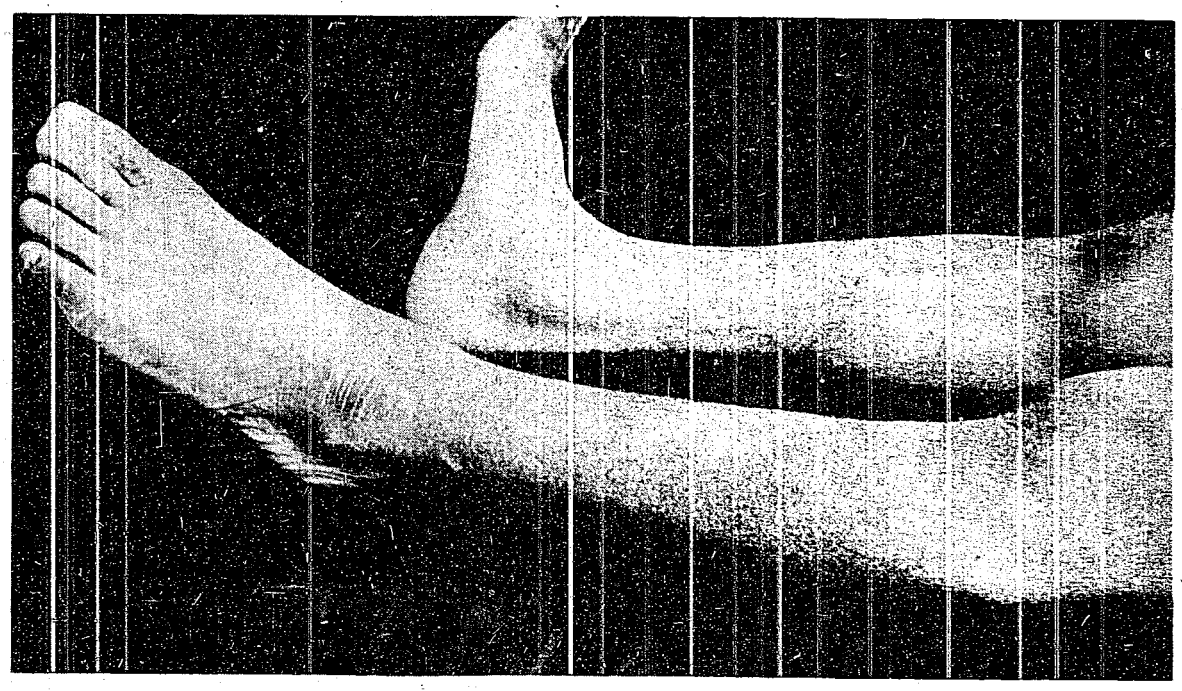
Four days after outbreak and before treatment.

35 days after beginning treatment. Complete recovery.

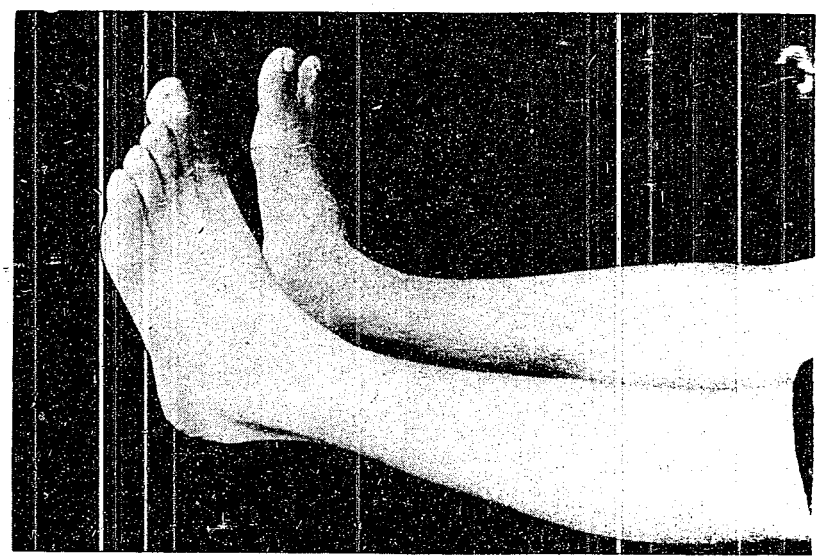


CASE (M) 1
Neuro-Paralysis of Fibular Nerve
Age 17 - Male
Treatment: 0.1 mg "Koha" Mk 1 given internally daily.

ENCLOSURE (M), continued



47 days after receiving wound.
No treatment.



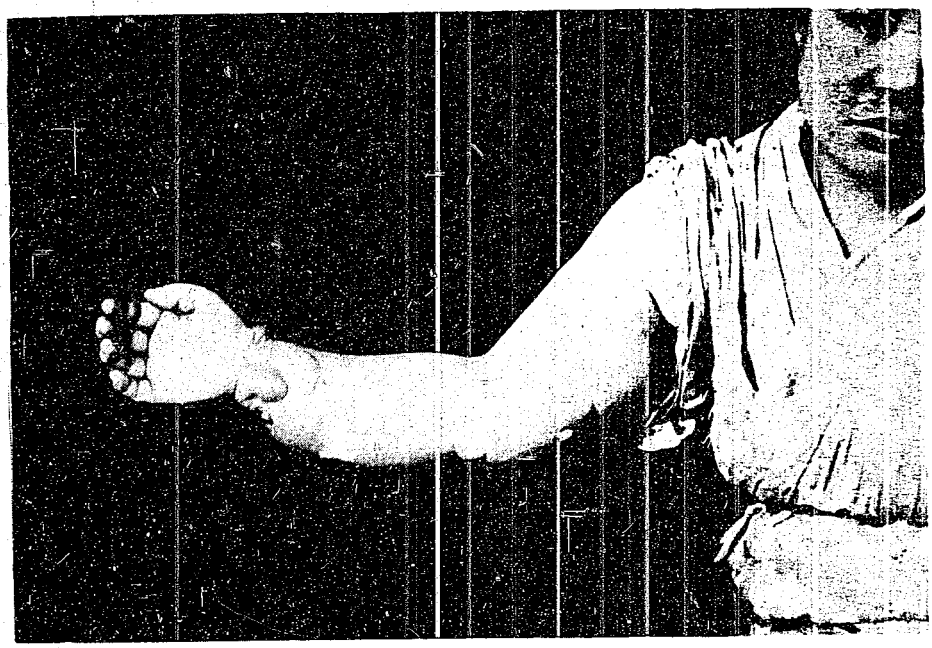
110 days after beginning treatment. Flexion of left foot impossible. No other abnormality.

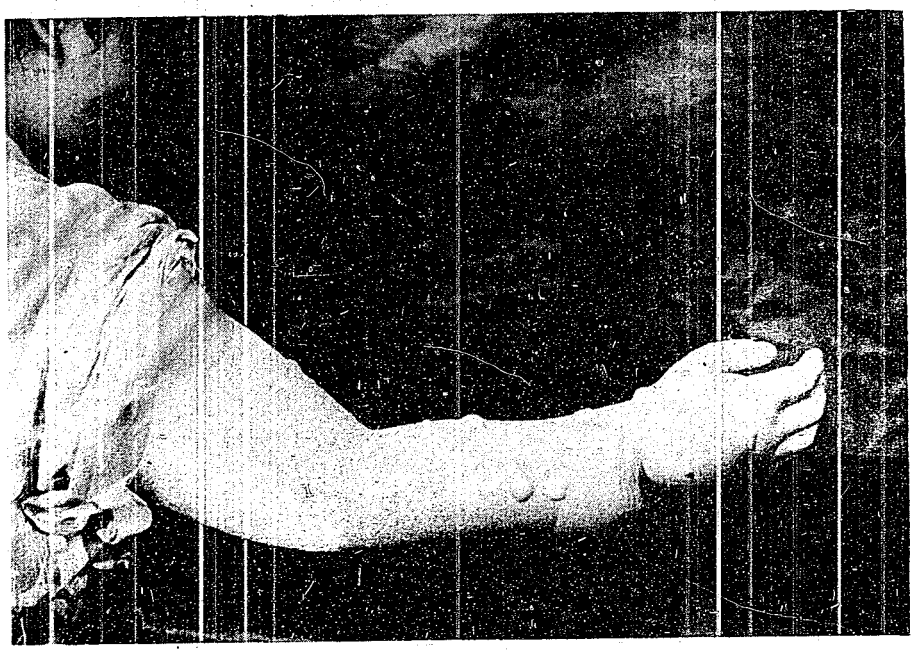
CASE (M)2
Aneurism From Knife Wound in the Thigh
(Also Neuro-Paralysis in Left Fibula)
Age 27 - Male
Treatment: 0.1 mg "Koha" Mk-1 given internally daily.

ENCLOSURE (N)

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

Before treatment. Day after burn.





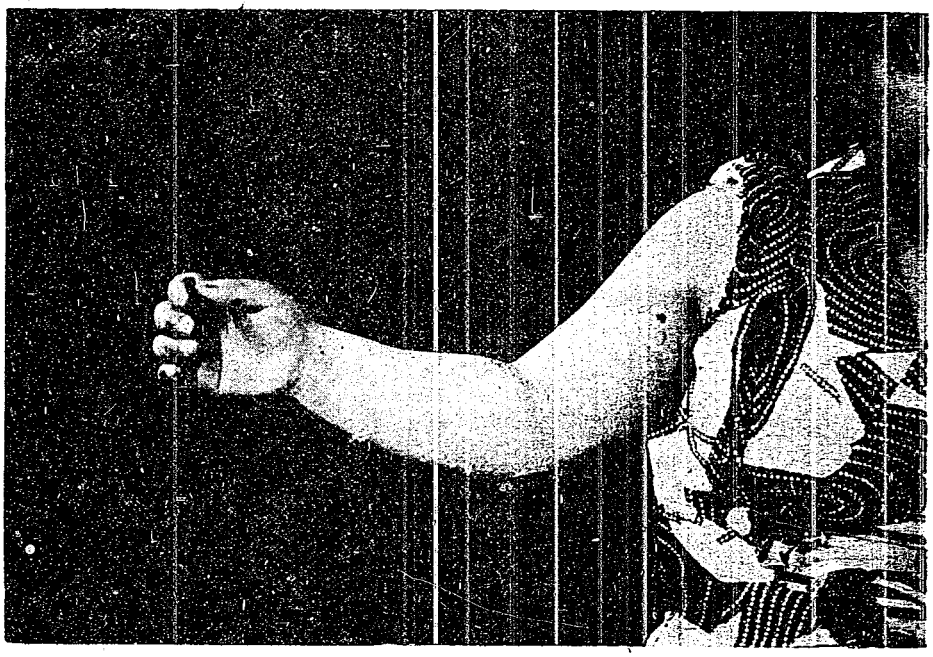
Same as above.

CASE (N) 1

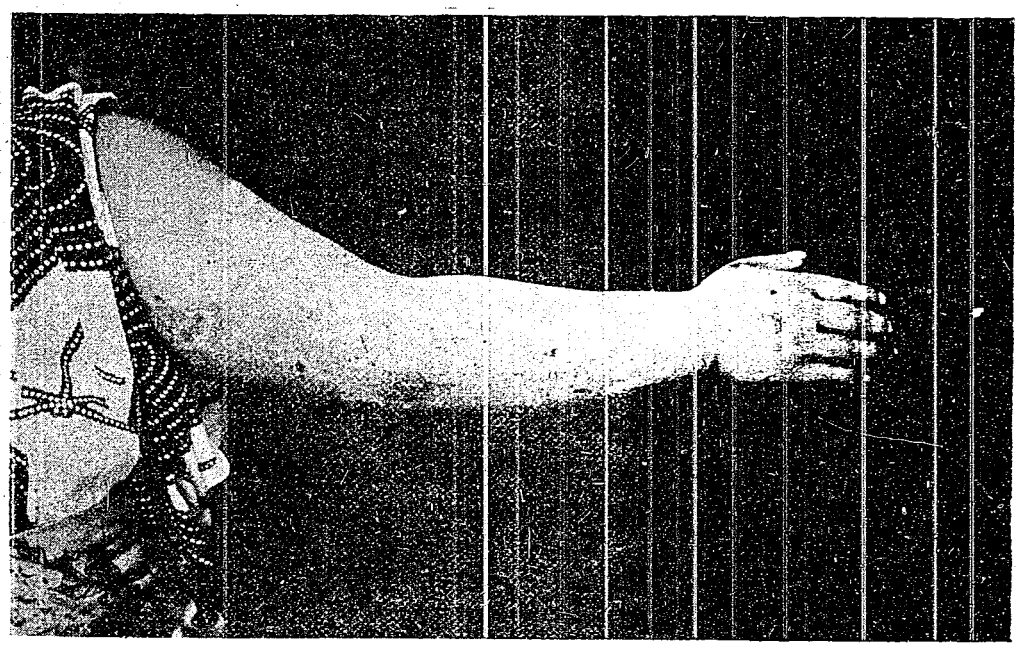
Second Degree Burns From Boiling Water
Age 28 - Female

Treatment: 0.25 mg of "Koha" Mk 1 given internally every day. Ichthyol applied locally.

ENCLOSURE (N), continued



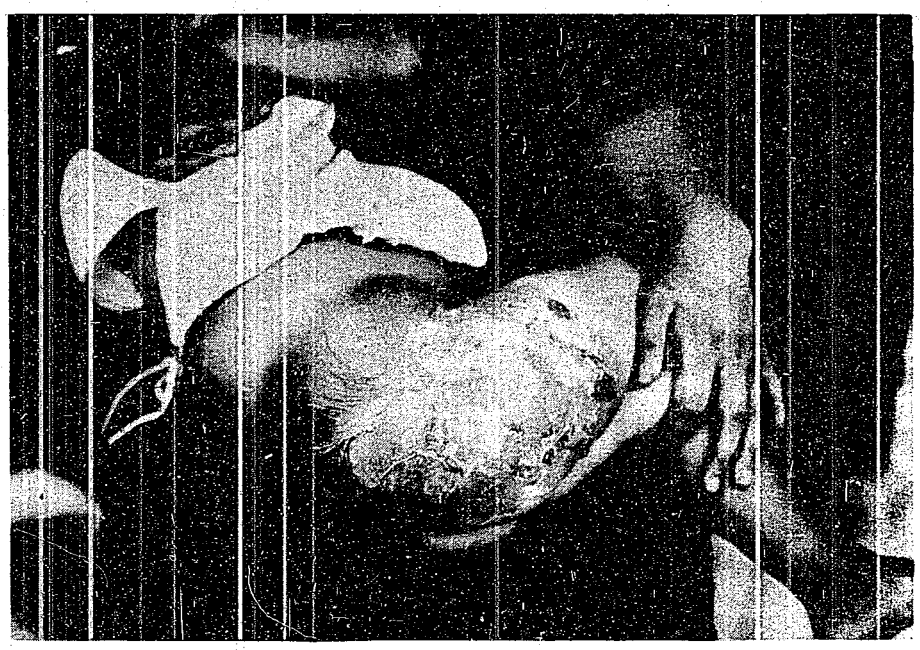
After 15 days.
Full treatment.



Same as above.

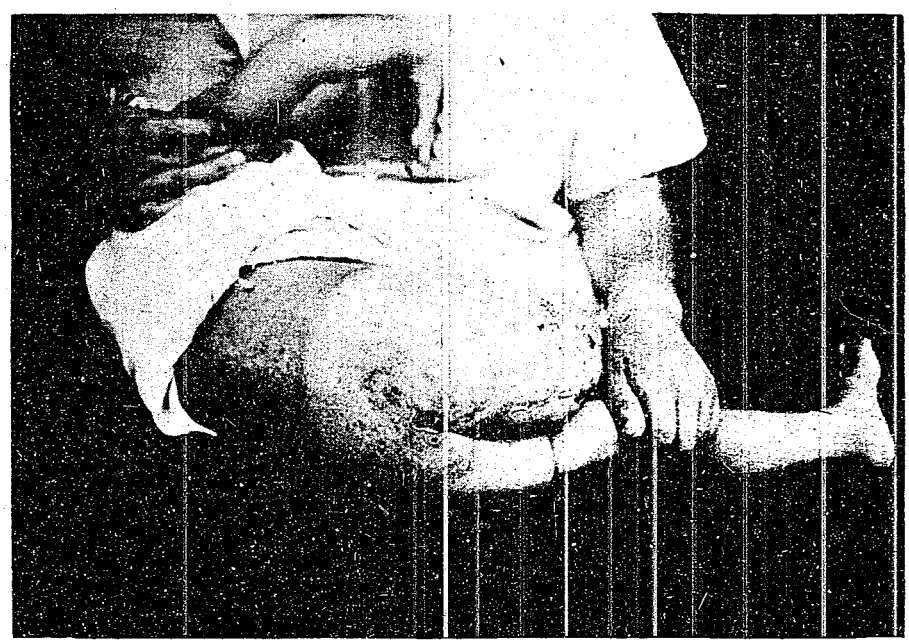
CASE (N)1
(continued)

ENCLOSURE (N), continued



Before treatment. Day after burn.

After six days of treatment.



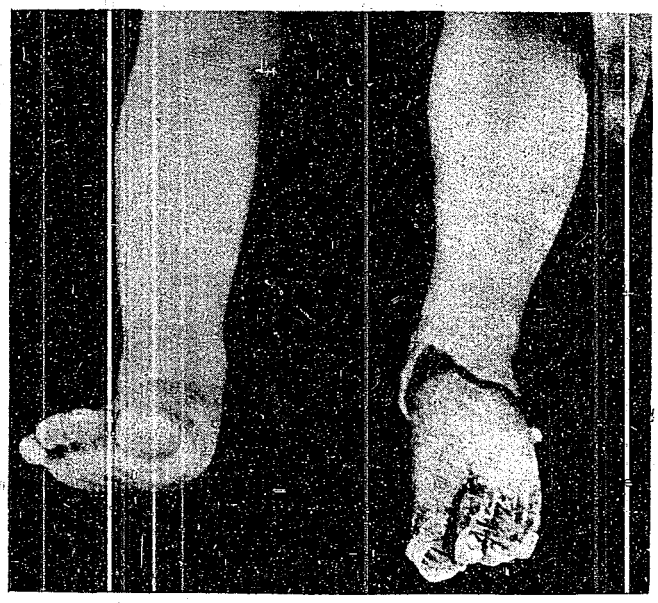
CASE (N)2

Second Degree Burns From Boiling Water
Age 2

Treatment: 0.1 mg "Koha" Mk 1 given internally daily. Ichthyol applied locally.

ENCLOSURE (N), continued

Before treatment.
Day after burn.



Same as above.

CASE (N)3

Second and Third Degree Burns From Boiling Water
Age 3

Treatment: 0.2 mg "Koha" Mk 1 given internally daily. Ichthyol applied locally.

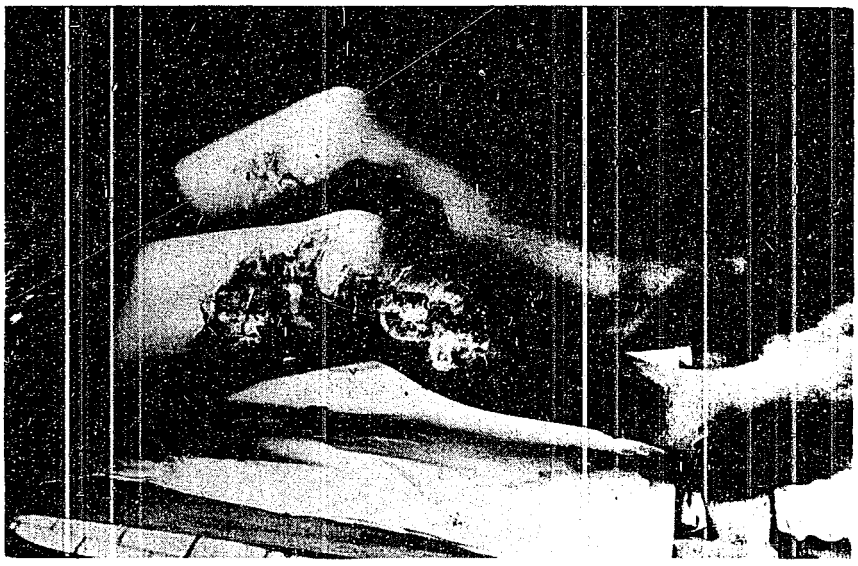
ENCLOSURE (N), continued

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.

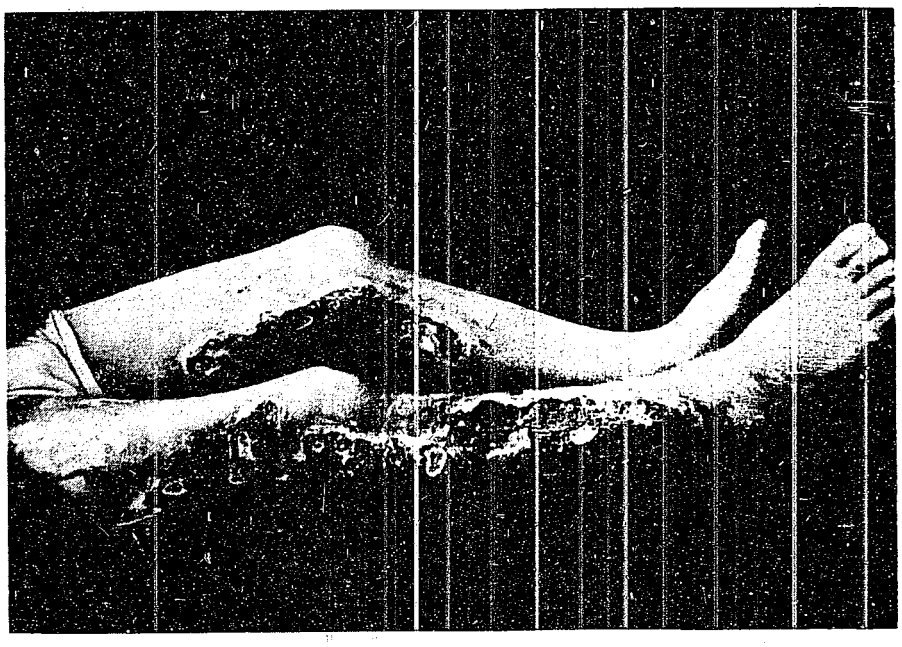
After 17 days of treatment. No fear of death after 10 days. Seven days thereafter Thiersch's grafting technique used.

CASE (N)4

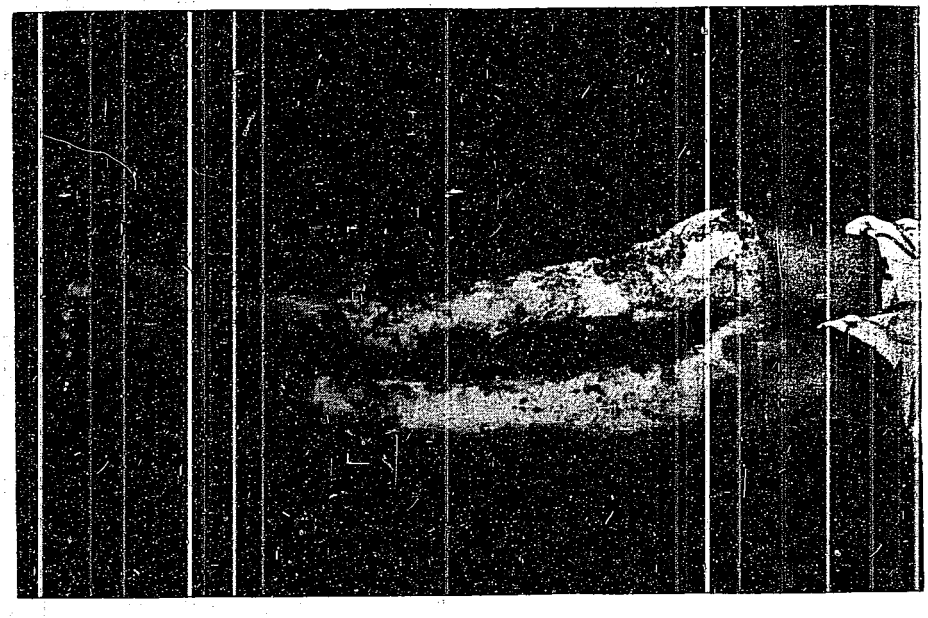
Third Degree Burns From Boiling Water
Age 19 - Female
(Patient is traumatic epileptic)

Treatment: 0.25 mg "Koha" Mk 1 given internally daily. Ichthyol applied locally.

ENCLOSURE (N), continued



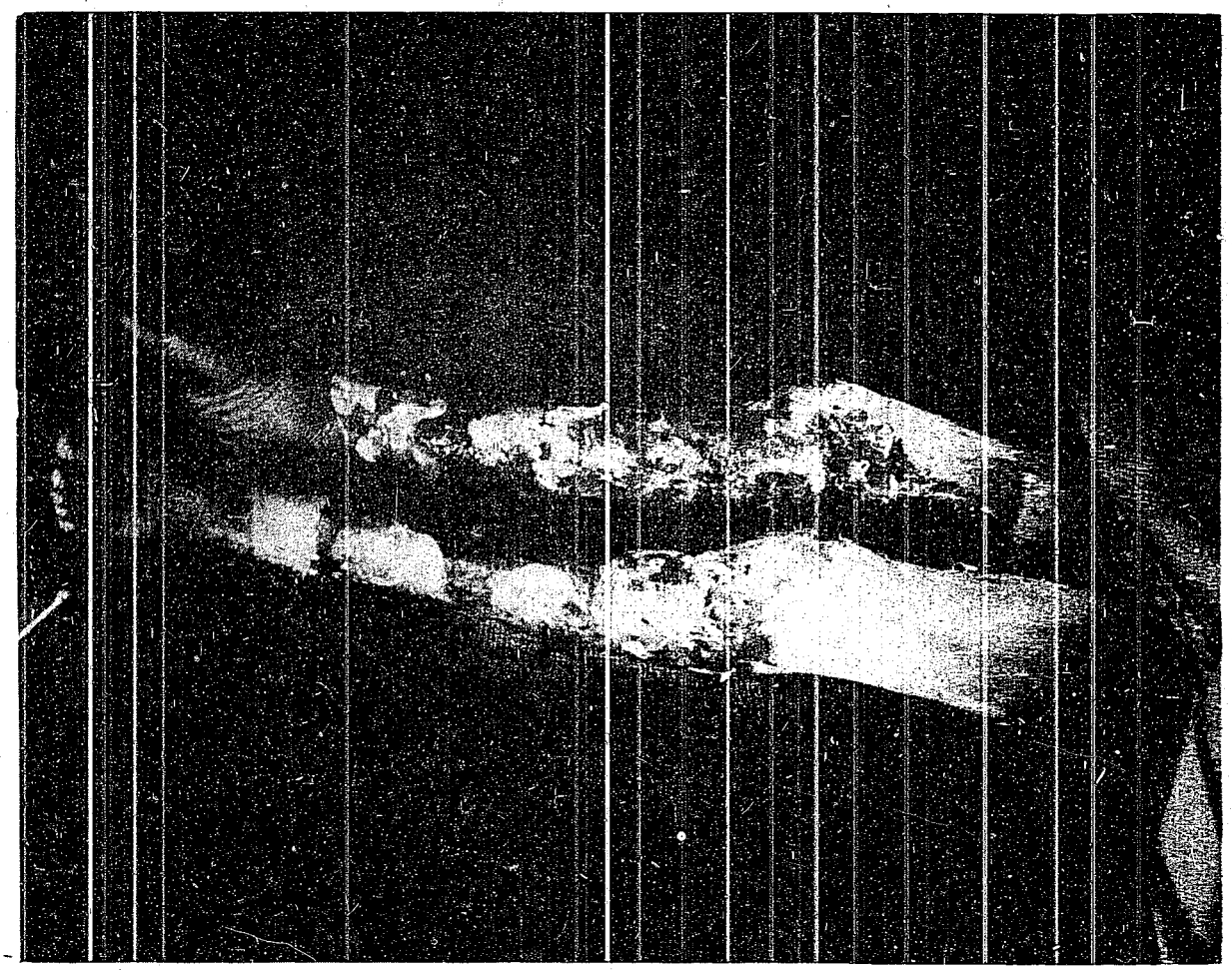
After 45 days of treatment.
12 days after grafting.



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

CASE (N)4
(continued)

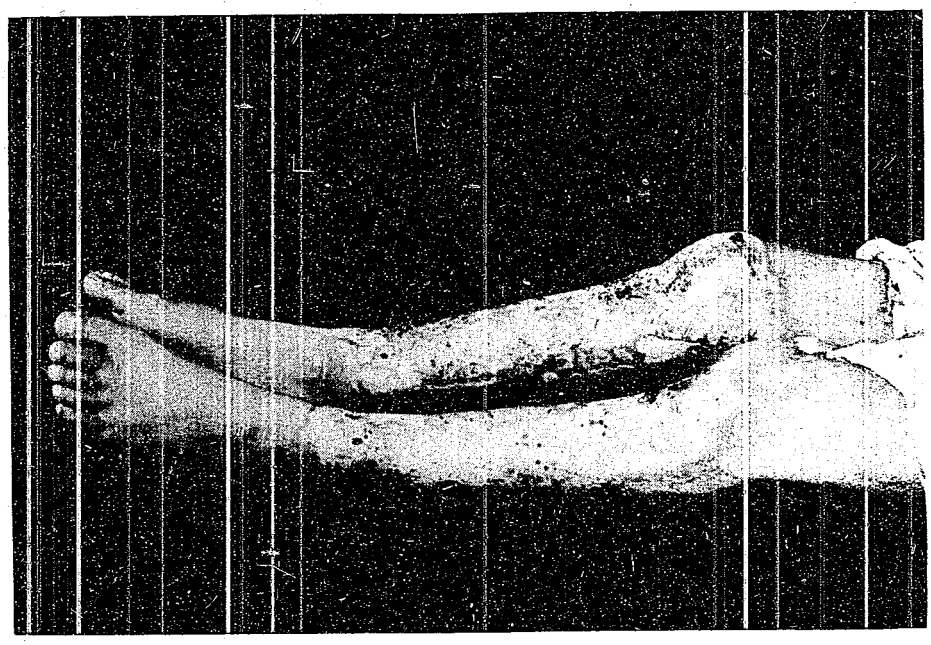
ENCLOSURE (N), continued



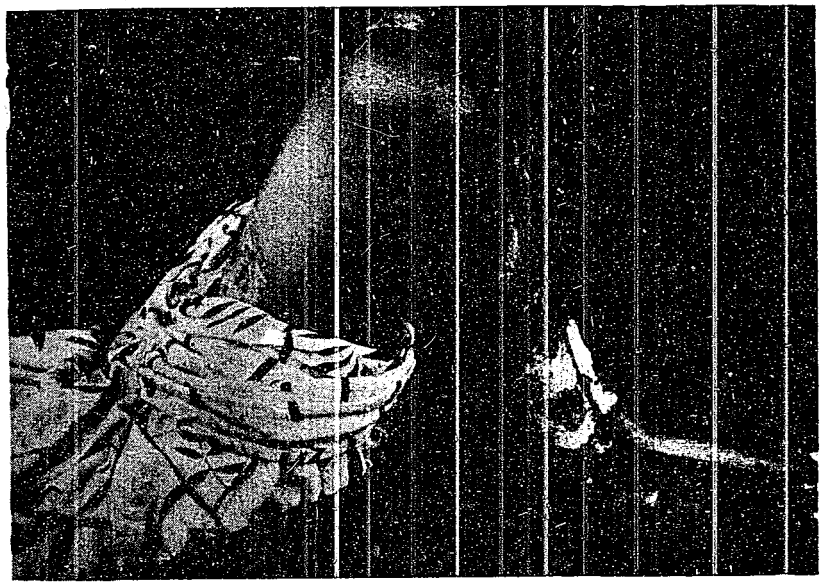
CASE (N)5
Burns From Burning Oil
Age 32

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.

ENCLOSURE (N), continued



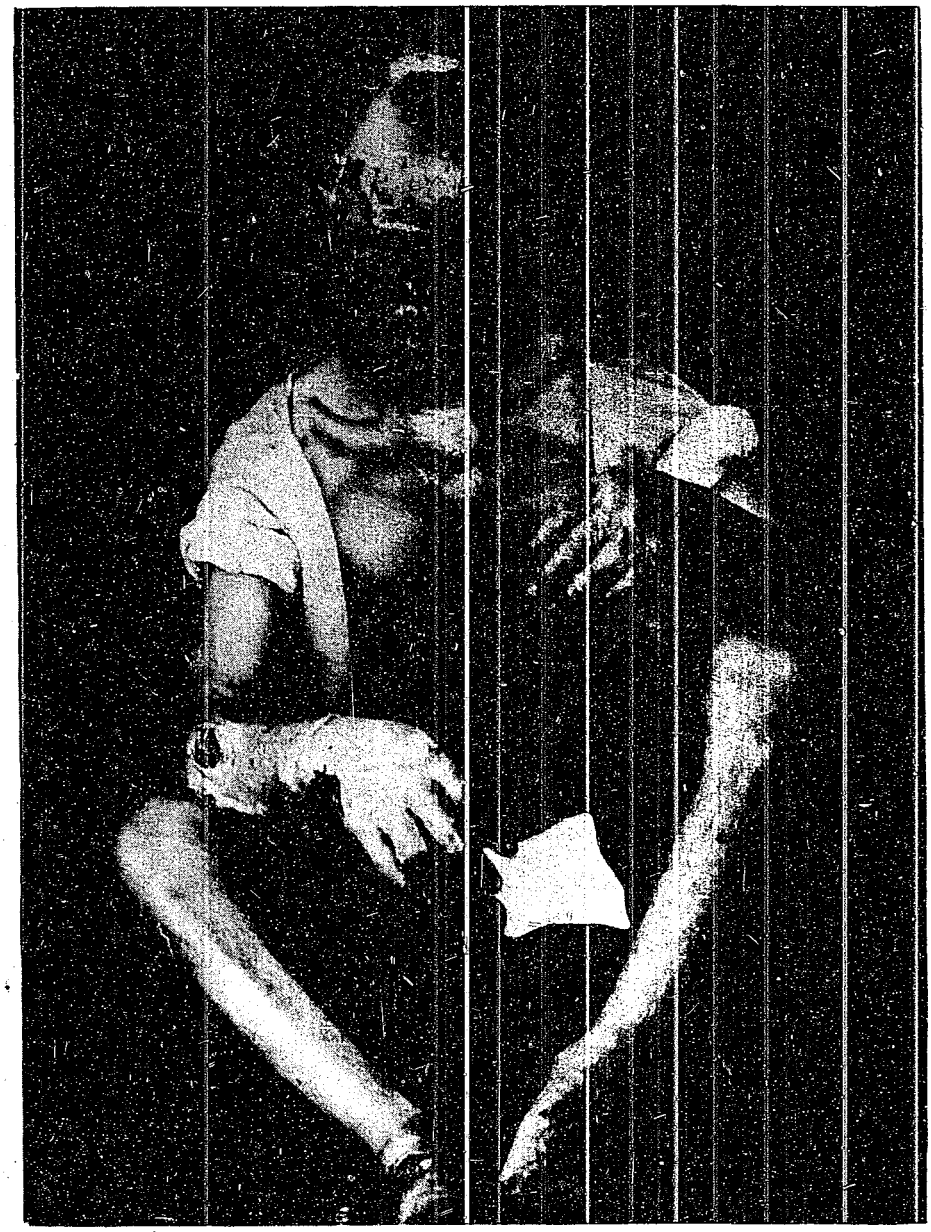
Condition after about 5½ months of treatment. Ulcers have completely healed. Hypodermis has recovered its elasticity. 0.1 mg of "Koha" Mk 1 given internally daily. Ichthyol applied locally.



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

CASE (N)5.
(continued)

ENCLOSURE (N), continued

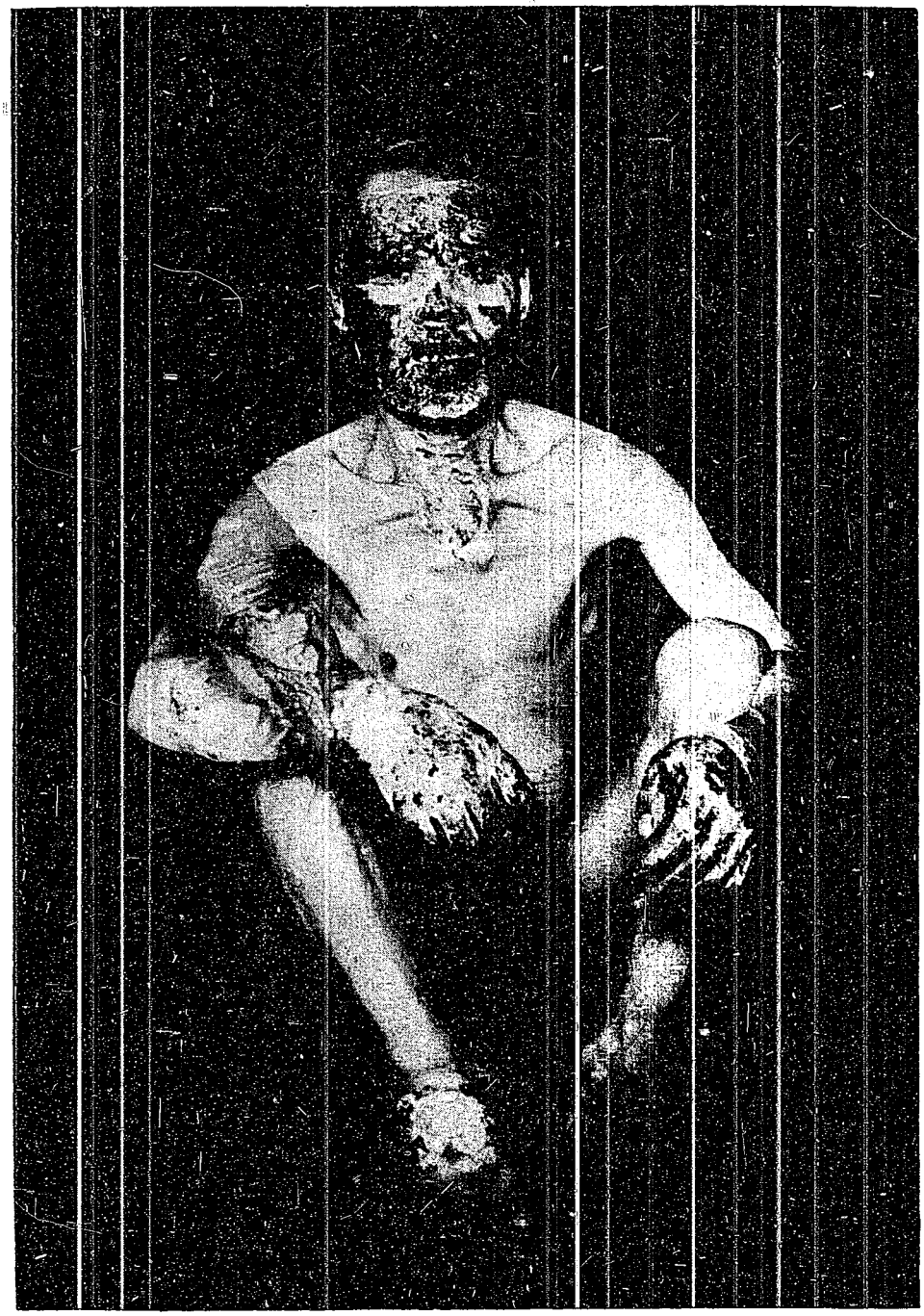


Before treatment.
Seven days after being burned.

CASE (N)6
Benzene Burns
Age 55

Treatment: 0.25 mg "Koha" Mk 1 given internally daily. Ichthyol - boric acid - water preparation applied locally.

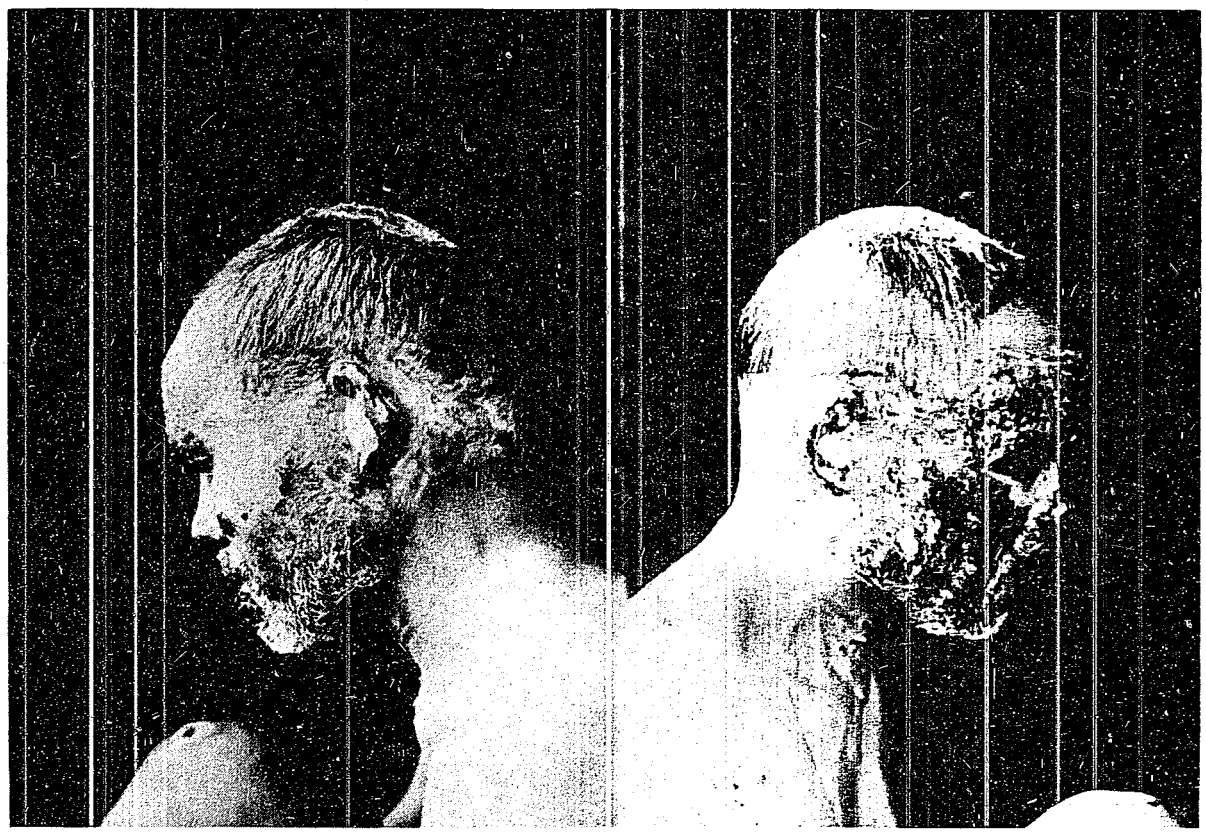
ENCLOSURE (N), continued



After eight days of treatment.

CASE (N)6 (continued)

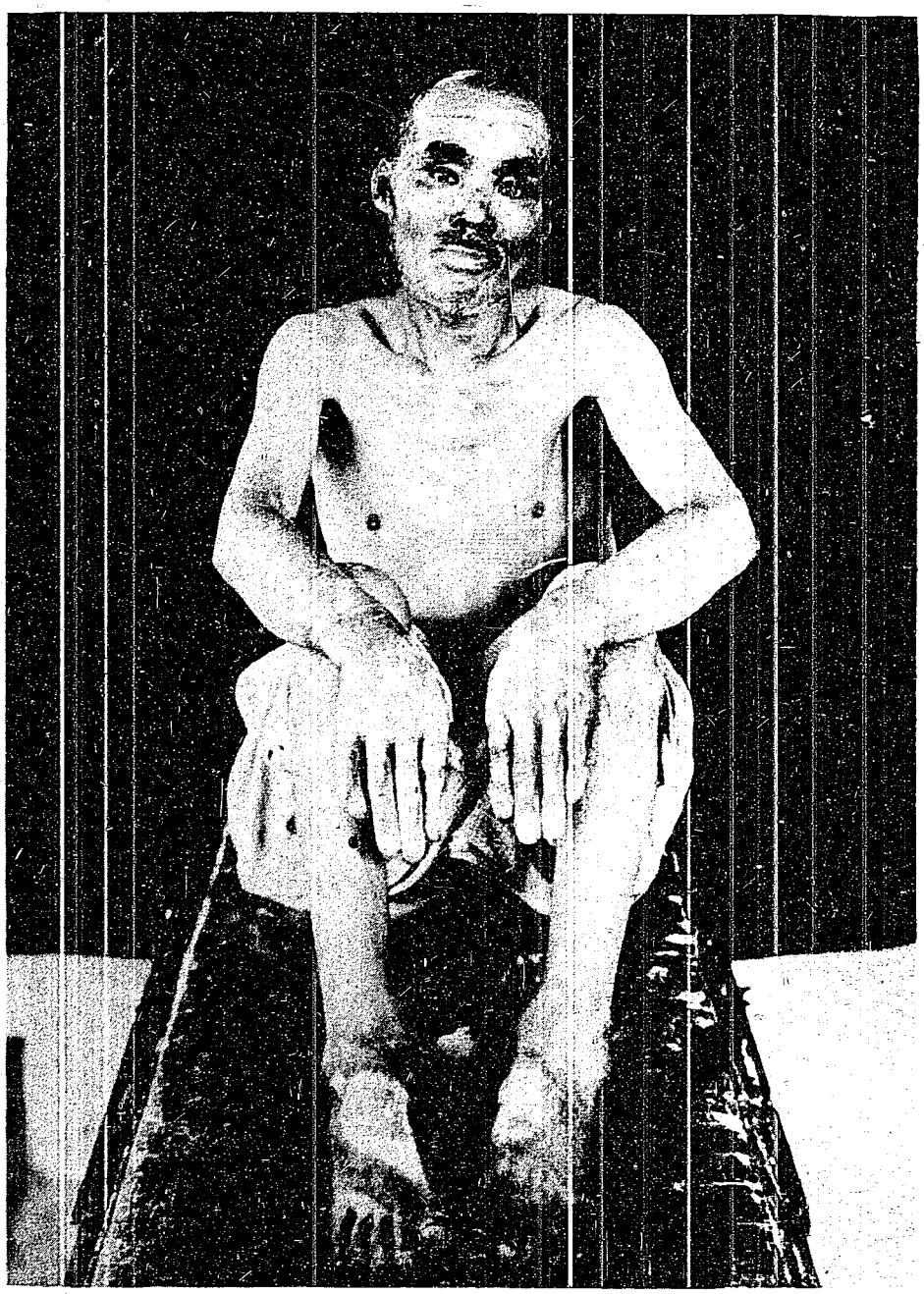
ENCLOSURE (N), continued



Same as front view.

CASE (N)6
(continued)

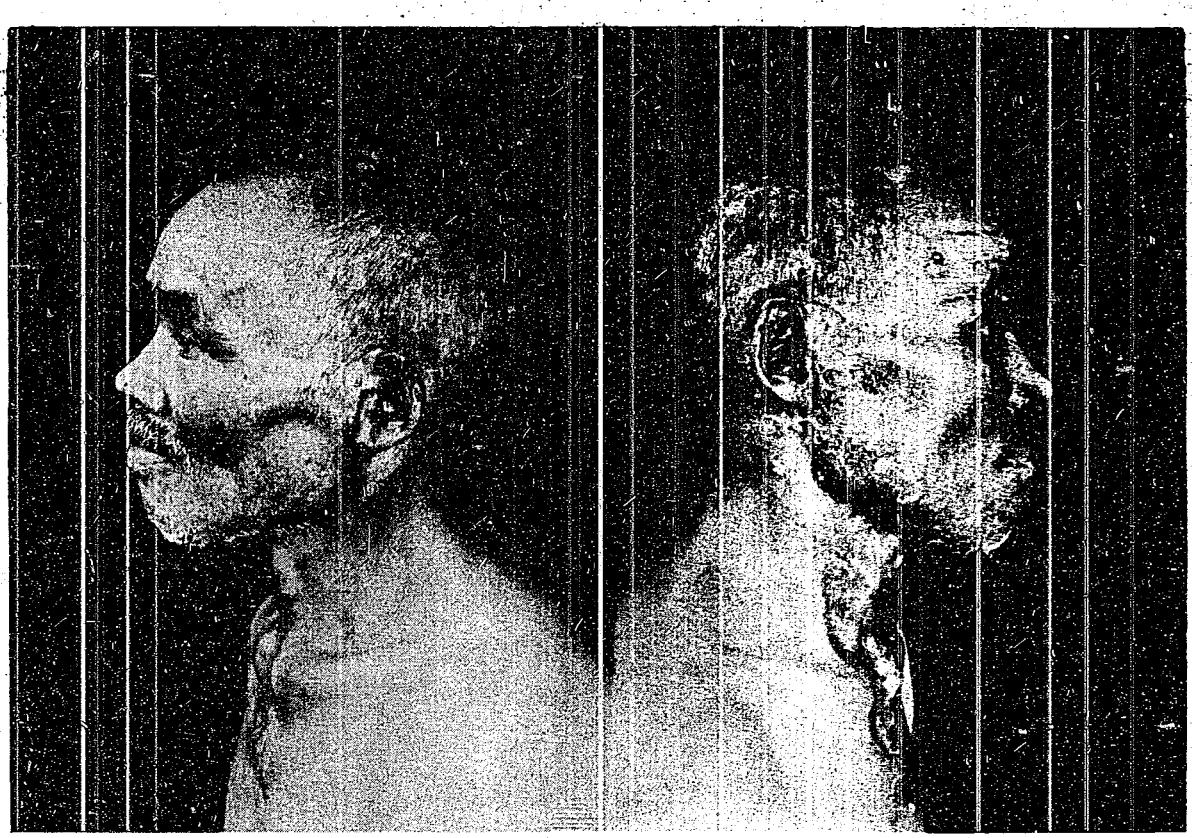
ENCLOSURE (N), continued



After 45 days of treatment. Only light wound scars remain.

CASE (N)6
(continued)

ENCLOSURE (N), continued

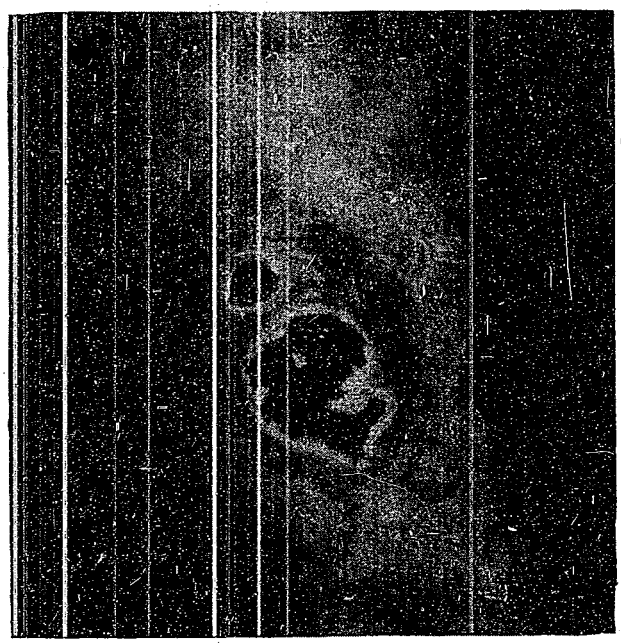


Same as front view.

CASE (N)6
(continued)

ENCLOSURE (O)

PHOTOGRAPHS SHOWING EFFECTS OF TREATMENT OF ULCERS OF THE LEG WITH "KOHA"



Before treatment.
20 days after appearance of ulcer.

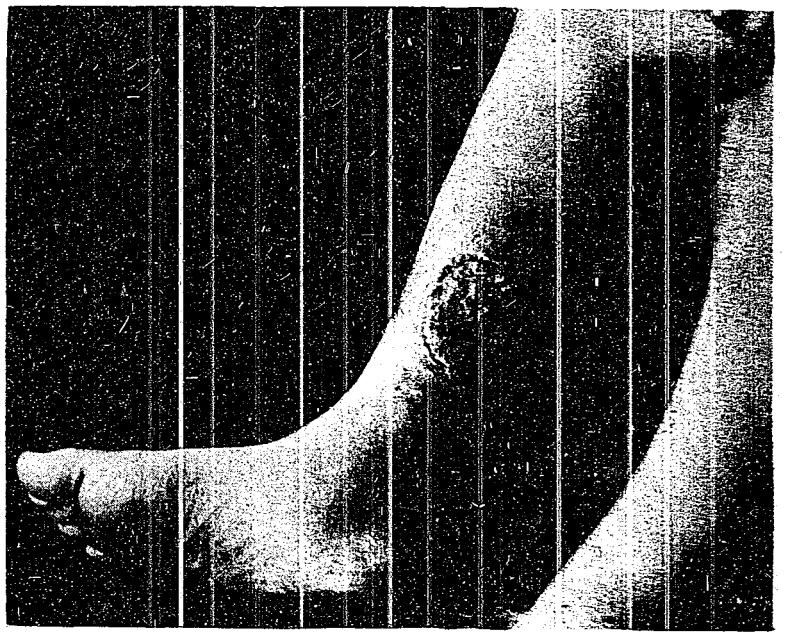
Out patient after 31 days.
Full course of treatment.

CASE (O) 1
Age 18 – Female

Treatment: 1.0 mg "Koha" Mk 1 administered internally once a day. Boric acid ointment applied locally.

ENCLOSURE (O), continued

Before treatment. 15 months after appearance of ulcer.

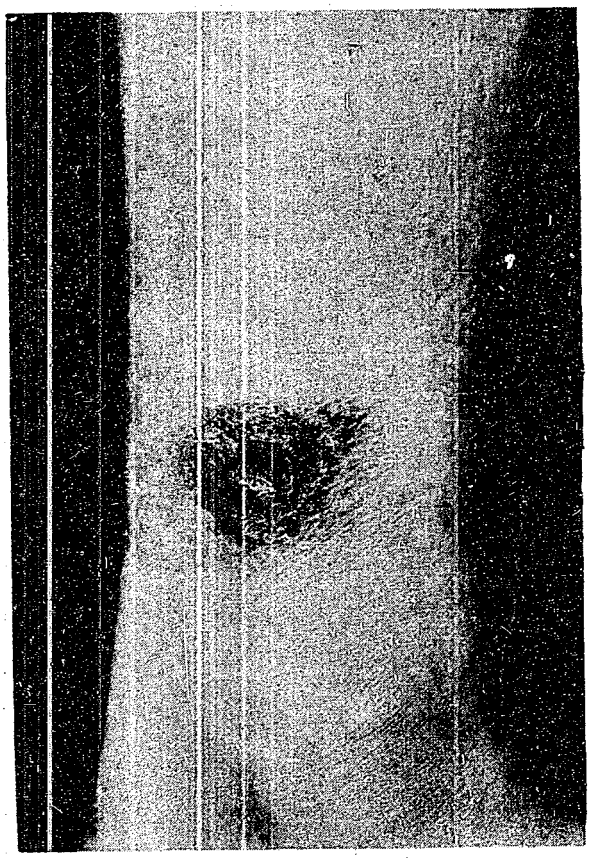


After 51 days of treatment. Full course. Hospitaliz d.

CASE (O)2
Age 25 - Female

Treatment: 0.01 mg "Koha" Nr 12 administered internally once a day. Rivanol gauze and boric acid-water-schthyol preparation applied locally.

ENCLOSURE (O), continued



Before treatment.
20 days after appearance of ulcer.

Out patient after 33 days of treatment.
Full course.

CASE (O)3
Age 17 - Female
Treatment: "Koha" gauze applied locally. Improvement s l ight.

ENCLOSURE (P)

PHOTOGRAPHS SHOWING EFFECTS OF " KOHA" TREATMENT ON TUBERCULAR LYMPHADENITES

Before Treatment

37 Days After Treatment

CASE (P) 1

ENCLOSURE (P), continued

Before Treatment

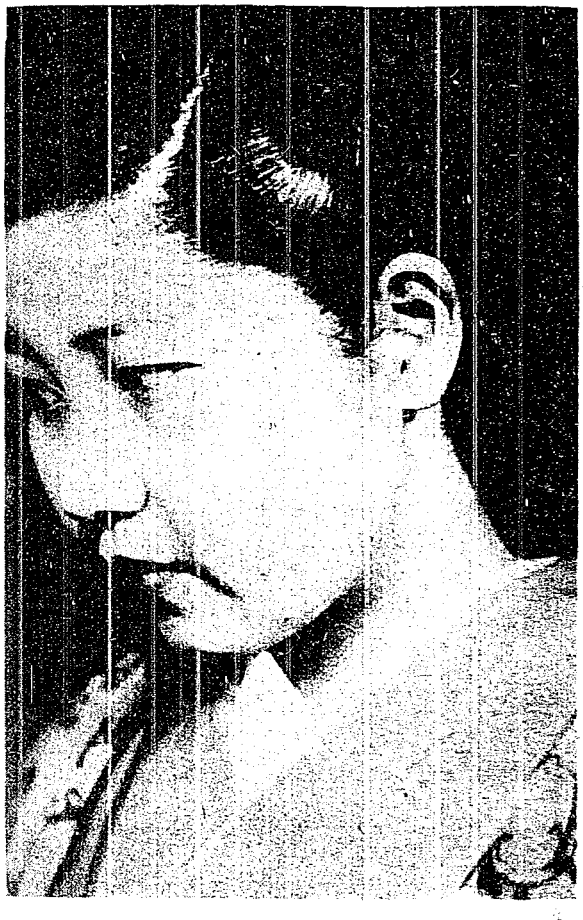
103 Days After Treatment

CASE (p)2

ENCLOSURE (P), continued

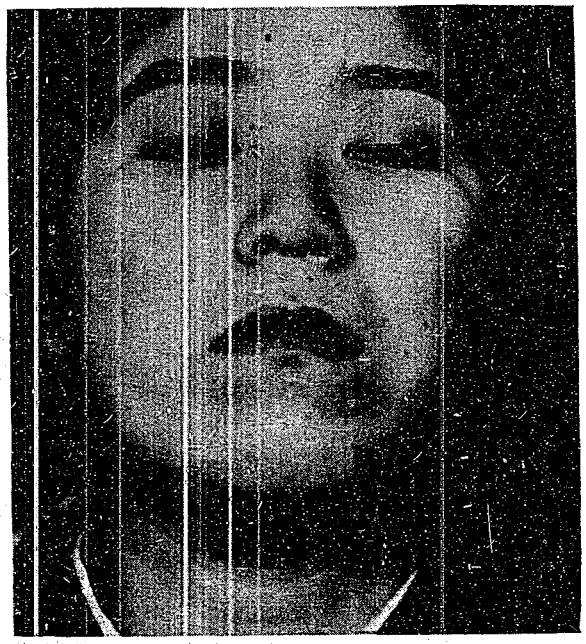
Before Treatment

15 Days
After
Treatment



CASE (p)3

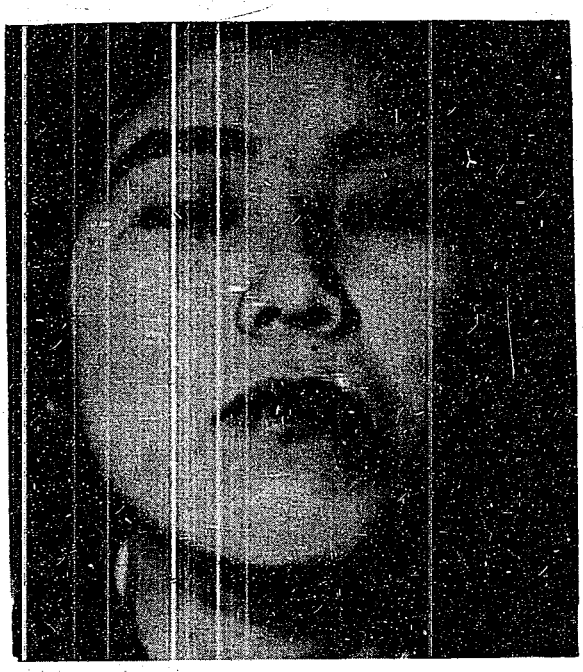
ENCLOSURE (P), continued



Before Treatment

After Treatment

66 Days After Treatment.
After 15 Intravenous Injections



CASE (P)4

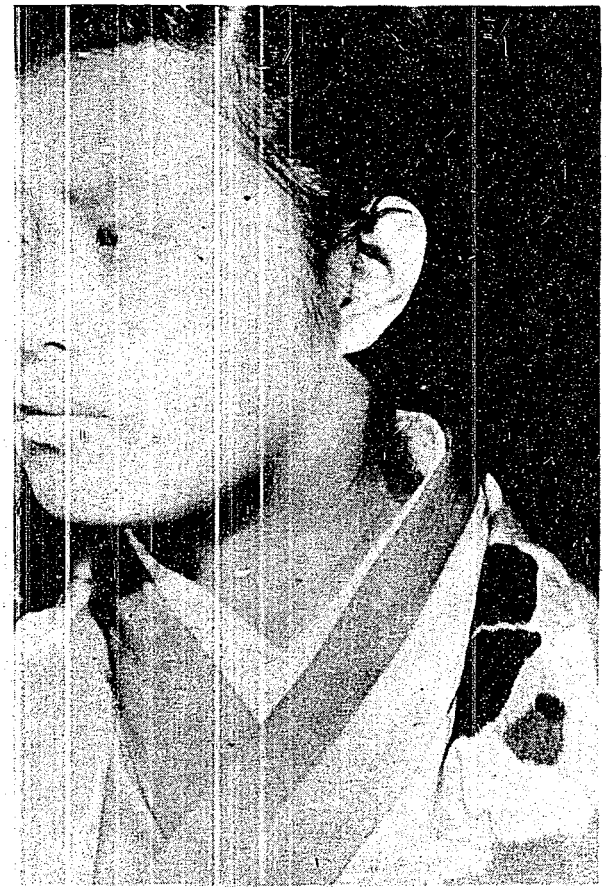
ENCLOSURE (P), continued

Ulcer Before Treatment

77 Days After Treatment

CASE (P)5

ENCLOSURE (P), continued



Before Treatment

440 Days After Treatment

CASE (P)6

ENCLOSURE (P), continued

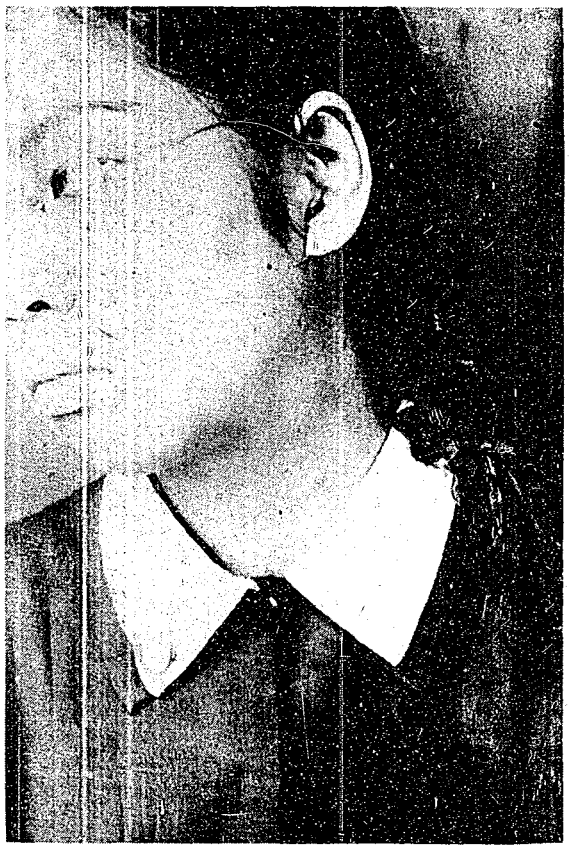
Before Treatment

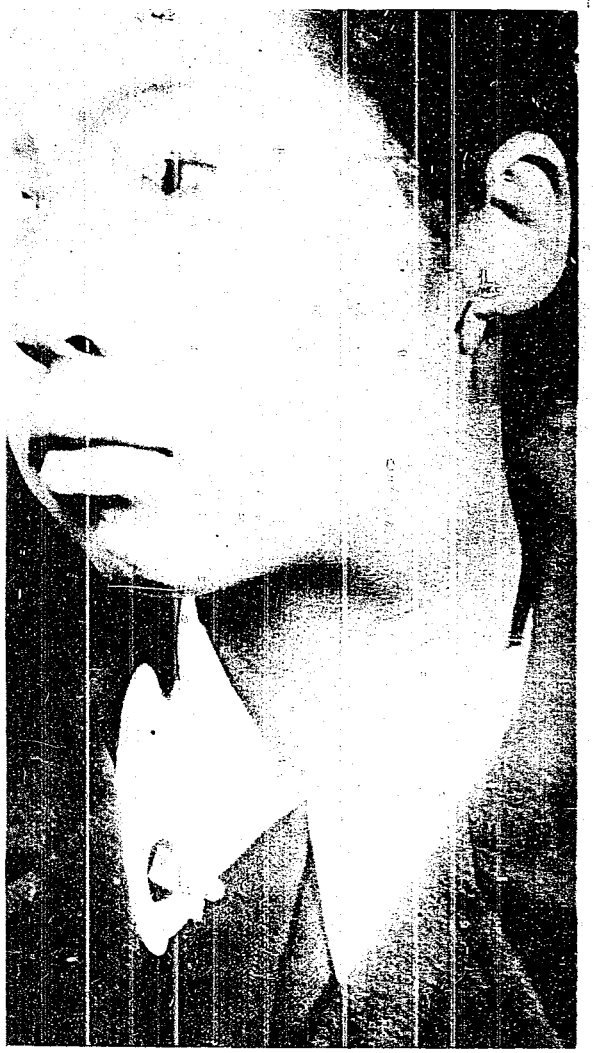
420 Days
After
Treatment

CASE (p)7

ENCLOSURE (P), continued

Before Treatment

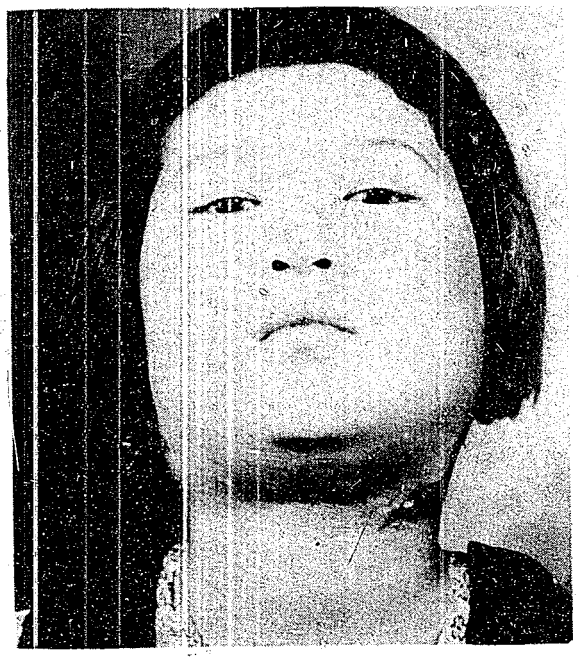




420 Days After Treatment

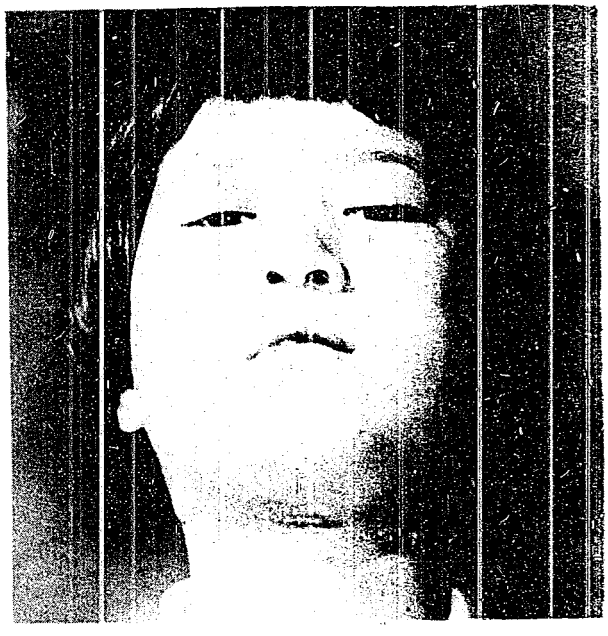
CASE (P)7

ENCLOSURE (P), continued



Before Treatment

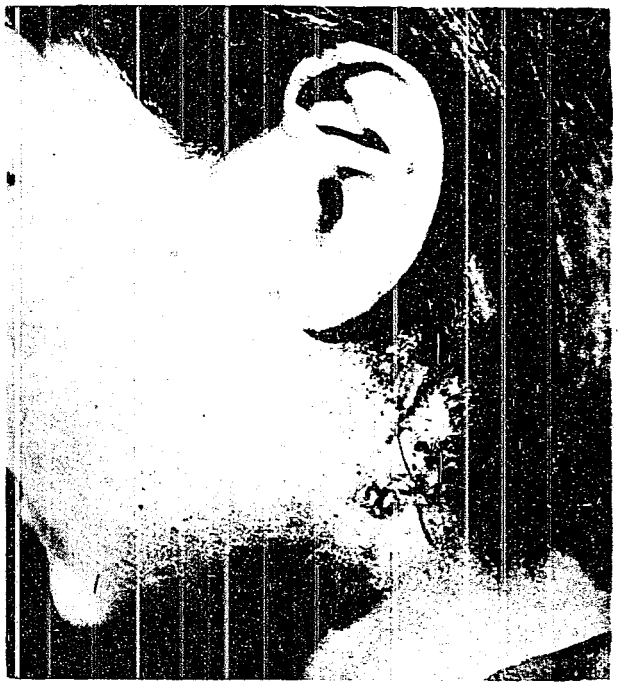
After 46 Days of Giving 0.1 mg of "Koha" Mk 1 Internally



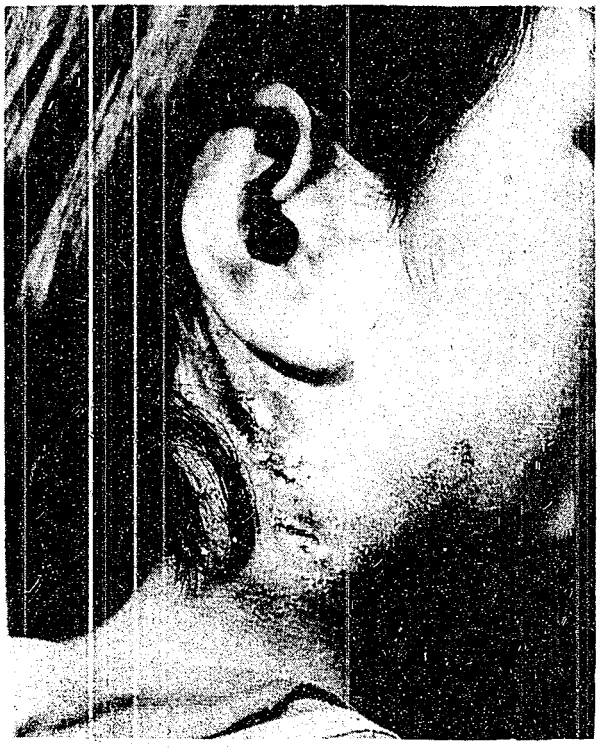
CASE (p)8

Treatment: "Koha" Mark 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.

ENCLOSURE (P), continued



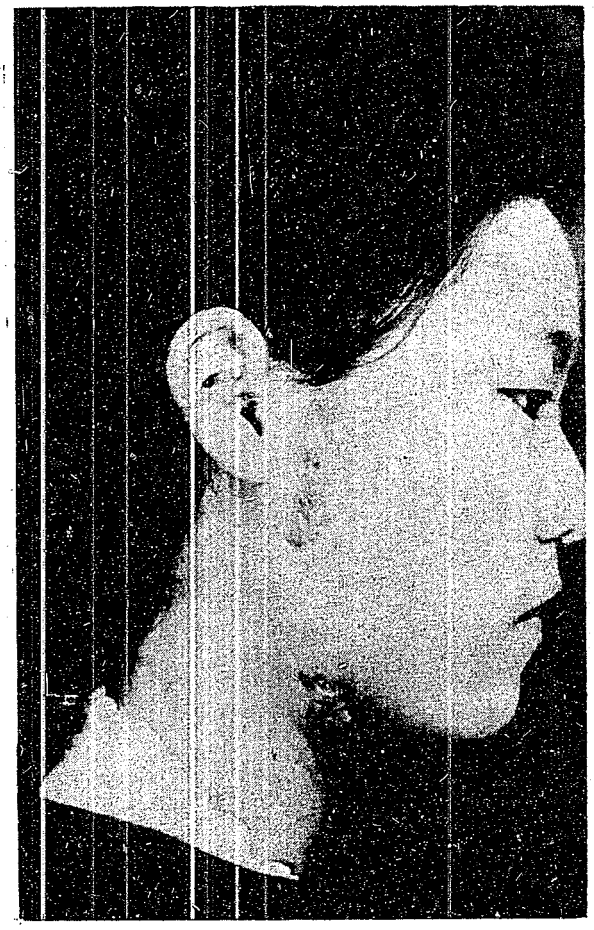
315 Days After Treatment Was Begun



315 Days After Treatment Was Begun

CASE (P)8 (continued)

ENCLOSURE (P), continued



Ulcer Before Treatment

126 Days After Treatment Was Begun

CASE (p)9

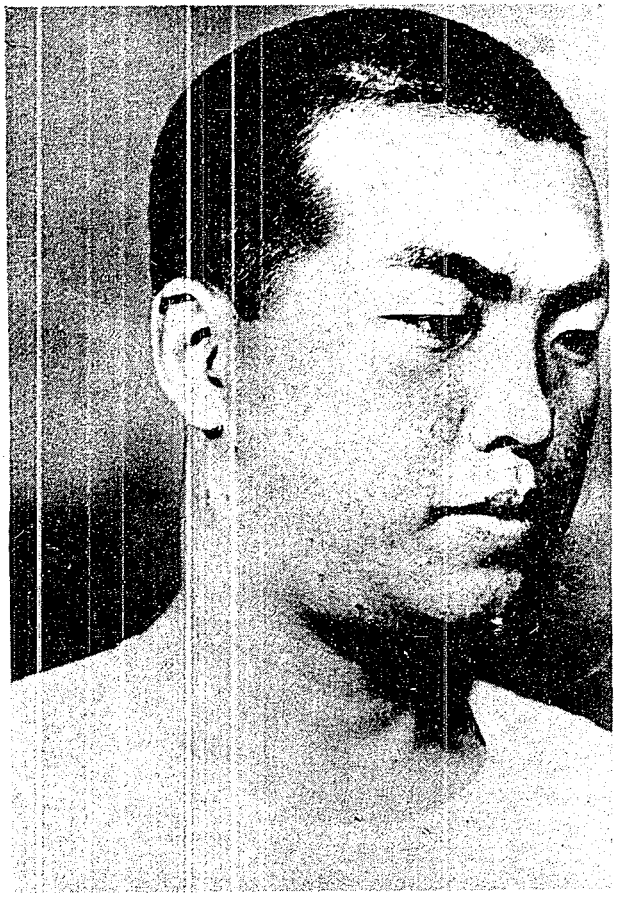
ENCLOSURE (P), continued

Before Treatment

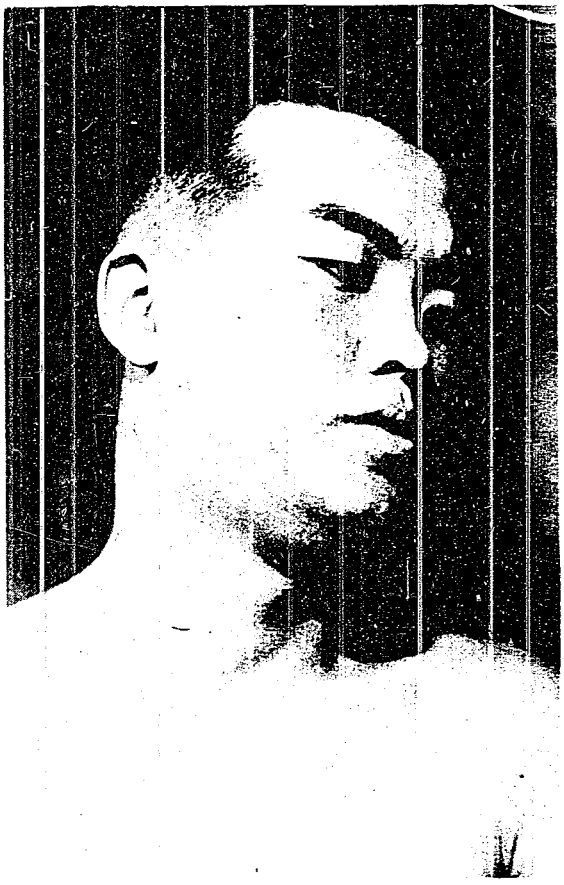
210 Days After Treatment Was Begun

CASE (p)10

ENCLOSURE (P), continued



Before Treatment



93 Days After Treatment

CASE (P)11

Treatment: 0.25 mg of "Koha" Mk 1 given internally every day.

ENCLOSURE (P), continued

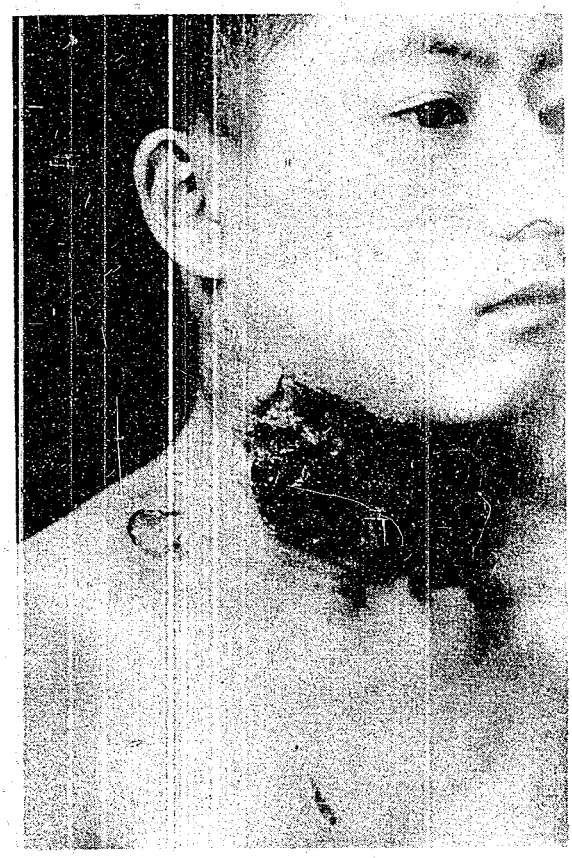
Before Treatment

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

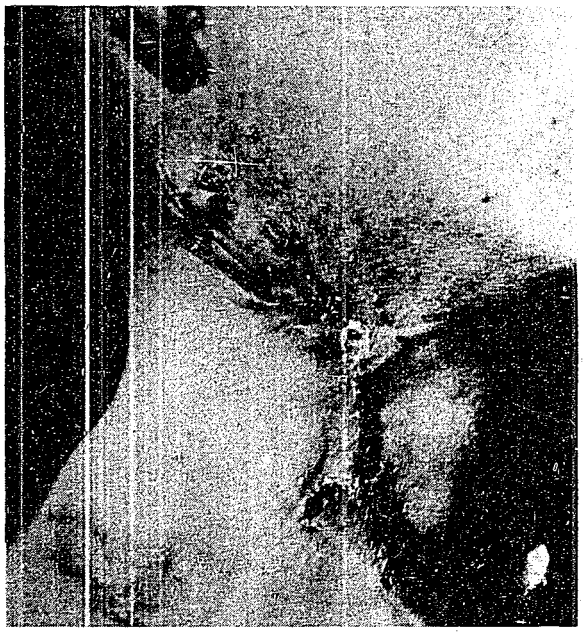


Before Treatment

During Treatment

CASE (P)13

ENCLOSURE (P), continued



During Treatment

After Treatment

During Treatment

CASE (P) 13

ENCLOSURE (P), continued

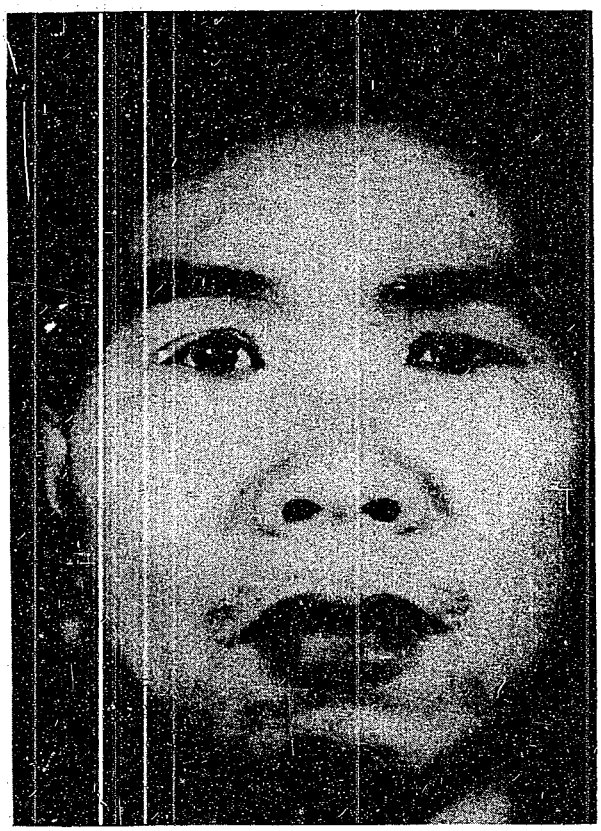
Before Treatment

335 Days After Beginning Treatment

CASE (P)14

ENCLOSURE (Q)

PHOTOGRAPHS SHOWING EFFECTS OF "KOHA TREATMENT ON TUBERCULAR LEPROSY



Before Treatment

After Treatment

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

Treatment: Following doses of "Koha" Mk 1 six times a week: 3.0 mg by anal suppository; 1.0 mg internally; 2.0 mg intramuscularly - twice a week: 3.0 mg anal suppository. Full course: 54 doses, totaling 291.0 mg of "Koha", given over period of 129 days.

ENCLOSURE (Q), continued

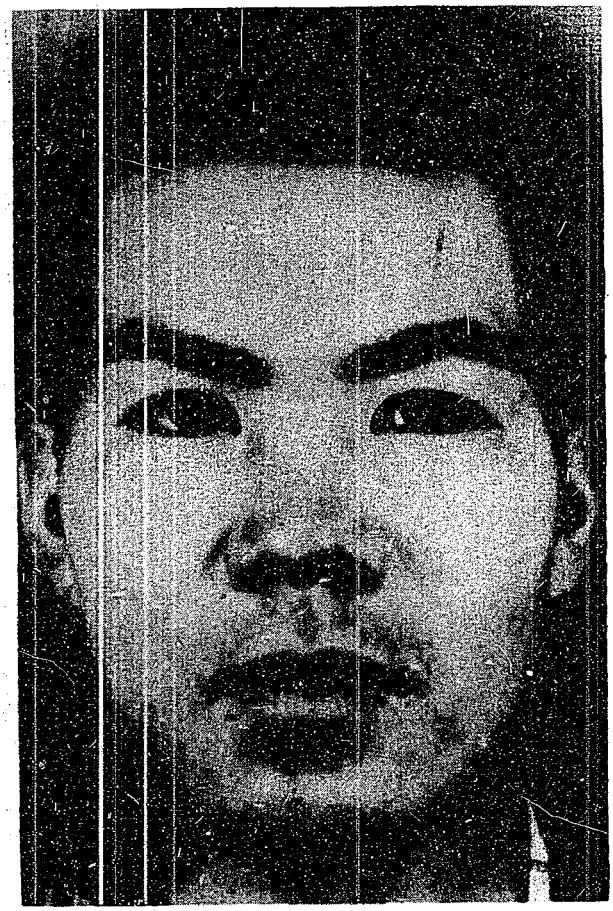
Before Treatment

After Treatment

CASE (Q)2
Primary Tubercular Leprosy
Age 16 - 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 136 days.

ENCLOSURE (Q), continued



Before Treatment

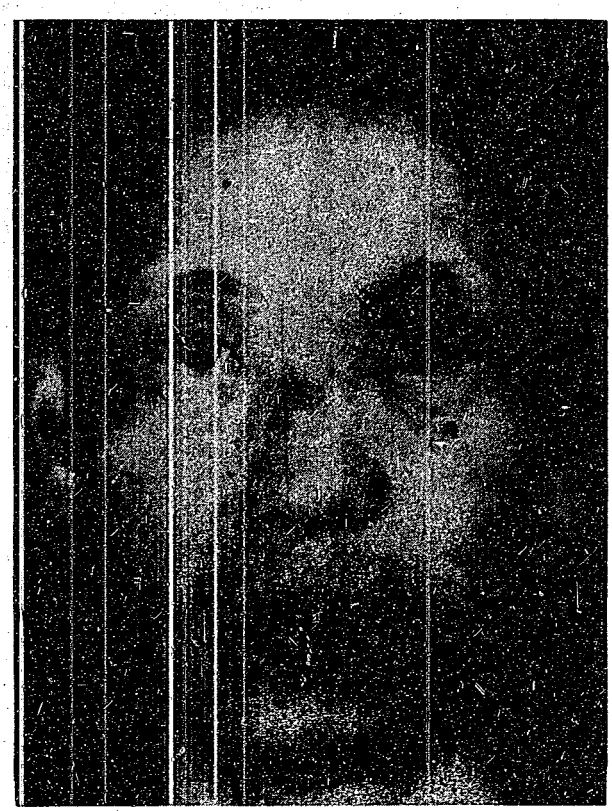
After Treatment

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 113 days.

ENCLOSURE (Q), continued

Before Treatment



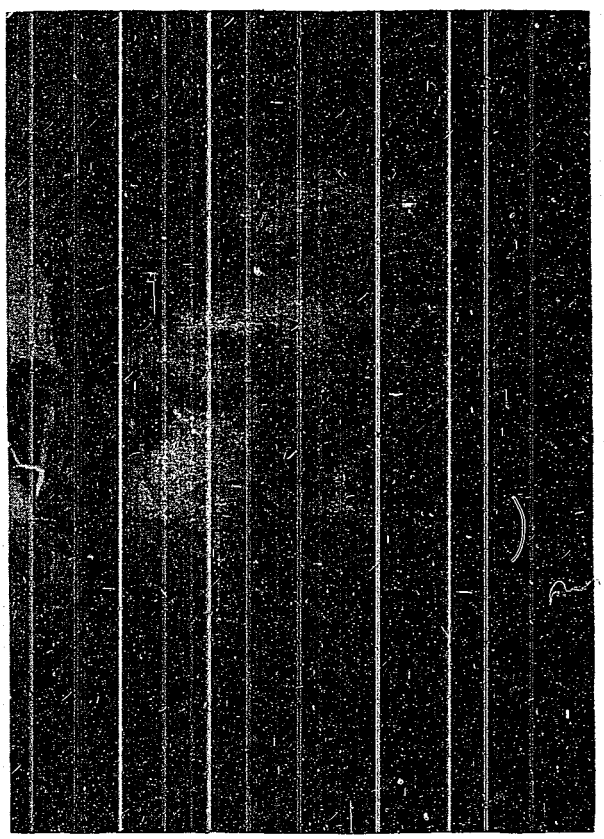
After Treatment

CASE (Q)4
Primary Tubercular Leprosy
Age 29 - Male

Treatment: "Koha" Mk 1 administered internally three to six times a week. Full course: 41 doses, totaling 41.0 mg of "Koha", given over period of 143 days.

ENCLOSURE (Q), continued

Before Treatment



After Treatment

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: 12 injections, totaling 12.0 mg of "Koha", given over a period of 24 days.

ENCLOSURE (Q), continued

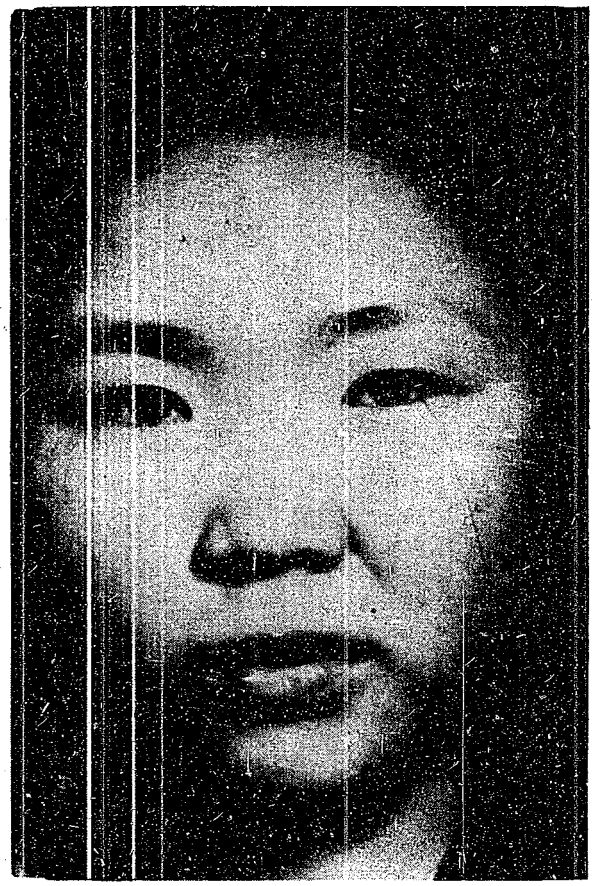
Before Treatment

After Treatment

CASE (Q)6
Primary Tubercular Leprosy
Age 23 - Male

Treatment: 3.0 mg "Koha" Mk 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



Before Treatment

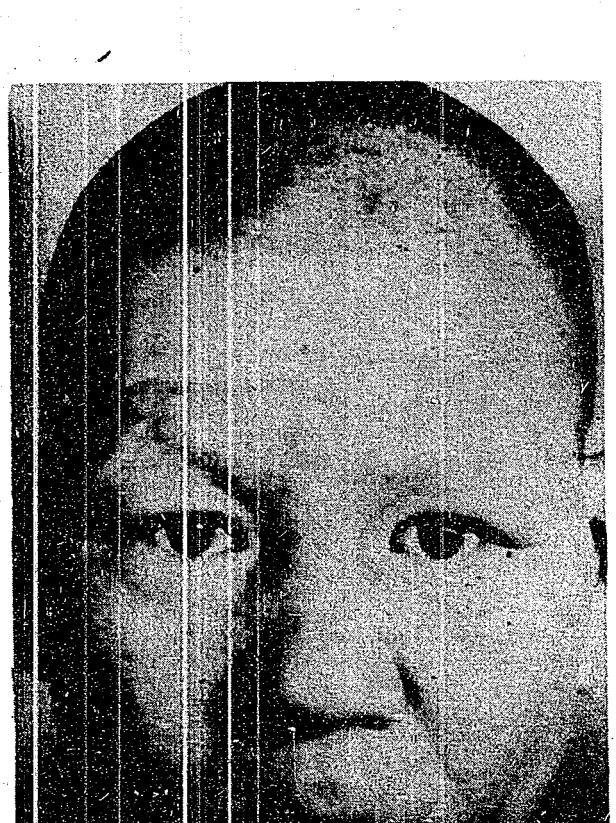
After Treatment

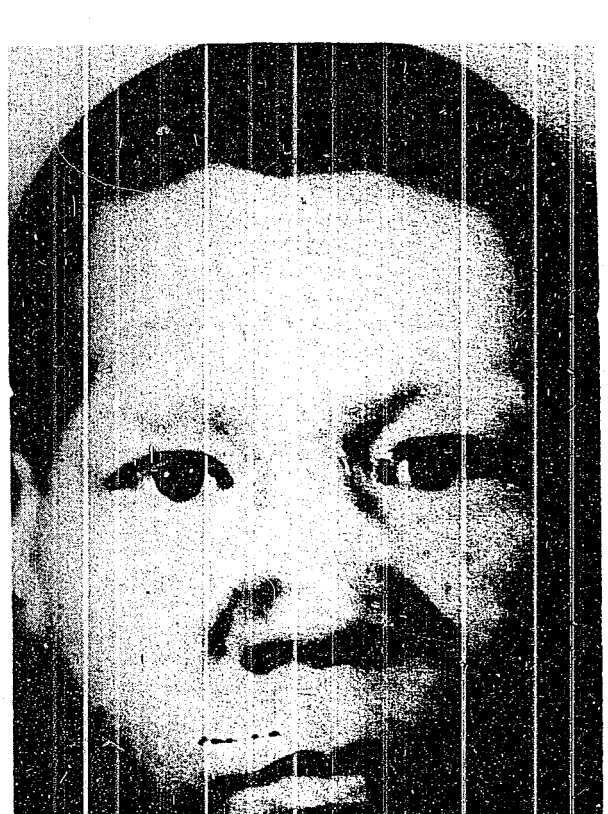
CASE (Q)7
Secondary Tubercular Leprosy
Age 18 - Female

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

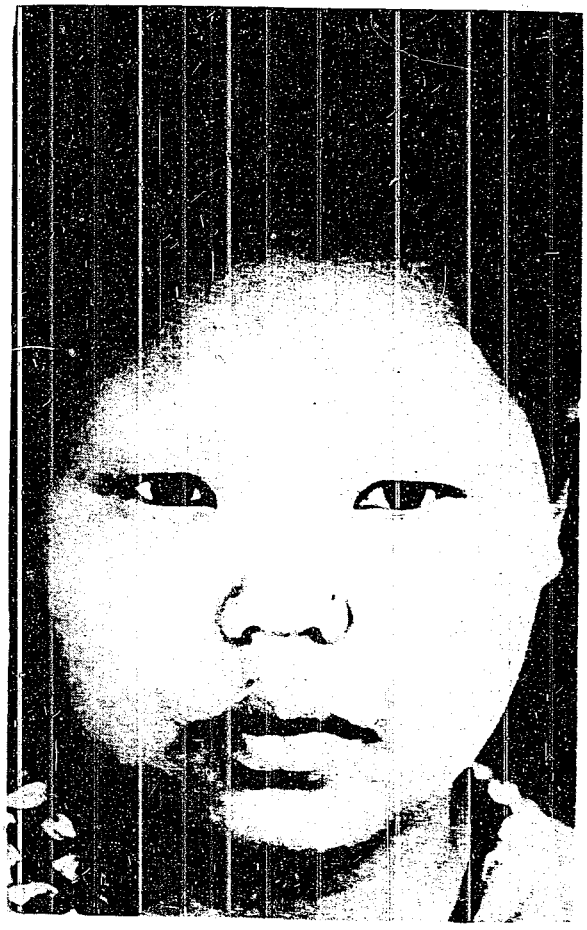
CASE (Q)8
Secondary Tubercular Leprosy
Age 32 - Male

Treatment: 0.1 mg "Koha" Mk 12 administered internally three times a week. Ten doses, totaling 1.0 mg of "Koha", given over a period of 32 days.

ENCLOSURE (Q), continued

Before Treatment

After Treatment



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

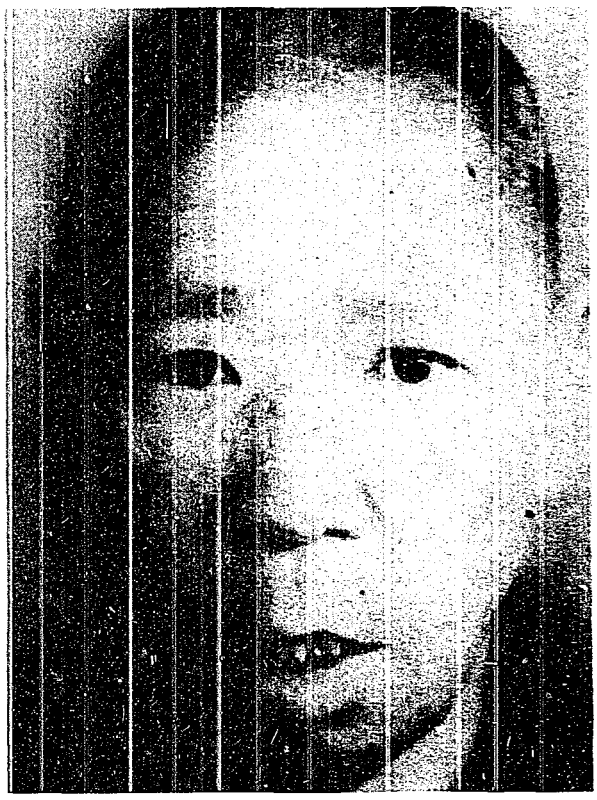
CASE (Q) 10
Secondary Tubercular Leprosy
Age 44 - Male

Treatment: 1.0 mg "Koha" Mk 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 (Q), continued

Before Treatment

After Treatment

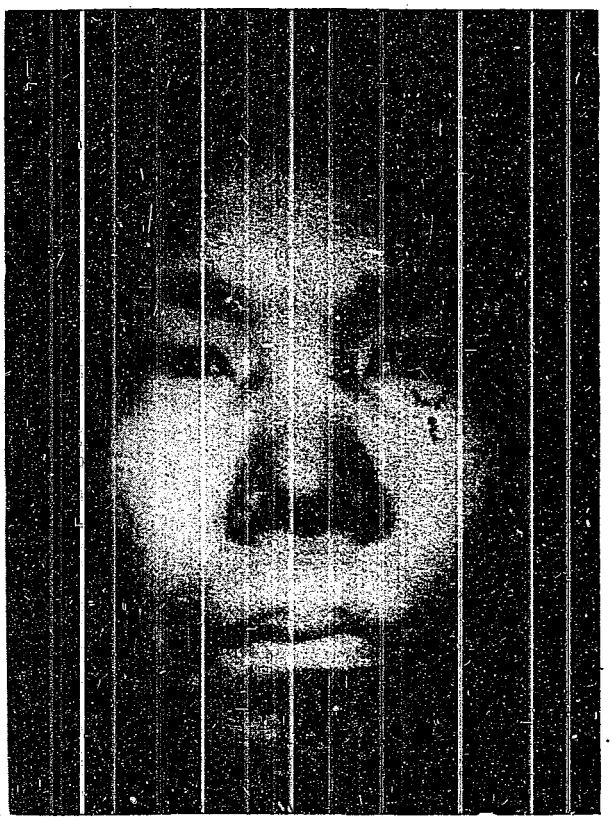


CASE (Q) 11
Secondary Tubercular Leprosy
Age 42 - Male

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

Before Treatment

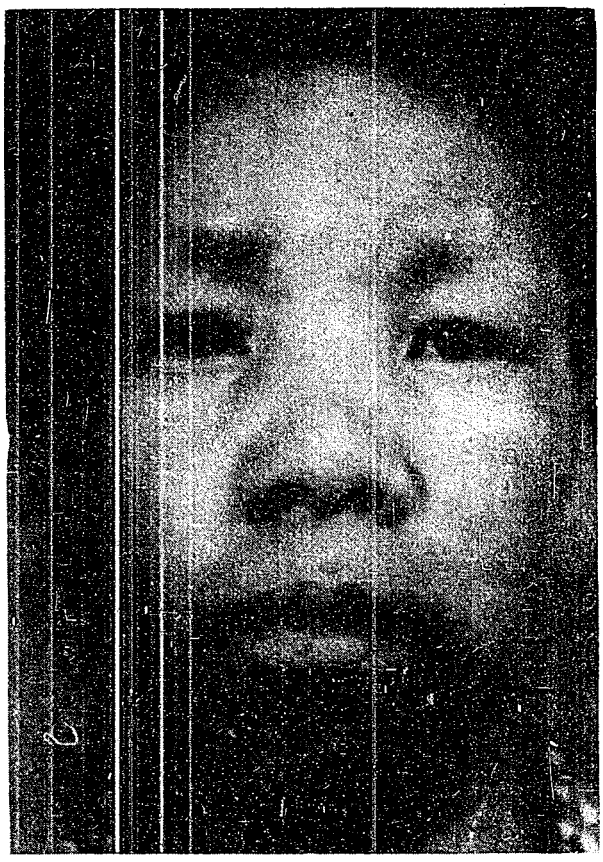


After Treatment

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



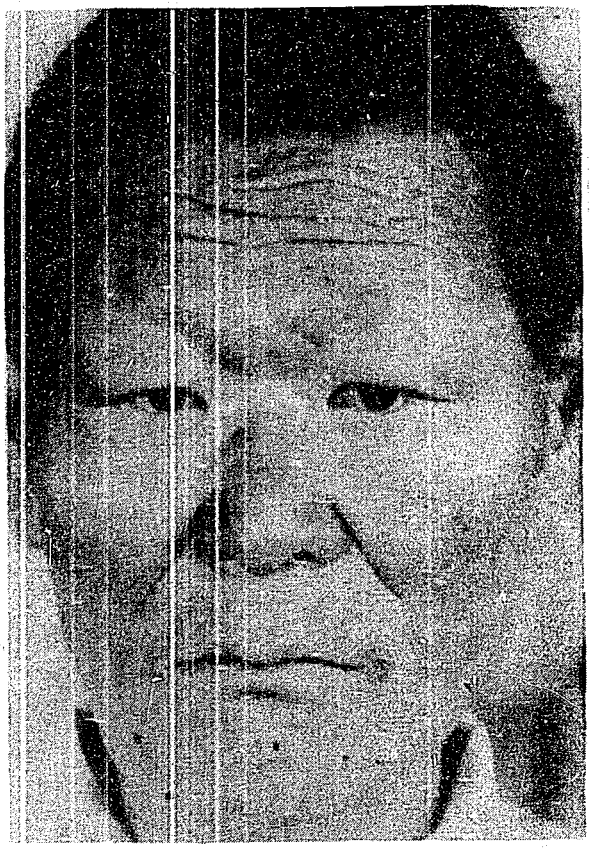
Before Treatment

After Treatment

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.

ENCLOSURE (Q), continued

Before Treatment



After Treatment

CASE (Q) 14
Secondary Tubercular Leprosy
Age 44 - Male

Treatment: "Koha" Mk 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 134 days.

ENCLOSURE (Q), continued

Before Treatment

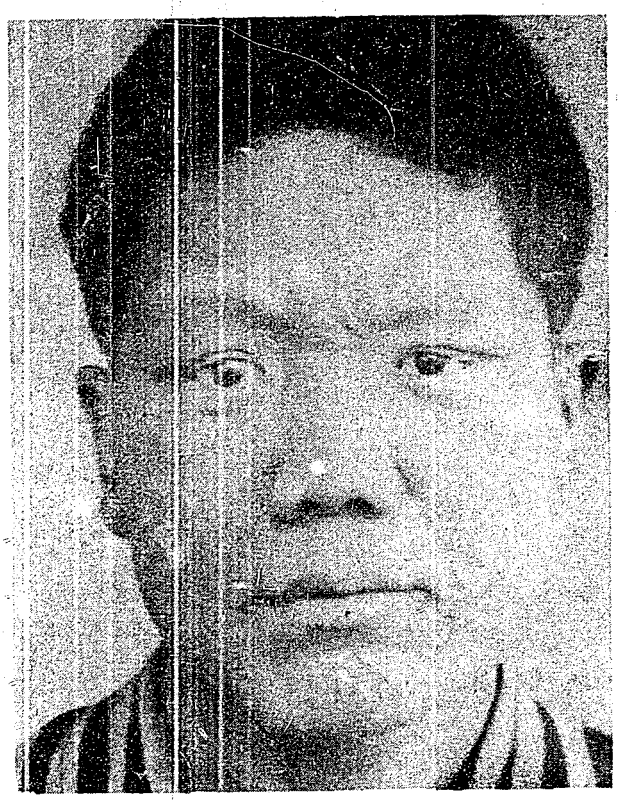
After Treatment

CASE (Q) 15
Secondary Tubercular Leprosy
Age 38 – Male

Treatment: 0.1 mg "Koha" Mk 12 administered internally twice a week. Full course: 10 doses, totaling 1.0 mg of "Koha", given over period of 32 days.

ENCLOSURE (Q), continued

Before Treatment

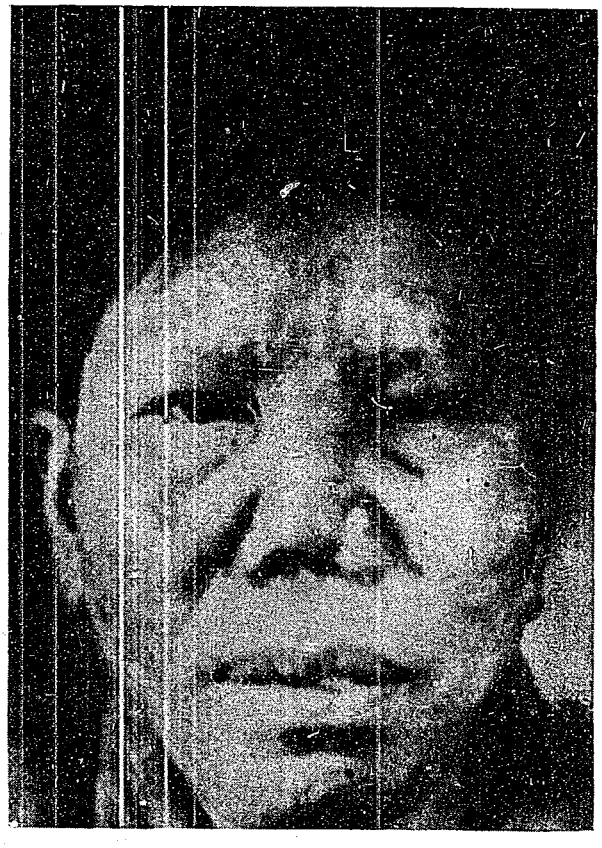


After Treatment

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

Treatment: 0.1 mg "Koha" Mk 1 given internally twice a week, and 0.1 mg "Koha" Mk 12 given internally twice a week. Full course: 27 doses, totaling 1.8 mg of "Koha" Mk 1 and 0.9 mg of "Koha" Mk 12, given over period of 154 days.

ENCLOSURE (Q), continued



Before Treatment

After Treatment

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

Treatment: 1.0 mg "Koha" Mk 1 given in spinal injection. 1.0 mg of "Koha" Mk 1 was injected intravenously three times a week, and 0.1 mg of "Koha" Mk 12 was administered three times a week. Full course: 17 doses, totaling 13.0 mg of "Koha" Mk 1 and 0.6 mg of "Koha" Mk 12, given over period of 121 days.

ENCLOSURE (Q), continued

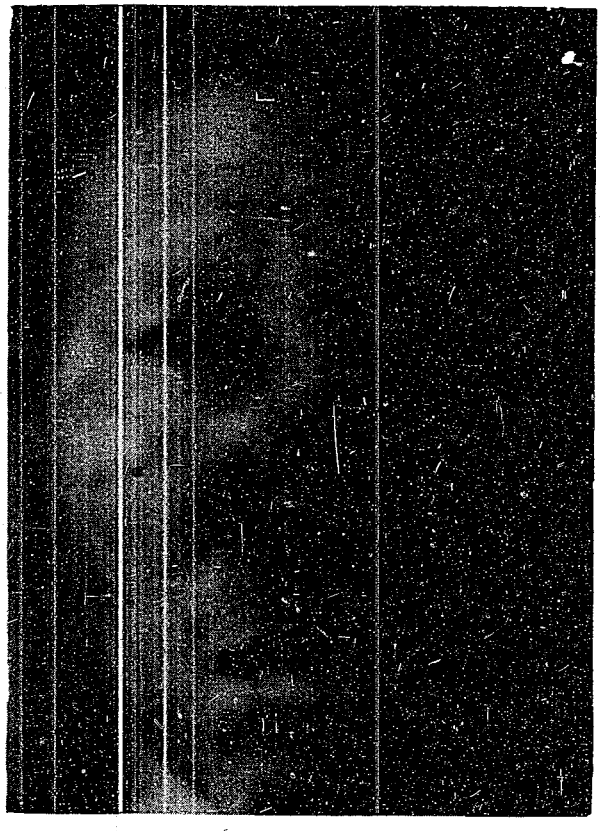
Before Treatment

After Treatment

CASE (Q) 18
Secondary Tubercular Leprosy
Age 21 - Male

Treatment: Following doses of "Koha" Mk 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" Mk 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.

ENCLOSURE (Q), continued



Before Treatment

After Treatment

CASE (Q) 19
Secondary Tubercular Leprosy
Age 38 - Male

Treatment: 0.1 mg "Koha" Mk 1 internally three times a week. Full course: 18 doses, totaling 1.8 mg of "Koha", given over period of 41 days.

ENCLOSURE (Q), continued

Before Treatment

After 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.

ENCLOSURE (Q), continued

Before Treatment

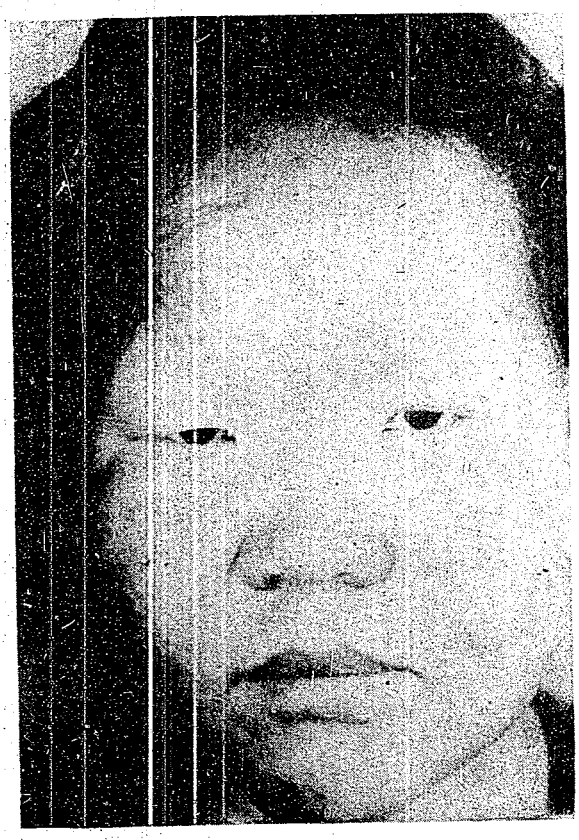
After Treatment

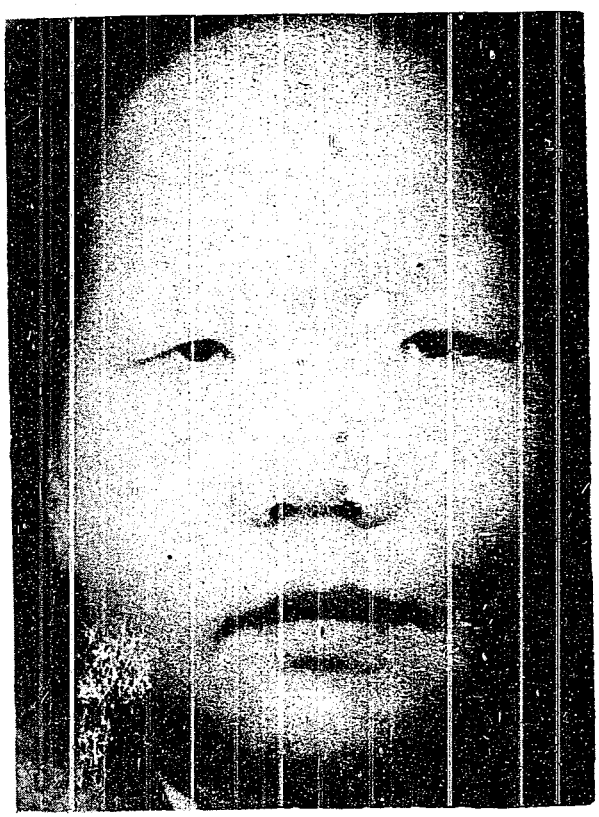
CASE (Q) 21
Advanced Tubercular Leprosy
Age 34 - Male

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



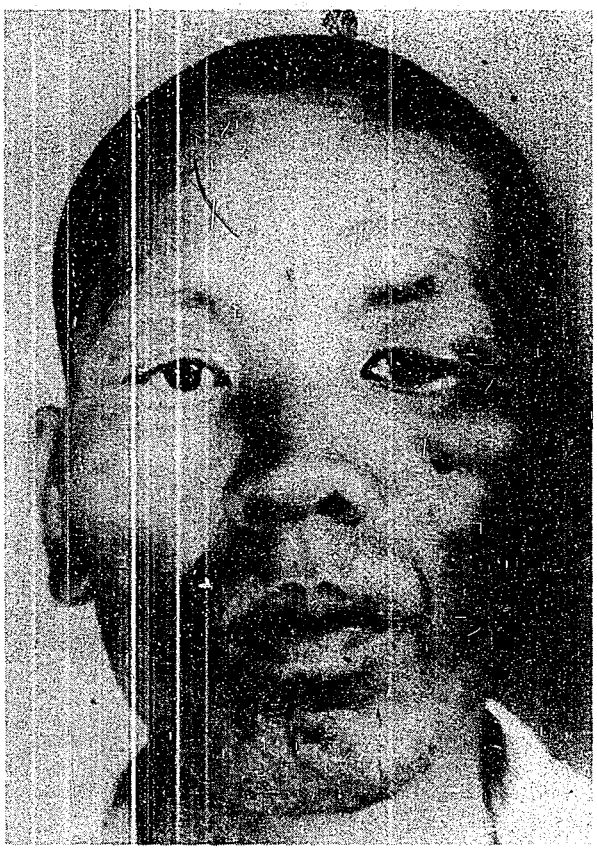


After Treatment

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.

ENCLOSURE (Q), continued



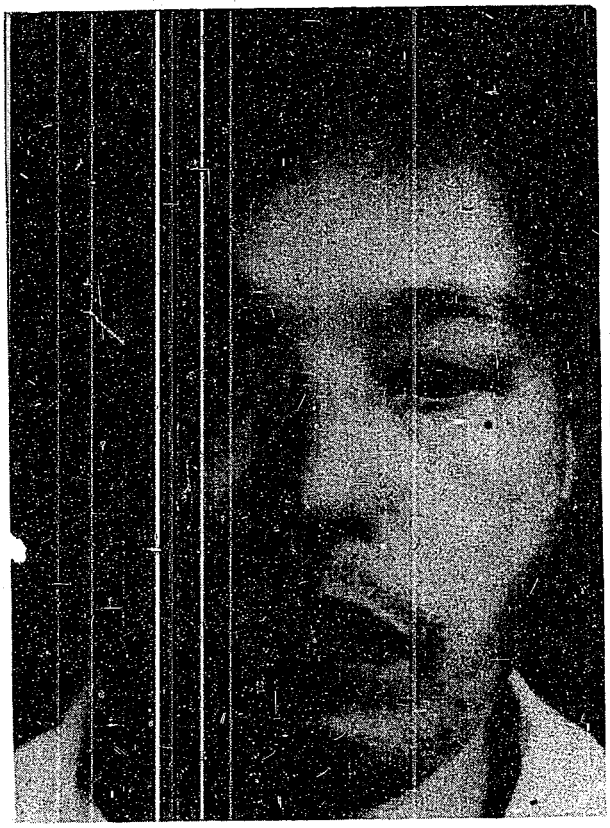
Before Treatment

After Treatment

CASE (Q)23
Advanced Tubercular Leprosy
Age 34 - Male
Treatment: 0.3 mg "Koha" Mk 12 internally each day. Full course: 15 doses, totaling 4.5 mg of "Koha", given over period of 15 days.

ENCLOSURE (Q), continued

Before Treatment

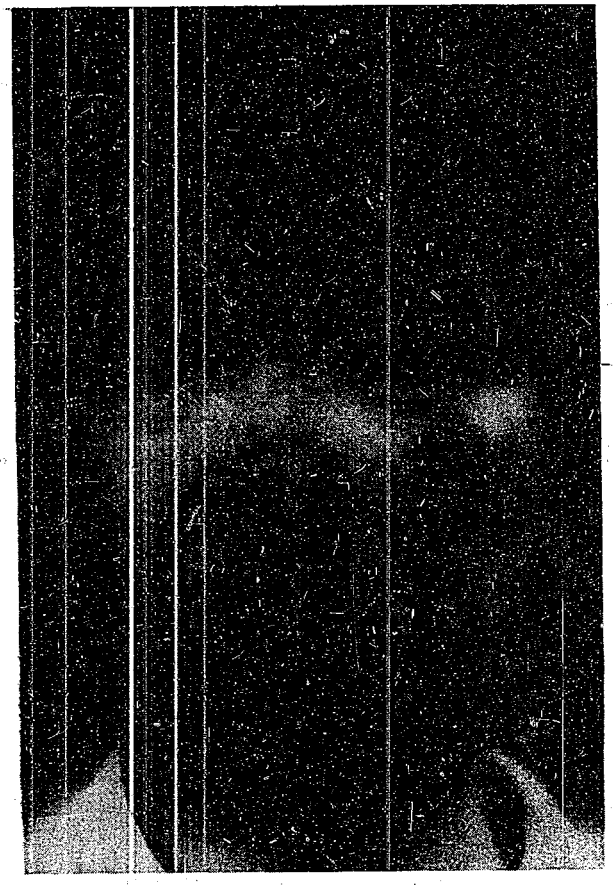


After Treatment

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

Treatment: 0.2 mg "Koha" Mk 1 internally twice a week. Full course: 24 doses. totaling 4.8 mg of "Koha", given over period of 106 days.

ENCLOSURE (Q), continued



Before Treatment

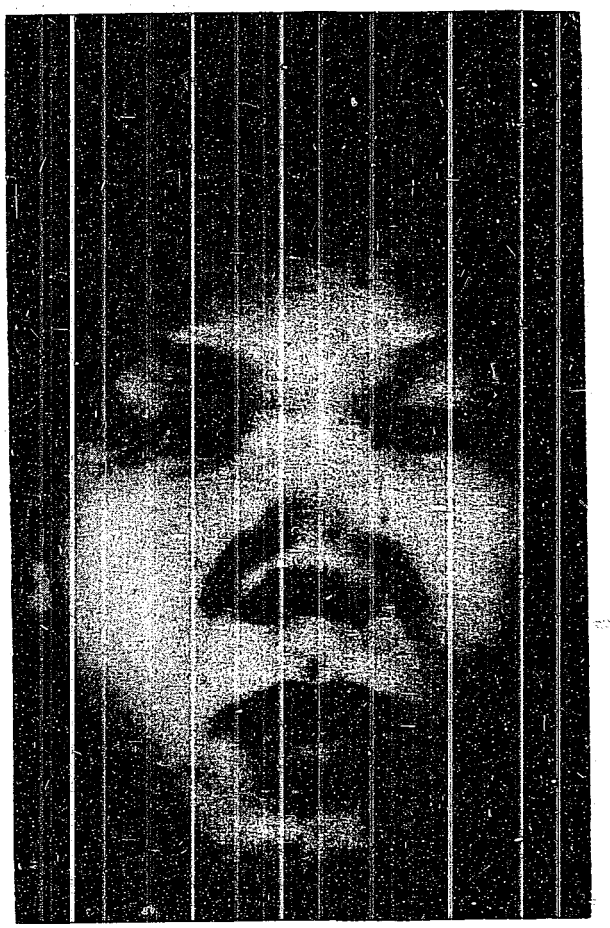
After Treatment

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

Treatment: 0.2 mg "Koha" Mk 12 internally three times a week. Full course: 14 doses, totaling 2.8 mg of "Koha", given over period of 32 days.

ENCLOSURE (Q), continued

Before Treatment



After Treatment

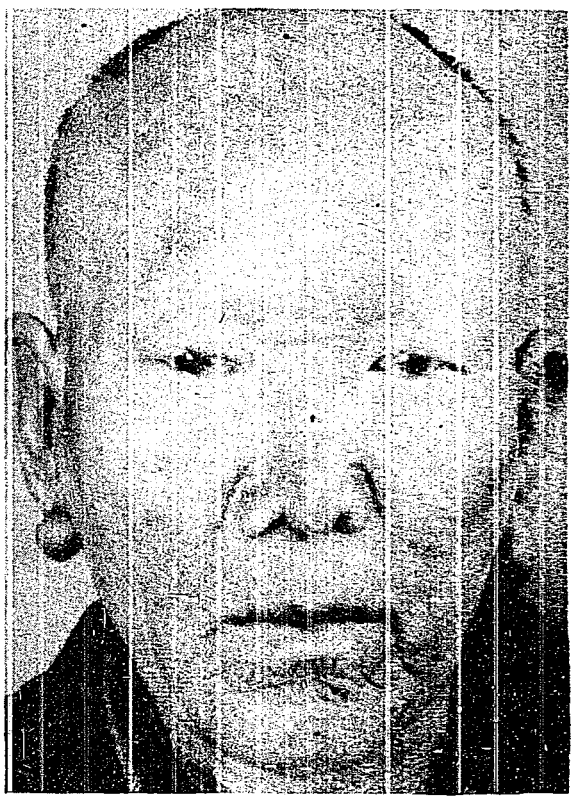
CASE (Q)26
Advanced Tubercular Leprosy
Age 43 - Female

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 (Q), continued

Before Treatment

After Treatment

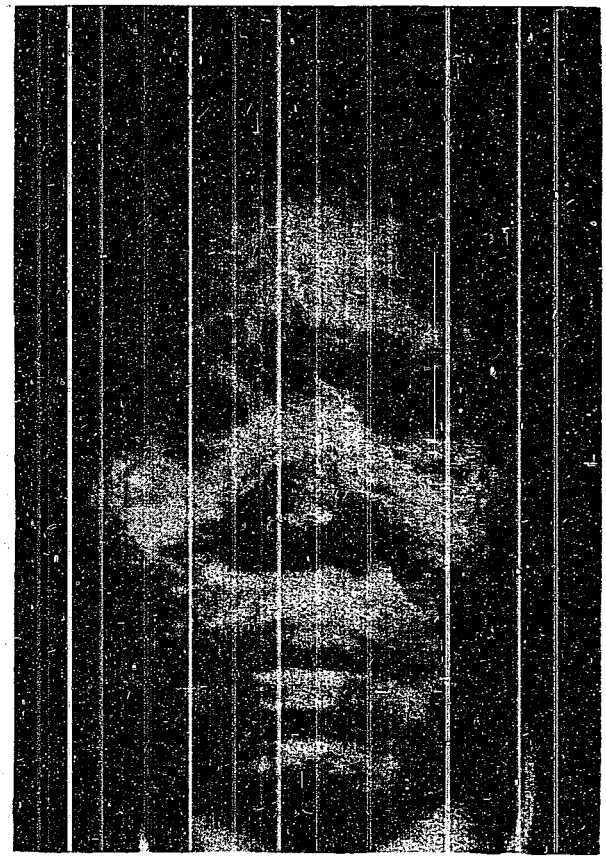


CASE (Q) 27
Advanced Tubercular Leprosy
Age 35 - Male

Treatment: 1.0 mg "Koha" Mk 1 injected three times a week. Full course: 12 injections, totaling 12 mg of "Koha", was given over period of 31 days.

ENCLOSURE (Q), continued

Before Treatment



After Treatment

CASE (Q) 28
Advance Tubercular Leprosy
Age 33 - Female

Treatment: 1.0 mg "Koha" Mk 1 administered internally three to six times a week. Full course: 52 doses, totaling 52.0 mg of "Koha", given over period of 172 days.

ENCLOSURE (Q), continued

Before Treatment

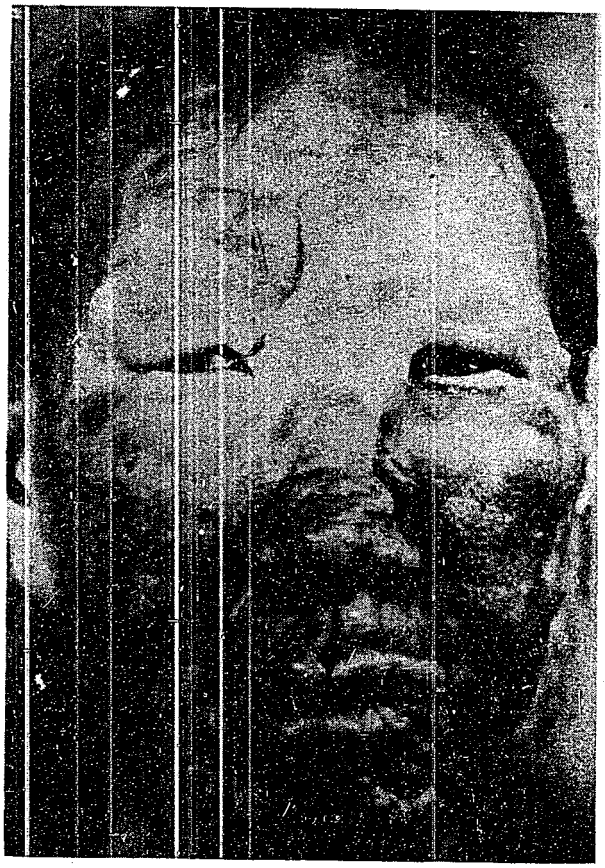
After Treatment

CASE (Q) 29
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

Before Treatment

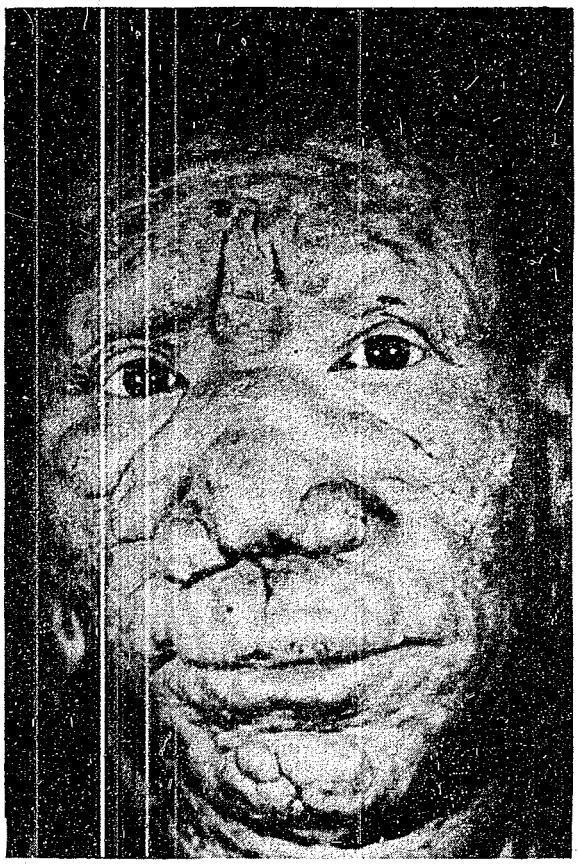


After Treatment

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

Treatment: "Koha" Mk 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 571.0 mg of "Koha", over period of 190 days.

ENCLOSURE (Q), continued



Before Treatment

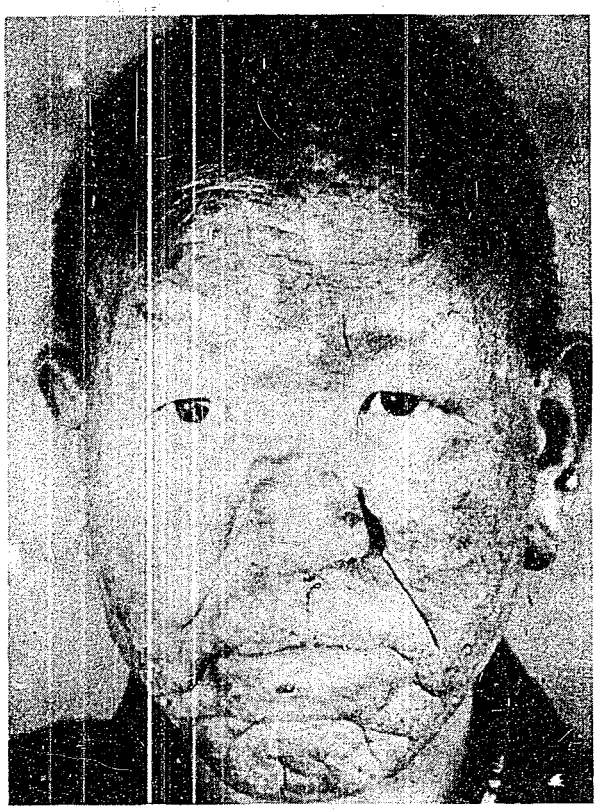
After Treatment

CASE (Q)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

Before Treatment



After Treatment

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.