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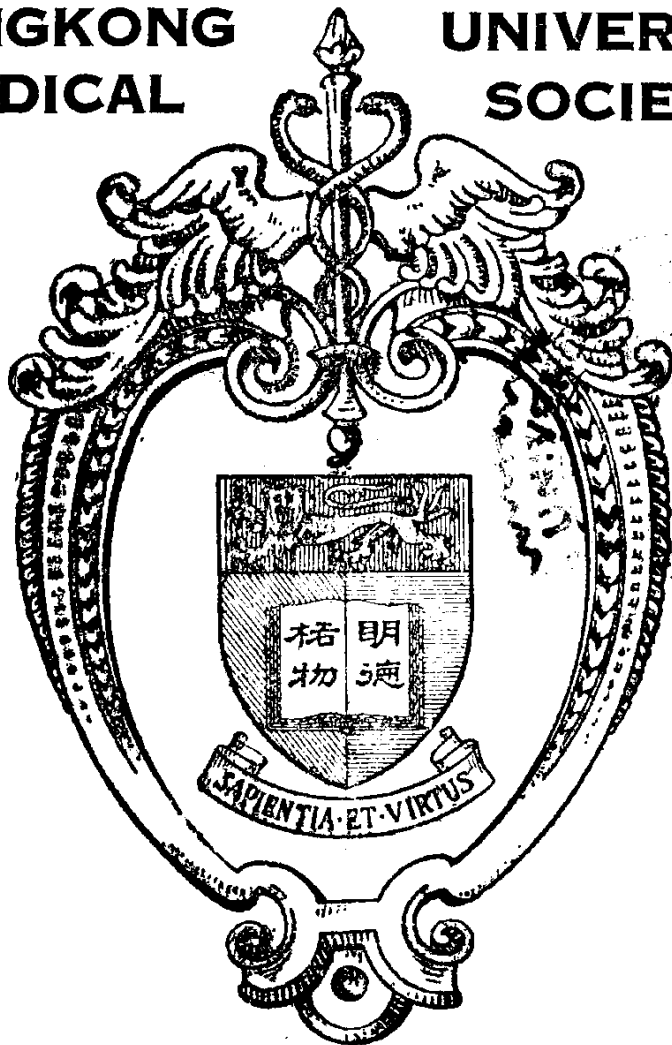
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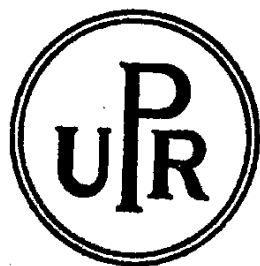
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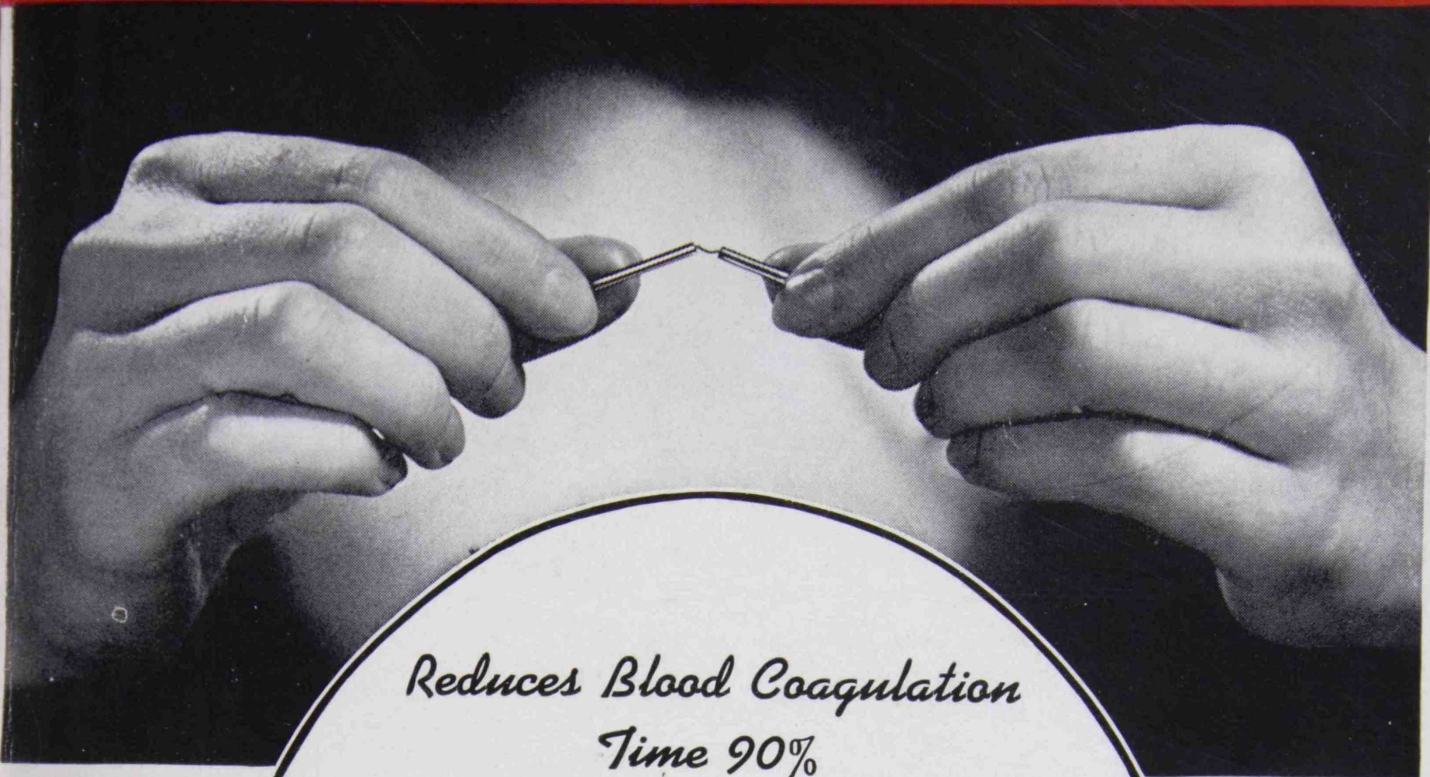
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## PRELIMINARY REPORT OF PELLAGRA OUTBREAK IN KOWLOON,

by

T. J. Hua & S. Y. Cheng,

Kwong Wah Hospital, Kowloon.

Since Casal first described pellagra in Spain under the name of mal de la rosa in 1762, the disease has been reported in greater or less degree from almost every part of the world. The geographical distribution of the disease up to 1936 has been ably and extensively reviewed by Stannus. In China typical cases were first reported by Jouveau-Doubreuil (1920). Recently Morris, Kwang and Kuo reported a series of 40 cases among the war refugees in Shanghai.

With the extension of the Sino-Japanese war to south China in 1936, the influx of refugees into the British colony, and the consequent soaring of the cost of living, the occurrence of deficiency diseases was but an expected and natural outcome. But although sporadic and rare cases showing symptoms suggestive of A, C, or D deficiency are seen, and beri-beri which is endemic here has been noticed to increase, especially the acute cardiac type, it was not until April 22nd, 1940 that we had our first typical case of pellagra at this hospital. Since then within a short period of four months we have had 420 cases. In submitting this report we are acutely aware of the incompleteness of our investigations, and as an explanation rather than an excuse we would state that this work was carried out under stringent conditions of time and facilities.

A total of 420 cases were treated, and of these 185 were males and 235 females. The monthly admissions are shown in a graphic form (graph 1), and it is seen that the outbreak occurred suddenly at the end of April, reached its zenith in June, and showed signs of decline by the end of August. The age incidence for male and female patients differed slightly; for the former the maximum incidence fell in the group 30-50 for the latter it occurred in the group 40-50. (graph 2).

The diet of the patients prior to the appearance of pellagra is interesting. It consisted mostly of rice, salted fish and vegetables with occasional meat and fruits. But since they spend on an average only 12 cents a day for their meals, they could not possibly have been able to afford sufficient quantities of the articles of food mentioned. In one of our patients prolonged restriction of diet advised by a herbalist was responsible for the appearance of pellagra.

Almost all our patients came from the slum districts of Kowloon. The female patients were mostly housewives of poor families, whilst coolies and other manual workers formed the majority of the male cases. Only one per cent. of the patients were actually unemployed.

The following clinical subgroups were recognized:—

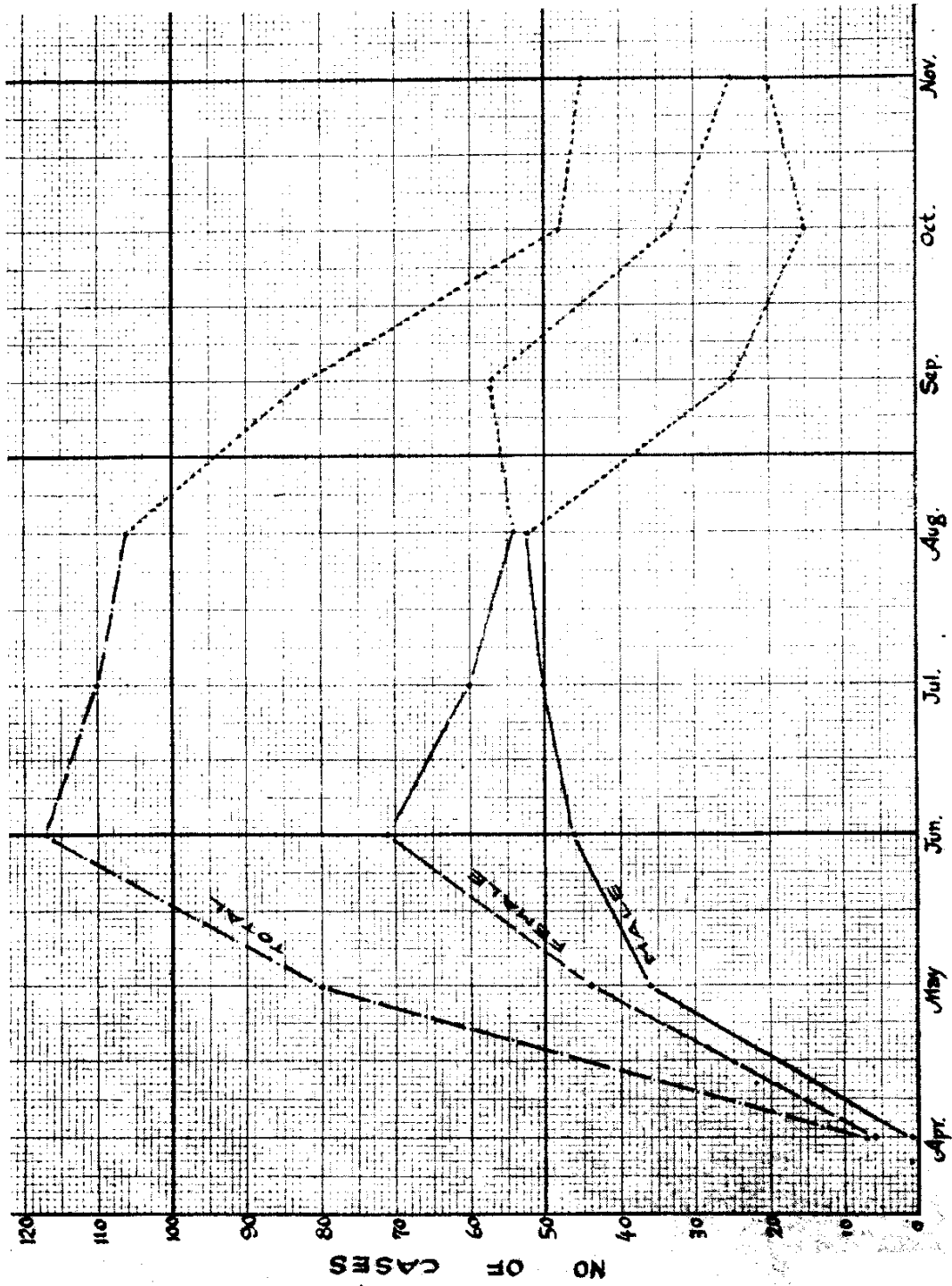
- (1) Cases with dermatitis alone.
- (2) Cases with dermatitis and diarrhoea.
- (3) Cases with dermatitis, diarrhoea and marked prostration, the so-called "pellagra typhus."
- (4) Cases presenting marked mental symptoms.

#### ILLUSTRATIVE CASES.

(1) Lee Tung, Chinese male, age 30, was admitted into this hospital on April 27, 1940. Patient was a bricklayer. He was a muscular and well-built individual. About one week before admission he experienced a burning sensation and numbness in both hands and feet and also in the back of the neck. Three days later he noticed redness of the skin in these regions. Soon afterwards there appeared vesicles and bullae which on rupture exuded a clear serous fluid. He then complained of bone pains and a sensation of epigastric constriction. On admission the skin over the dorsal aspects of both hands and feet was dark brown and indurated with scattered denuded areas left by the ruptured bullae. There was slight secondary infection with redness and oedema and the pigmentation was sharply defined and symmetrical. The skin over the back of the neck was likewise pigmented and sharply defined but induration was not so marked. There was angular stomatitis with glossitis and dysphagia. The skin of the perineum and on the medial aspects of the thighs was also pigmented but less sharply defined. (Fig: 1). He was put on the usual hospital diet with the addition of 2 pints of milk, 6 drachms of marmite and 2 eggs a day. The skin lesions were treated on general surgical principles with eusol dressings for few days and thereafter sterile paraffin gauze dressing to counteract the dryness of the skin.

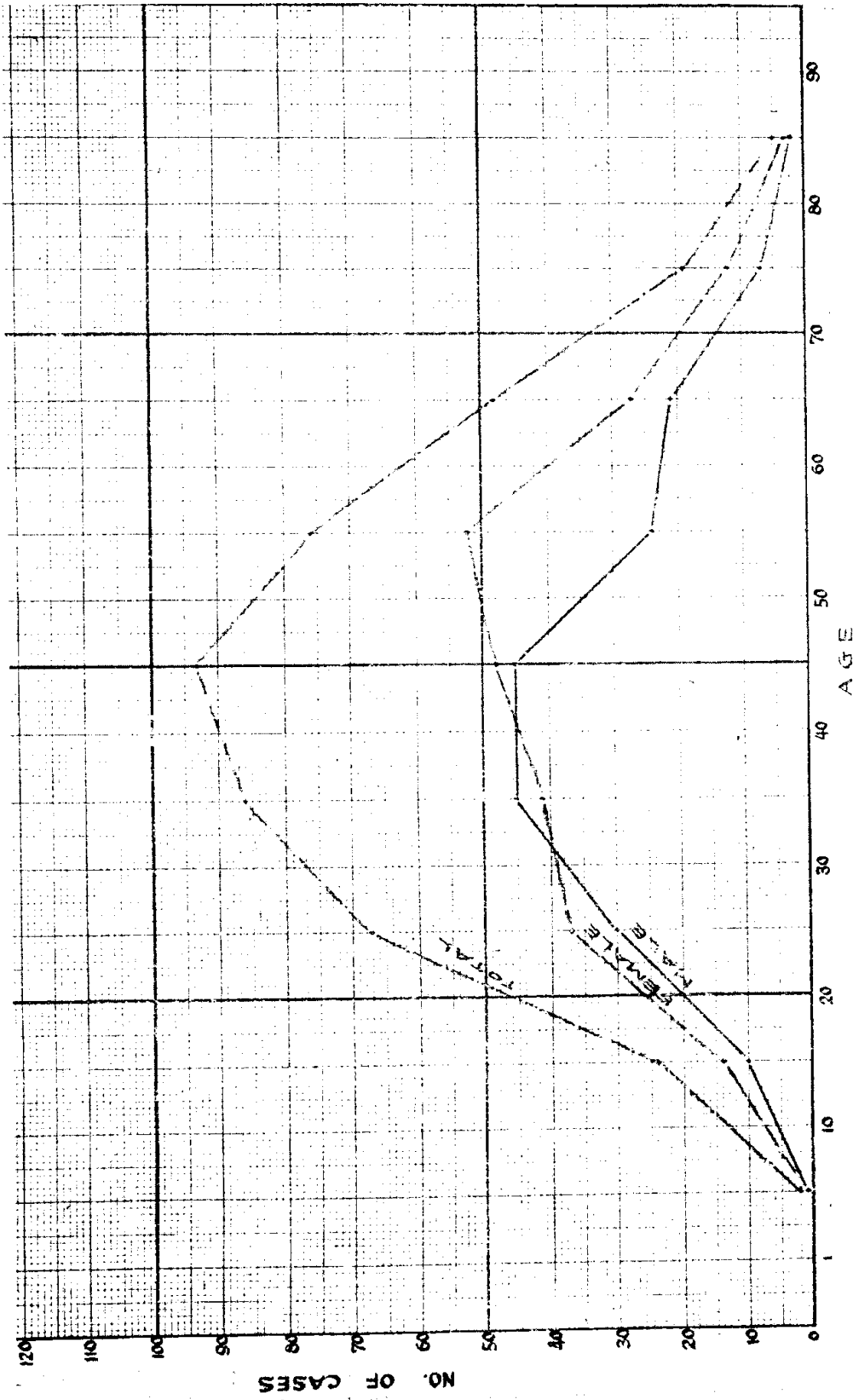
By May 6th i.e. ten days after admission there was no dysphagia, the stomatitis and glossitis had subsided and the skin lesions were dry and undergoing desquamation. (Fig: 2). Epigastric discomfort and bone pains were still present. The blood W. R. was negative.

CHART SHOWING SEASONAL INCIDENCE



GRAPH I

CHART SHOWING AGE INCIDENCE



GRAPH II

He was discharged on June 10, 1940 when the desquamation of the skin lesions on the hands and feet was complete with slight persistent pigmentation at the margins. (Fig: 3). The pigmentation of the neck and the perineum still persisted but there had been no desquamation.

There was no history of previous attacks or of the occurrence of pellagra among members of the same family. There was, however, a history of an impoverished diet of rice, salted fish and pickled vegetable for two and a half months.

(2) Young Bo, a Chinese widow aged 26, was admitted into this hospital on May 6, 1940. She was a worker in a sewing factory. She had been living on a diet of rice, salted fish and pickles for about 6 months. Three months before admission patient experienced attacks of burning, and tingling sensations in the limbs. There was loss of appetite and occasional attacks of nausea and epigastric discomfort. About a week later patient noticed the appearance of redness on the back of both hands, forearms, elbows, and the lower part of arms. Ten days later there appeared a similar condition on the back of both feet and on the face. The erythema was followed by the formation of bullae and superficial ulceration when they ruptured. Coincident with this there was diarrhoea with watery stools which lasted for about two weeks and subsided by itself without any special treatment. Amenorrhoea had been present since the onset of the disease. On admission there was severe dermatitis of the limbs and the face which showed a typical butterfly distribution. Severe folliculitis i.e. inflammation of the hair follicles with retention of sebaceous secretion, was noticed. (Fig: 4). Pigmentation of the perianal skin and vulvitis were noticed. Patient was put on similar treatment to the previous case. Two week later the tongue looked moist, smooth and slightly fissured and the skin condition had cleared up with slight persistent pigmentation. (Fig: 5). By then she had developed mild symptoms of beri-beri. She was treated accordingly and was discharged on June 6, 1940.

(3) Leong Sze, a Chinese widow aged 60, admitted on May 22, 1940. She had been living on a diet which consisted of rice, salted fish and very occasionally a little meat. She spent 8 to 9 cents a day for her meals. She had been suffering from dysphagia, and dermatitis of the hands and feet for about three weeks and diarrhoea with blood and mucus in stool for two days. On admission she was dull and apathetic (Fig: 6) and there was severe glossitis. The stool showed no cysts or amoebae but there were cytological suggestions of bacillary dysentery for which she was given the appropriate treatment with the addition of Nicobion by mouth. The prostration became progressively worse and she was in muttering delirium on June 6. She died on June 7, 1940 a few hours after the picture was taken.

(4) Chu Mui Ngan, a Chinese girl aged 20, was admitted into this hospital on June 7, 1940. One month before admission she had suffered from diarrhoea with watery stools for about two weeks which was followed, during convalescence, by numbness and weakness of limbs. Two weeks before admission patient first noticed redness of hands, feet, forearms and legs which was preceded by a sensation of heat and followed by bulla formation and superficial ulceration. On admission she had a typical raw beef tongue, dysphagia, and dermatitis of the limbs. There was no diarrhoea, mental or nervous symptoms. However on the next day patient became delirious with tremor of the lips and spasmodic twitchings of the fingers and toes. There was incontinence of urine and faeces. This condition persisted and on June 11, the patient was noticed to have a markedly rigid neck and showed a strongly positive Kernig's sign. At this time the skin lesions were actually improving and there was commencing desquamation. A lumbar puncture was performed; the pressure was increased but the cerebrospinal fluid was clear and showed no increase of cells or globulin or the presence of organisms. Nicobion 100 mg. tds given. On June 12 condition was not improved and she was given an injection of 0.4 gm. of nicotinic amide. (Nicobion 4 ampoules). For the following three days she was given a daily injection of 0.2 gm. of Nicobion with apparently no improvement whatsoever. On June 14 it was found necessary to give her 40 c.c. of 50% glucose and 2 c.c. of cardatone intravenously. On June 16 patient recovered consciousness, almost suddenly, talked intelligibly and was indeed quite cheerful. There was no neck rigidity and tremor of fingers or toes. Neither was there any incontinence of urine and faeces. On June 17 patient was able to get up and walk about in the ward. The glossitis had subsided and there was no dysphagia. The subsequent recovery of the case was uneventful.

#### DISCUSSION OF SYMPTOMS.

*Dermatitis.* With the exception of two cases of pellagra sine pellagra, all cases reported in this series had dermatitis of greater or lesser degree. The relative frequency of involvement of the various parts of the body is here presented in a tabular form:—

	Face	Neck	Hands	Forearms	Feet	Legs	Perineum
No. of Cases....	17	28	309	71	328	66	266
Percentage.....	4%	7%	73.6%	17%	78.1%	16%	63.1%

The back was involved only in one case of a wood chopper who was in the habit of exposing his back during working hours. It is to be noted that the soles, the palms and the anterior abdominal wall were not involved in any of the cases. The lesions of the perineum and that of the skin overlying bony points such as the ischial tuberosities, the greater trochanters and the sacrum and the elbow



were not identical with those of the hands and the feet. Their appearance was not invariably preceded by a burning sensation or other form of paraesthesia, neither were they so sharply demarcated. No vesicles or bullae were formed and no desquamation occurred. Indeed the lesions were just patches of dry, dark, indurated non-elastic skin with ill-defined margins. It is what one might call a "pre-bed sore" stage of undernutrition of skin.

The extent of the skin lesions at any particular site is usually delimited at the first appearance of the erythema and has no tendency to subsequent local extension. In fact the redness usually appeared first at the periphery of the involved area on both sides of the body simultaneously. Different parts of the body, however, may be and usually are involved at different times, at intervals of a few days. (Fig: 7). Vesicle and bulla formation usually occurs after the application of some form of counter-irritation, though not infrequently it appears spontaneously. (Fig: 8). With the rupture of the bullae a mild degree of secondary infection is the rule, sometimes accompanied by inflammatory oedema and enlargement of the neighbouring lymph nodes. In non-infected cases the involved skin became dry and detached from the underlying tissues and cast off. Before desquamation it presents an appearance reminiscent of a tannic acid treated burn. (Fig: 10). Persistent pigmentation after desquamation varies in degree, is usually more marked at the margins, and depends to a certain degree on secondary infection. (Fig: 11). It is our experience that the skin lesions, if kept clean, have a tendency to spontaneous recovery.

That sunlight does in certain cases act as a definite precipitating factor for the appearance of dermatitis is well illustrated in one of our cases. Yan Oi, a Chinese male aged 51, was admitted on July 25, 1940. He had suffered from dysentery for three weeks about one and a half months ago. Two weeks before admission he resumed his work as a wood chopper. It was his habit to work, like other wood choppers, wearing the minimum amount of clothing. He felt smarting pain all over the exposed parts of the body, and the next morning bullae developed on both upper limbs, the neck, the back, the dorsal aspect of both feet and the front of both ankles. The subsequent rupture of the bullae resulted in superficial ulceration. On admission it was found that apart from the skin lesions there was glossitis, angular stomatitis and dysphagia. There were no nervous or mental symptoms. He made a rapid recovery and was discharged on August 1, 1940 after eight days in hospital.

While deficiency of vitamin B<sub>2</sub> as a cause of pellagra may be considered proved there are many problems in connection with this disease which are as yet unsettled. Among such problems is the symmetrical distribution of dermatitis. We have one case which suggests

that nervous influences play a part in its pathogenesis. Wong Kung, a Chinese female, aged 55 was admitted on June 15, 1940. She had suffered from a hemiplegia for five years, and two weeks before admission she began to complain of dysphagia. Soon afterwards she noticed the appearance of red patches on the dorsal aspects of right hand and foot. She also complained of diarrhoea with 'tarry' stools. She was emaciated and weak. On admission it was found that she had a left spastic hemiplegia. There was no facial paralysis. Blepharitis was present on both sides and there was marked angular stomatitis, glossitis, and gingivitis. There was also extensive ulcerative vulvitis and ulceration of the anus and inflamed external piles. There was erythema, pigmentation and superficial ulceration of the back of the right hand and a red patch over the right elbow. Over the right foot there was a dark pigmented area about the size of a dollar below and in front of the lateral malleolus. The left limbs showed no signs of dermatitis. She died about twenty hours after admission, before arrangements could be made to have a photograph taken.

*Folliculitis.* This was noted in a few cases. It is an inflammation of the hair follicles with pigmentation round the hair-roots and sometimes also retention of sebaceous secretions. (Fig: 12).

*Blepharitis.* This occurred in 46 cases, 17 male and 29 female. The blepharitis is usually mild and affects especially the canthal regions, giving rise to moist, slightly reddened eyelids and a mucous or mucopurulent discharge. It cleared up readily with a simple boracic lotion and dietetic treatment.

*Stomatitis.* This occurred in 69 cases i.e. 16.4% of our series. It varies in severity from a generalized ulcerative stomatitis with snail-track ulcers on the inner sides of the cheeks simulating secondary syphilis to a mild angular stomatitis manifested by a moist bluish-white appearance of the angles of the mouth. The buccal mucous membrane in severe cases looked red and angry.

*Glossitis.* This also varies in severity and the appearance differs according to the stage in which it is first seen. In the acute stage the whole tongue is red and swollen, with enlarged hyperaemic papillae giving rise to the typical appearance of a raw-beef tongue. (Fig: 13). It is difficult or almost completely impossible for these patients to protrude the tongue. Dysphagia, of course is present. At this stage, it responds readily to Nicobion injections. In less severe cases the inflammation is confined to the edge and the tip of the tongue. After recovery the tongue is moist, clean and fissured. In a number of cases there is a certain amount of permanent enlargement and impairment of motility. The fissures are often arranged in such a manner as to give the tongue a leaf-like appearance. The smoothness is due to the atrophy of the papillae. Glossitis was noticed in 183 cases, i.e. 43.3%.

*Gingivitis.* This occurred in 127 cases i.e. 30% Gingivitis as such cannot be considered as a symptom of pellagra except when present as a part of generalized stomatitis. In the absence of the latter it usually occurs in association with septic teeth and pyorrhoea alveolaris, and is then to be considered as an independent condition rather than as a manifestation of pellagra.

*Pharyngitis.* This was not specially looked for in every case, hence its frequency cannot be reported, but in the few cases in which it was noted the pharyngitis was mild in degree and the mucous membrane presented the ordinary catarrhal appearance.

*Dysphagia.* This usually occurs as an early symptom in pellagra and is then due to one or more of the following conditions:—Stomatitis, glossitis, gingivitis and pharyngitis. No case of laryngitis was noted.

*Vulvitis.* Vulvitis occurred in 65 cases, i.e. 15%. It is usually a mild catarrhal condition, but in some cases it is severe and showed extensive ulceration. (Fig: 14). It responded readily to nicotinic amide treatment and castor oil and zinc oxide dressing.

*Amenorrhoea.* This is one of the most constant symptoms of pellagra in women. It occurred in about 85% of our female cases in the reproductive period of life. Its causation is obscure, and the degree of anaemia found in such patients was not severe enough to account for the occurrence of the symptom.

*Sensation of epigastric constriction.* This curious symptom was present in 62% of cases. It was an early symptom and did not respond to alkali treatment.

*Diarrhoea.* This was complained of in 202 cases i.e. 48%. It usually occurred early in the course of the disease. The stool at onset was usually watery, but, later on blood and mucus were sometimes passed. Tenesmus and abdominal griping appeared in the more severe cases. The cytology of the stool in such cases was suggestive of dysentery, but as no cultures were performed, it is not possible to report on the frequency of true bacillary dysentery as a complication.

*Nervous symptoms.* Headache was observed in 65 cases. Insomnia was a frequent and early symptom at onset, being present in about 72% of cases. Delirium was noted in 16 cases, i.e. about 5%. Mania was noted in 4 cases.

*Retrobulbar neuritis.* No ophthalmoscopic examinations were made to discover signs of this condition but none of our cases complained of dimness of vision.

#### CONCOMITANT AFFECTIONS.

*Beri-beri.* Symptoms of beri-beri were noted on admission in 253 cases, i.e. 56% of our series.

*Vitamin A Deficiency.* A few cases with symptoms suggesting vitamin A deficiency such as coarse dry skin and dryness and brittleness of hair were noted, but no case of xerophthalmia or night-blindness was encountered.

*Malaria.* Malarial infection was present in 32 cases.

*Scabies.* Seventy-two of our cases had scabies on admission.

*Haemorrhoids.* Piles were noted in 7 cases.

*Syphilis.* The blood W. R. was positive in only 17 cases.

*Pulmonary Tuberculosis.* Physical signs of active lesions were detected in 9 cases.

*Dislocation of the temporo-mandibular joints.* Two cases of recurrent dislocation of the jaw were met with.

*Recurrences.* Seven of our cases were re-admitted within two months of discharge with recurrence of symptoms of pellagra. The second attack was usually more severe and many of them died. The small number of re-admissions may not represent the true incidence of recurrence as many of our patients were so poor that they could not possibly afford an adequate diet after discharge.

*Pregnancy and Labour in Pellagra.* Four of our cases were admitted to the maternity ward with well established symptoms and signs of pellagra. All of them were delivered at full term. Two of the babies were still-born, while the other two were healthy and showed no signs of illness during their stay at the hospital. The nature of the labour in each case was normal.

#### TREATMENT.

Apart from symptomatic treatment, the treatment given was mainly dietetic. The hospital diet, as can be seen from the table, is quite a liberal one. After making the usual allowance of 10% for the portion of food that escapes digestion and absorption, the total calorie value comes to 2713 C., which is quite sufficient for a man at rest. The vitamin content also would seem to be sufficient. However, this diet was not well tolerated by cases with digestive disturbances; it was found necessary to give such cases a more digestible diet such as arrowroot, albumen water, and glucose. As soon as the digestive disturbances had subsided every attempt was made to give a high calorie, high protein, high vitamin-G diet. For this purpose two pints of milk, and two eggs were given daily in addition to the hospital full diet to those who could take it. Marmite, fresh baker's yeast, dried yeast powder, and liver were tried on groups of cases. It is our clinical impression that they stand in the following order of efficacy; milk, marmite, dried yeast powder, liver and fresh baker's yeast. The last two were found unsatisfactory, as the patients usually objected to taking the liver diet after a few days and fresh baker's yeast produced but little therapeutic effect. Nicobion by mouth or

by injection was given to cases with mental symptoms and those with severe lesions of the mucous surfaces, and was found most efficacious. Lately we have given nicotinic acid by mouth and found the results satisfactory but not so remarkable as those produced by nicotinic amide.

HOSPITAL FULL DIET.

Items	Quantity	Protein	Fat	Carbo- hydrate	Calcium	Phos- phorus	Iron	Vitamins						Calories	
								A	B	C	D	E	G		
RICE	20 oz. 567 G.	37	2.7	440	0.27	0.6464	0.0057	—	+	—	—	—	—	—	1973
MEAT	2 oz. 56.7 G.	5.35	34	0.53	0.0034	0.5727	0.0008	+	++	±	—	—	—	—	339
FISH	2 oz. 56.7 G.	10.65	0.43	0.14	0.017	0.8618	0.0010	—	—	—	—	—	—	—	48
GREEN VEGETABLE	8 oz. 228 G.	3.65	0.43	4.4	0.3215	0.0661	0.0089	++	++	+++	+	+	+	+	36
SOYA BEAN PRODUCT	5 oz. 142 G.	9.8	4.7	1.8	0.3877	0.1363	0.0031	+	++	—	—	—	—	—	92
GROUND NUT OIL	2 oz. 56.7 G.	—	56.7	—	—	—	—	±	—	—	—	—	—	—	527
TOTAL		66.45	98.96	446.9	1.000	1.000	0.0195								3015

All calculations in the above table are based on "Shanghai Foods" by Read, Lee and Cheng.

## MORTALITY :

We had 137 deaths in the series, i.e., a mortality rate of 32.6%. After correcting for cases who were admitted in a moribund condition and died soon after admission, and those who died of other diseases while undergoing treatment, we had 101 deaths, or a rate of 24.5%. The age incidence of the fatal cases is here presented in a tabular form.

The mortality when presented under the clinical groups (see page 2) brings out striking points:—

Group 1	163 cases	15 deaths	9.2%
Group 2	208 cases	73 deaths	35%
Group 3	5 cases	5 deaths	100%
Group 4	39 cases	8 deaths	21%

## PROGNOSIS :

We have found that the extremes of age affect the prognosis adversely. Debilitated patients usually succumbed early in the course of the disease. Mental symptoms such as mania, delirium and confusion when present should lead one to give a guarded prognosis. Intractable diarrhoea and the 'typhoid state' make the case almost hopeless.

## NOTES OF LABORATORY WORK.

120 specimens of stools were examined for ova with the following results :

Ascariasis .....	40 cases
Trichuriasis .....	7 cases
Ankylostomiasis .....	3 cases
Clonorchiasis .....	2 cases

63 cases had a red and white cell count and a differential count done. The results of these examinations showed the average red cell count to be 3,500,000, the average haemoglobin 65%, and the average relative lymphocytosis to be 48%.

Nicotinic acid estimations were performed on 19 specimens of blood and 21 specimens of urine by Mr. K. T. Liu, Secretary of the Nutrition Research Committee. The average nicotinic acid content of blood was 0.31 mg.% in acute cases and in convalescent cases 0.55

mg.%. Eight specimens of blood obtained from healthy young adults had an average nicotinic acid content of 0.75 mg.%. The average daily urinary excretion of nicotinic acid was 0.61 mg. in acute cases and 1.86 mg. in convalescent cases.

## SUMMARY.

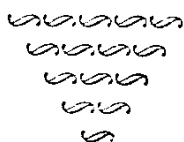
- 1 420 cases of pellagra are reported.
- 2 The symptomatology is described and discussed.
- 3 The epidemiological aspects are briefly touched upon.
4. A summary of the laboratory work done so far is reported.

## ACKNOWLEDGMENTS.

We are indebted to Dr. P. S. Selwyn-Clarke, the Honorable Director of Medical Services, for his constant encouragement and the supply of literature for reference, to acting Prof. P. B. Wilkinson for his instructive criticism, to Mr. K. T. Liu for the estimation of nicotinic acid. We wish also to express our thanks to Messrs. Olivier-Chine for the supply of nicotinic amide for injection (Nicobion).

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<i>Fig. No.</i>	<i>Name</i>	<i>Sex</i>	<i>Age</i>	<i>Notes on Illustrative Lesions.</i>
1	LEE TUNG	M.	30	Showing symmetrical well defined pigmentation over region of ischial tuberosities and medial aspects of the thighs.
2	LEE TUNG	M.	30	Showing the dry dermatitis undergoing desquamation.
3	LEE TUNG	M.	30	Showing distribution of dermatitis of hands and back of neck.
4	YOUNG BO	F.	26	Showing dermatitis of upper limbs and folliculitis of face.
5	YOUNG BO	F.	26	Showing healed dermatitis with some persisting pigmentation.
6	LEONG SZE	F.	60	Showing apathetic look in a case with dermatitis, diarrhoea and marked prostration.
7	TANG CHUNG	M.	42	Showing erythematous stage of dermatitis on dorsum of hands and desquamating stage on feet.
8	CHU MIU	F.	18	Showing dermatitis of neck and hands with bulla formation.
9	TSANG KWONG MUI	M.	50	Showing dermatitis of hands, feet, neck and front of chest.
10	YUEN KIN	M.	30	Showing dermatitis of feet with marked pigmentation simulating a burn which has been treated with tannic acid.
11	LEE TUNG	M.	30	Showing persistent marginal pigmentation following desquamation of skin.
12	LAU YUK	F.	25	Showing folliculitis on the lateral aspect of the lower limbs.
13	LEONG SAM	F.	52	Showing glossitis with deep, furrowed, glistening surface.
14	YUEN CHIK	F.	35	Showing marked ulcerative vulvitis and inflamed external piles.
15	LAU MUI	F.	20	A case of pellagra complicating pregnancy showing early stage of dermatitis of the face involving areas round eyebrow, bridge of nose, cheek and upper lip in symmetrical distribution.



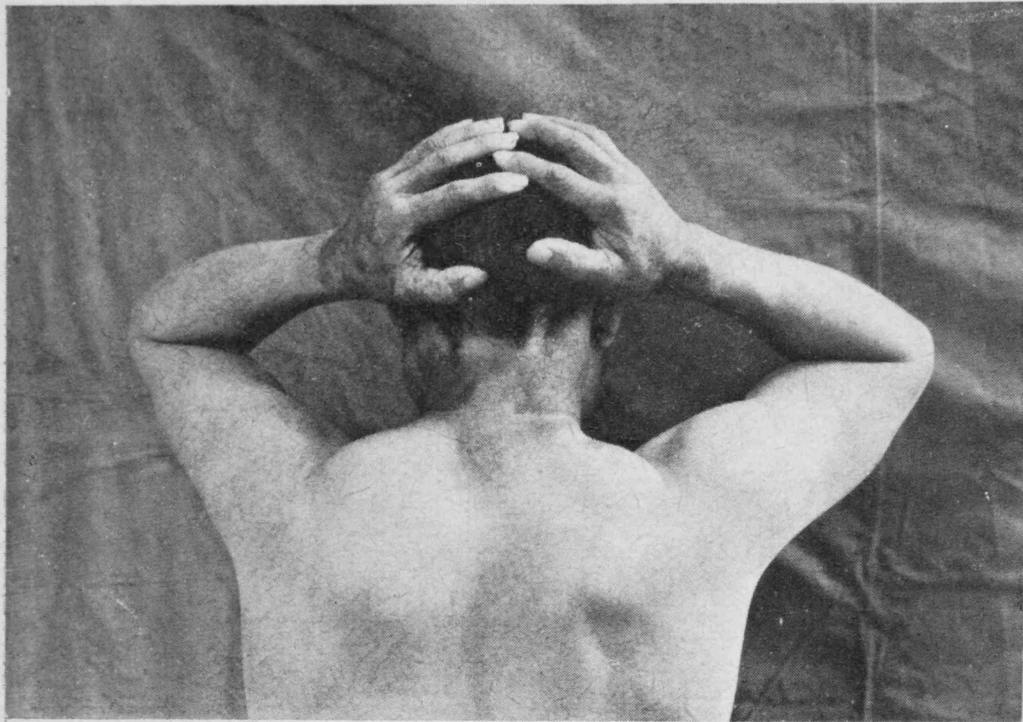


Fig. No. 3.

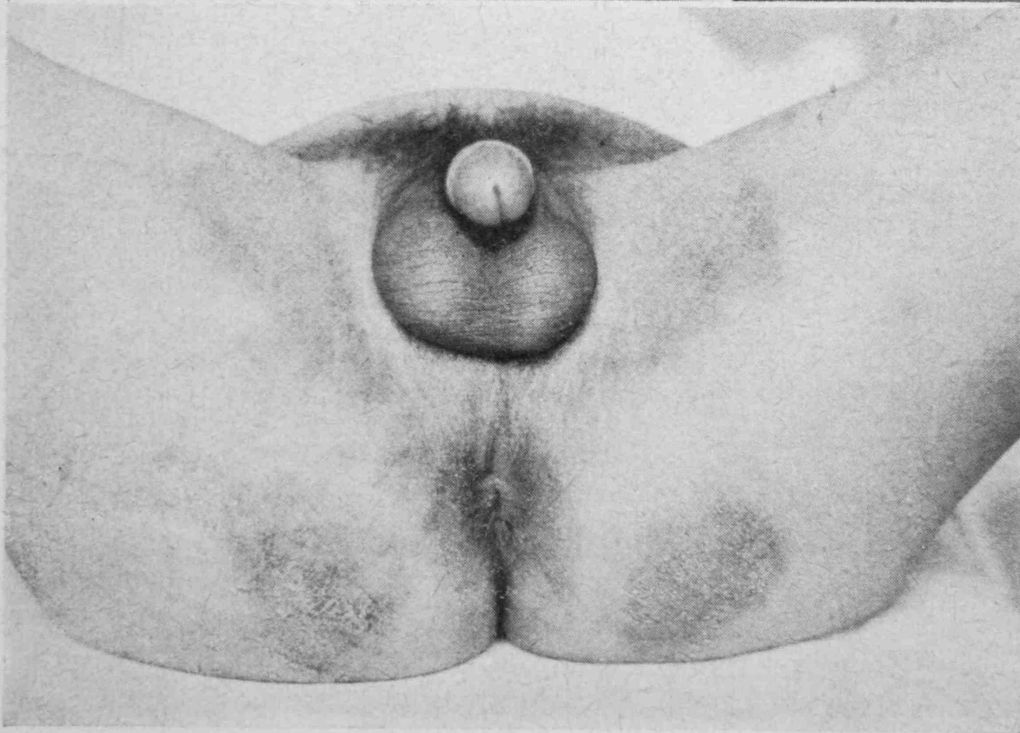


Fig. No. 1.

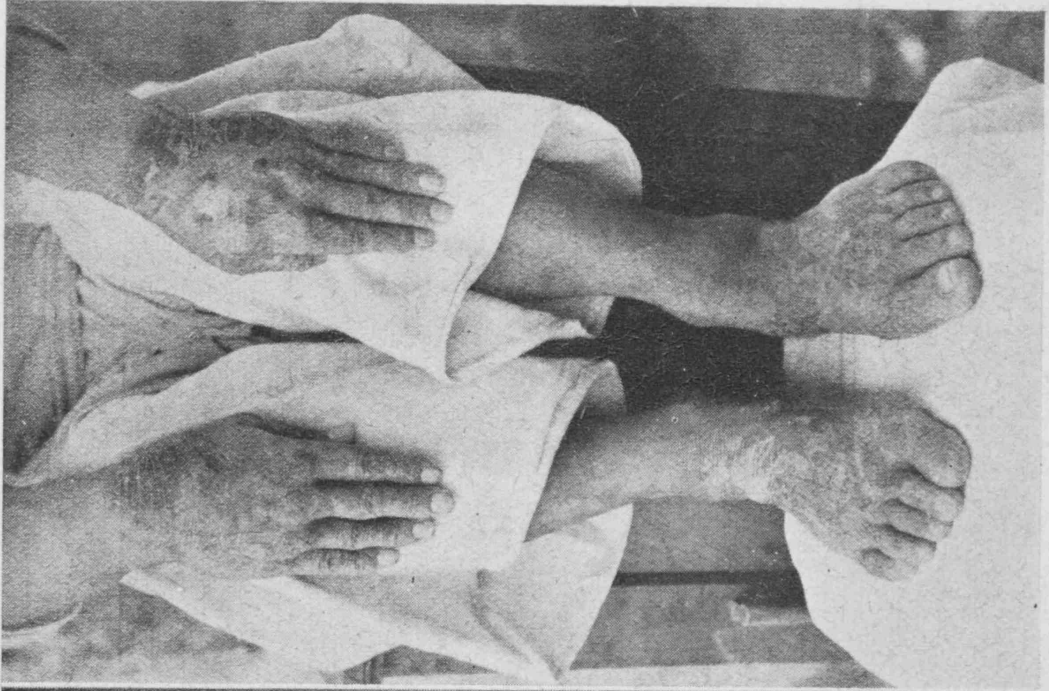


Fig. No. 2.



Fig. No. 4.



Fig. No. 5.



Fig. No. 8.

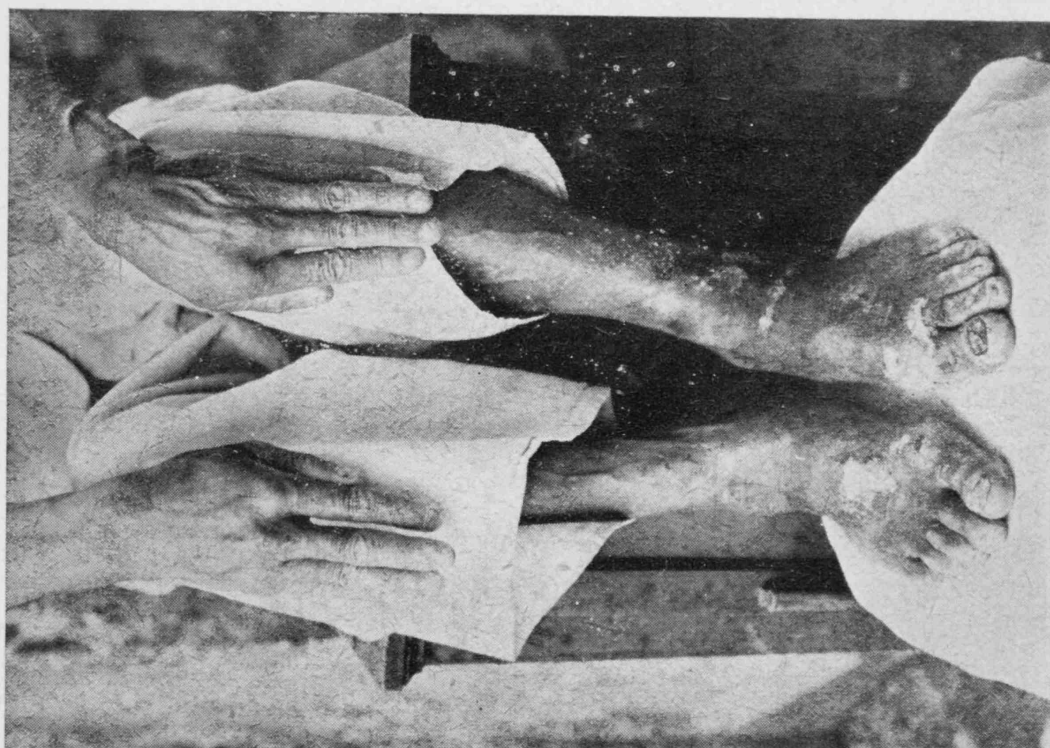


Fig. No. 7.



Fig. No. 9.

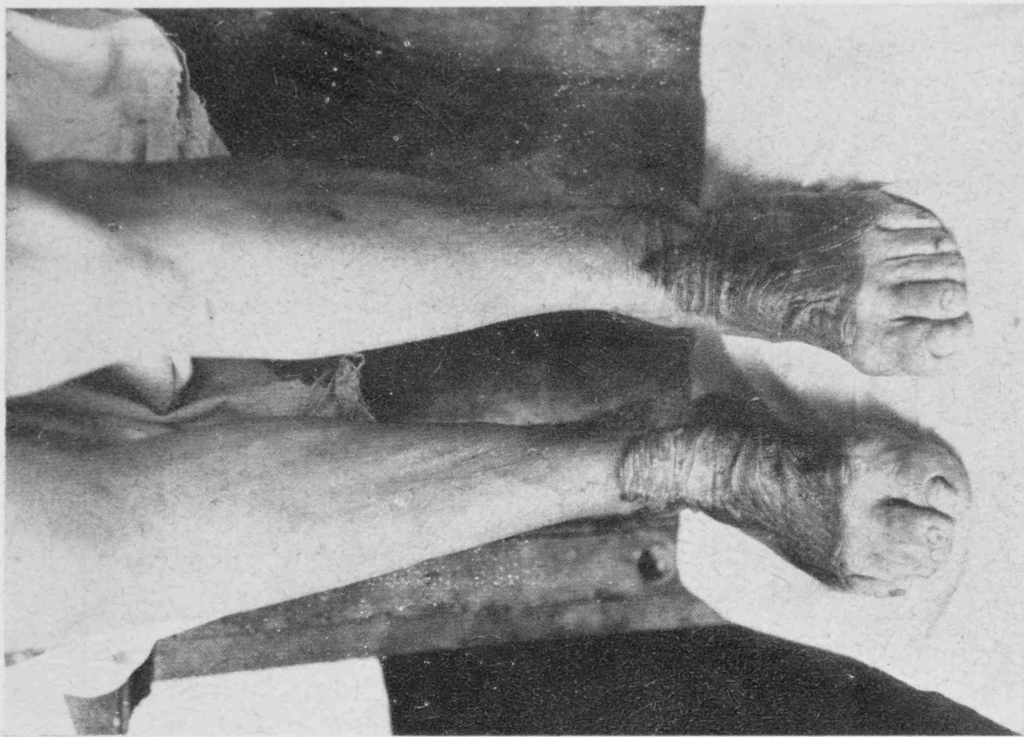


Fig. No. 10.

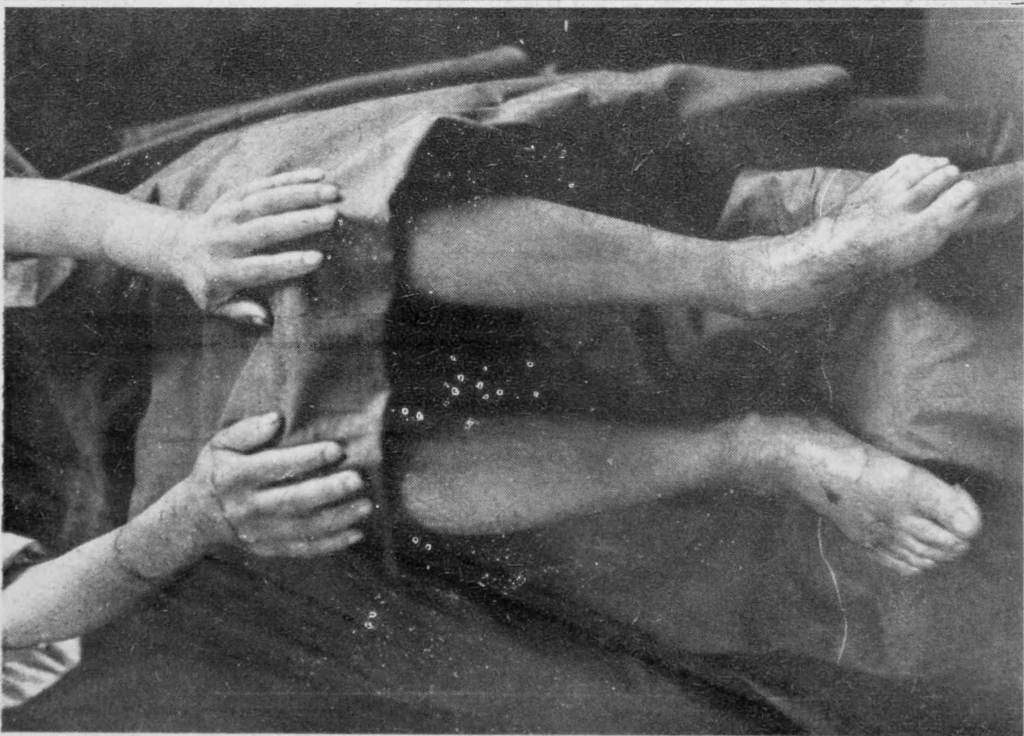


Fig. No. 11.

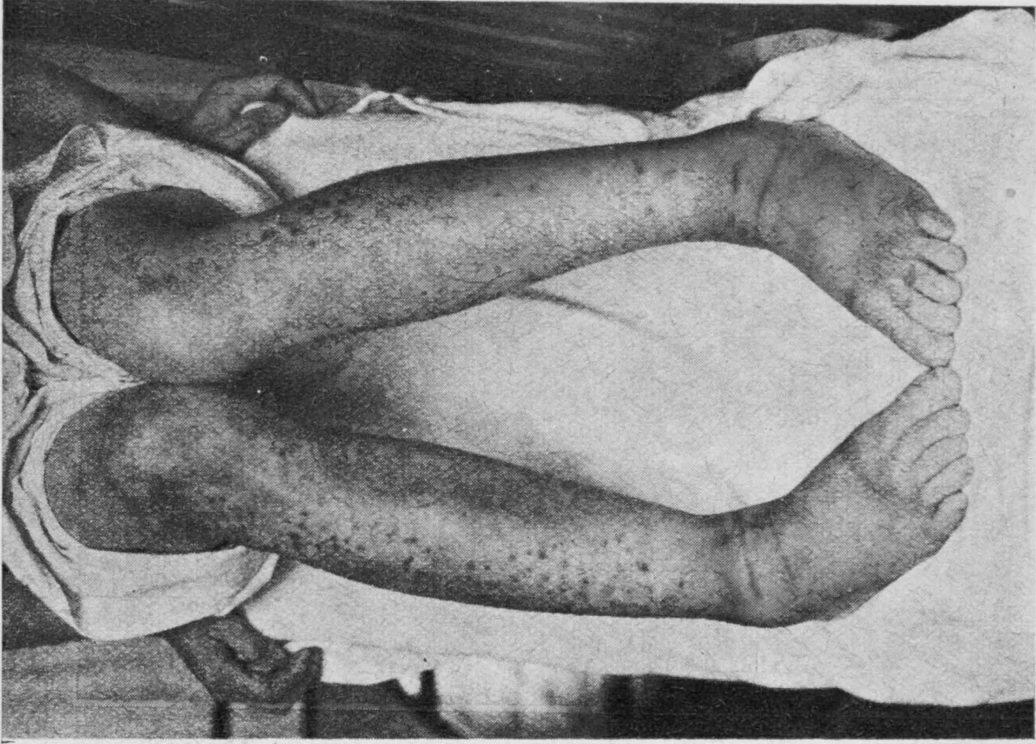


Fig. No. 12.



Fig. No. 13.

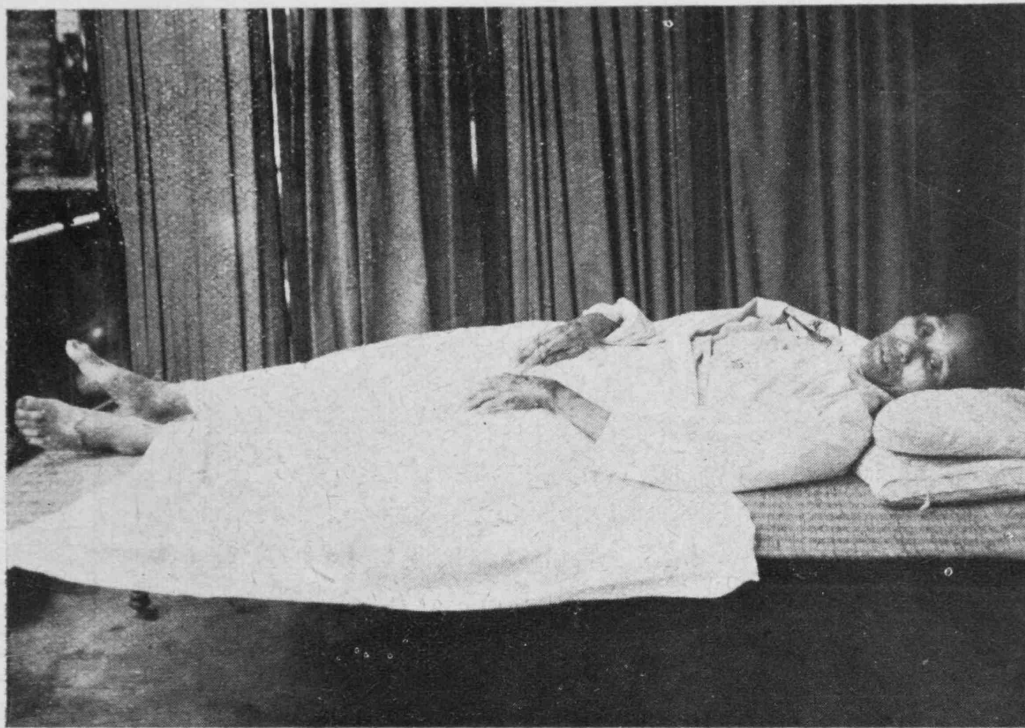


Fig. No. 6.

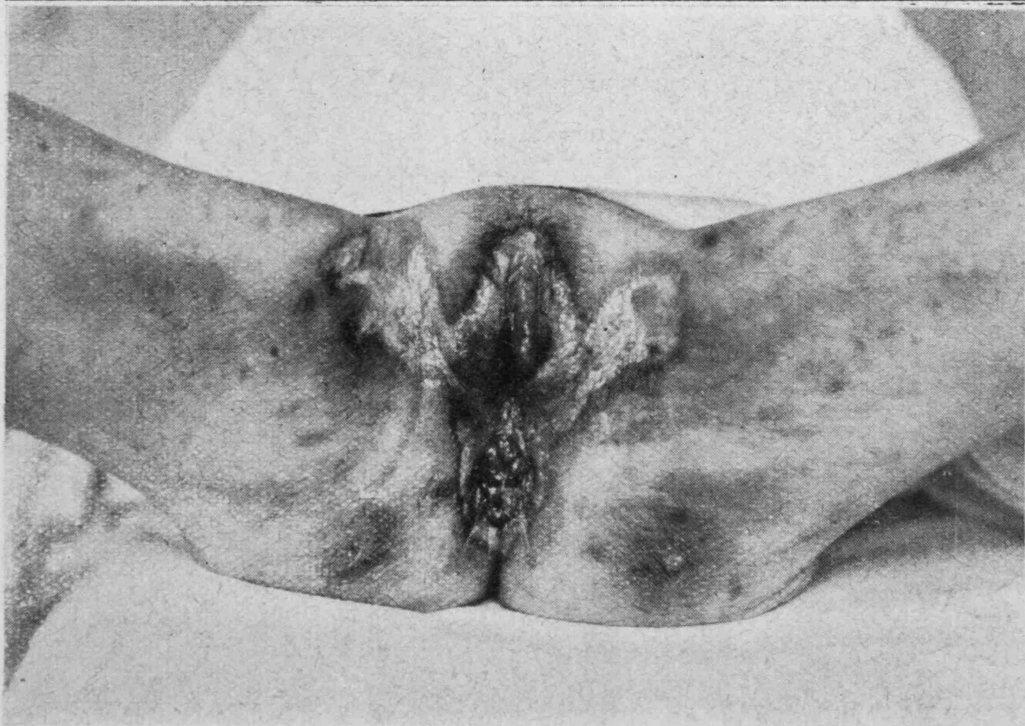


Fig. No. 14.



Fig. No. 15.



## RETROBULBAR NEURITIS DUE TO AN AVITAMINOSIS,

by

P. B. Wilkinson

and

Au King,

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## INTRODUCTION.

Unemployment, over-crowding and starvation wages have all helped to make the standard of living fall in Hong Kong during the last two years. This fall in the standard of living has, of course, affected mainly the poorer people who have become more and more prone to diseases of malnutrition. Beri-beri we have always with us, but pellagra, rare in Hong Kong till now, has become a scourge during the last six months.

Many of the victims of this generalised malnutrition have shown signs and symptoms attributable to a deficiency of more than one vitamin, and this has made exact diagnosis difficult in some cases. It is the object of this paper to describe a group of patients suffering from a retrobulbar neuritis apparently due to an avitaminosis. This syndrome has only been observed in Hong Kong since June this year and it seems to be one of the rarest of the nutritional disorders occurring here, for we have only been able to collect fifteen cases since our attention was first drawn to it six months ago.

## CLINICAL PICTURE.

All these patients tell the same story. Vision which has hitherto been perfectly normal becomes gradually or suddenly dim and this defect progresses until in some cases central vision is reduced to finger counting only. Two of the patients in this group of fifteen said they had had similar attacks before, and one of them said spontaneously that the attack was cured by improving her diet.

Other symptoms which occurred while the visual loss was coming on were soreness of the tongue, giddiness, palpitation, acroparaesthesiae and weakness of the limbs. In one case scrotal eczema had accompanied the visual loss and in another there had been marked oedema of the eyelids during the course of the disease. Two of the patients gave a history of recurrent attacks of oedema of the ankles during the two years preceding the visual loss, and both had noticed that this swelling disappeared if beans were introduced into the diet. *Perlèche* was noted in two of the patients on their admission to hospital and

one of these men showed changes similar to perlèche at the external canthi. Neither of these men had complained of sore mouth or sore tongue during the onset of the visual loss.

One of the four women in this group was an undoubted pellagrin palpitation and giddiness.who gave a history of some months diarrhoea. On admission she showed marked pigmentation of the hands and feet and her visual defect had already progressed to left sided optic atrophy. We include her in this series as we have reason to think that this syndrome is a pellagrous condition and not an entity sui generis. She was the only patient in the series who showed definite evidence of dermatitis. No other cases showed pigmentation, phrynoderma, lichen pilaris or linear skin lesions.

On examining the eyes the media were found to be normal in all cases. Externally the eyes showed no evidence of an avitaminosis A, though Bitot's spots and xerophthalmia have both been common in Hong Kong during the last year. In every case save two the pupillary reactions to direct light were found to be sluggish, and the contraction was poorly maintained. The consensual reflex, and the reactions of the pupils on convergence and shading were normal. The fundi were normal in eleven of these patients, the remaining four showing varying degrees of optic atrophy. The commonest and earliest change is the appearance of temporal pallor. All the patients showing optic atrophy had been ill for at least two or three months and it is therefore likely that temporal pallor does not supervene until 8 to 10 weeks after the onset of visual defect. In the one classical pellagrin in the series the whole of the left disc was atrophic on admission and thinning of the retinal vessels was conspicuous. The atrophy had evidently been coming on for some months as the patient said she "had been knocking into things on her left side" recently. She was the only patient who failed to respond to treatment and it seems probable that if this condition is neglected it may lead ultimately to an irrecoverable optic atrophy. This is, of course, the usual fate of many an optic nerve attacked by retrobulbar neuritis, whatever the aetiology of the neuritis. Photophobia was a rare symptom and only one patient complained of it and then only on being asked directly. In two of these cases the visual loss was found to be more marked in one eye than the other, but all the other cases showed an equal reduction of vision in both eyes. The loss estimated by Snellen's test types ranged from  $\frac{6}{18}$  in the early cases to less than  $\frac{6}{60}$  or even finger counting at 3 feet in the more long standing cases.

Perimetric and X-ray examinations were made whenever possible. In all cases save two perimetric observations showed a concentric or quadrantic constriction of the visual fields. In one case one field only showed constriction and in one case the fields to red and green were markedly constricted while those for white remained normal. In only two cases were quadrantic losses found. One peculiar point which emerged from these field examinations was that in no case was it possible to demonstrate a central or paracentral scotoma to white, red or green with any type of illumination. In several cases the observations were checked by both of us independently and there is no doubt that scotomata were absent. Comment will be made later on the value of field observations as a means of assessing the effect of treatment.

Skiagrams of the skull were taken in eight of the cases, but apart from a slight degree of erosion of the posterior clinoid processes found in two of the skiagrams they showed no significant changes. It was clear that the erosion of the posterior clinoid processes was not connected aetiologically with the loss of vision. Examination of the nervous system and the cerebrospinal fluid was likewise negative in the majority of cases. Three of the cases showed a loss of knee or ankle jerks or both and in two cases there was a definite exaggeration of the knee jerks without, however, any weakness or spasticity. No objective sensory loss to any form of testing was demonstrable in any case. The plantar responses in all cases were flexor and there was no disturbance of sphincter control.

None of the patients in this group showed any mental changes, nor was evidence of mental disease found in their family histories.

The cerebrospinal fluid was normal in the thirteen cases where it was examined and the blood and fluid Kahn reactions were uniformly negative. The blood pictures were normal in twelve of these patients. Three showed a mild degree of hypochromic anaemia.

The appended tables show in tabular form the symptoms, signs and laboratory findings in these cases, and the two diets used in this investigation. The visual fields are shown in the appendix.

#### AETIOLOGY.

These points may be of aetiological significance. All our patients come from the poorer classes. Six of them were unemployed at the time of onset of the disease. The disparity between the sexes, eleven men to four women, is probably not significant as our numbers were so small, and for the same reason it would be unwise to stress the

fact that all save one of our patients were over 20 years of age, and that this condition has only been seen here once in a child.

The mode of onset was gradual in the majority of the cases. The longest history was ten months, the shortest one week and the average duration of the visual loss before advice was sought was just over three months. Two of the patients had suffered before from a similar failure of vision which had recovered spontaneously.

Undoubtedly the factor of greatest aetiological importance is the change in diet which has recently been forced upon so many of the poorer people in Hong Kong. The increasing amount of unemployment in the colony has inevitably led to dietetic restrictions, and in all the cases in this group we found that the diet was, or had recently become, unbalanced. This parallels exactly the state of affairs found in taking the history of pellagra patients. With striking unanimity these pellagrins link the onset of their disease to their economically enforced abandonment of salt or other fish. All the patients in this group, and it is noteworthy that six of them were unemployed, complained about their food when they were specifically questioned about diet. Three had been compelled to make changes in their diet during the last few months because of the recent rise in prices and four said they never had meat of any kind. The common dietetic history was that two meals were eaten daily, each one consisting mainly of rice, vegetables and fish. The rice was invariably polished, the fish almost invariably salt. It is easy to realise that first class protein is conspicuously lacking from such diets, and the lower class Chinese who rarely eat eggs or cheese are dependent almost entirely on meat for their first class protein. A scarcity of meat is so common in these diet histories that there seems little doubt that a relative deprivation of first class protein is the precipitating if not the causal factor in producing this picture.

#### THERAPY.

It was abundantly clear after the examination of the first two or three cases in this group that we were dealing with a retrobulbar neuritis due to some nutritional defect and appropriate therapy did much to strengthen that supposition. First of all we tried dried yeast in small daily doses and found that 1 drachm three times a day if continued long enough would bring about a cure as shown by the return of visual acuity towards normal and by widening of the visual fields.

As the symptoms presented by this group resembled closely the early symptoms of pellagra we tested the effect of nicotinic acid on 11 of the cases. Knowing that nicotinic acid, though marvellously

	Sex.	Age.	Occupation.	Date seen.	Previous attacks of defective vision.	Duration visual loss.	V.A. on Admission.
Case I.	Female	50.	Unemployed.	29. 6.40.	None.	3 weeks.	R.V.A. $\frac{6}{60}$ . L.V.A. $\frac{6}{60}$ .
Case II.	Male	48.	Motor driver.	23. 8.40.	One 10 years ago. Recovered without treatment.	1 week.	R.V.A. $\frac{6}{60}$ . L.V.A. $\frac{6}{60}$ .
Case III.	Male	42.	Unemployed.	28. 8.40.	None.	7 months.	R.V.A. $\frac{6}{60}$ . L.V.A. Counts fingers at 3 feet.
Case IV.	Male	40.	Policeman.	12. 9.40.	One in 1923. Recovered without treatment.	2 weeks.	R.V.A. $\frac{6}{60}$ . L.V.A. $\frac{6}{60}$ .
Case V.	Female	22.	Unemployed.	25. 9.40.	None.	10 months.	R.V.A. $\frac{6}{60}$ . L.V.A. $\frac{6}{60}$ .
Case VI.	Male	30.	Tailor.	26. 9.40.	None.	1 month.	R.V.A. $\frac{6}{60}$ . L.V.A. $\frac{6}{60}$ .
Case VII.	Male	21.	Unemployed.	2.10.40.	None.	2 months.	R.V.A. $\frac{6}{36}$ . L.V.A. $\frac{6}{36}$ . Partly B.S.
Case VIII.	Male	31.	Unemployed.	2.10.40.	None.	2 months.	R.V.A. $\frac{6}{60}$ . L.V.A. $\frac{6}{60}$ .
Case IX.	Male	30.	Carpenter.	9.10.40.	None.	6 months.	R.V.A. $\frac{6}{18}$ . L.V.A. $\frac{6}{18}$ .
Case X.	Male	45.	Unemployed.	9.10.40.	None.	2 months.	R.V.A. $\frac{6}{18}$ . L.V.A. $\frac{6}{18}$ . partly.
Case XI.	Male	35.	Policeman.	11.10.40.	None.	2 weeks.	R.V.A. $\frac{6}{36}$ . partly. L.V.A. $\frac{6}{12}$ .
Case XII.	Female	40.	Housewife.	12.10.40.	None.	5 months.	R.V.A. $\frac{6}{24}$ . L.V.A. $\frac{6}{18}$ .
Case XIII.	Male	38.	Motor driver.	21.11.40.	None. Had conjunctivitis 6 months ago. V. A. then was 6/6.	1 month.	R.V.A. 6/36 L.V.A. 6/36
Case XIV.	Male	12.	School child	20.11.40.	None.	Not certain. Visual loss detected at routine school inspection.	R.V.A. 6/24 L.V.A. 6/24
Case XV.	Male	46.	Hawker.	9.12.40.	None.	6 months.	R.V.A. 6/18 partly. L.V.A. 6/18 partly.

TABLE SHOWING SIGNS, SYMPTOMS AND TREATMENT.

<i>Pupils.</i>	<i>Optic Discs.</i>	<i>Fields.</i>	<i>Reflexes.</i>	<i>Associated symptoms.</i>	<i>C.S.F.</i>
Semidilated. Sluggish to light. Contr: poorly maintained.	L.O.D. pale 2 1/2 mos: later bilat: O.A.	—	K.J. O O. A.J. O O.	Palpitation, diarrhoea, sore tongue, pigmentation hands and feet for "a few months."	Not examined
React sluggishly to light. Contr: poorly maintained.	Normal.	Uniform constriction. No scotoma.	Normal.	Giddiness on getting up from recumbent position. No glossitis. No dermatitis.	Normal.
React sluggishly to light. Contr: poorly maintained.	Normal.	Uniform constriction. No scotoma.	K.J. present. A.J. O O.	Numbness lips, face, fingers, toes for 7 months. No glossitis or dermatitis.	Normal.
React sluggishly to light. Contr: poorly maintained.	Normal.	Uniform constriction. No scotoma.	Normal.	Scrotal eczema for last 2 months. No glossitis or dermatitis.	Normal.
Direct light reaction sluggish.	Temporal pallor both discs.	No scotoma. Restricted in upper quadr: B.S.	Normal.	Puffy eyelids, tingling face, lips, fingers, palpitation and giddiness for 10 months. No dermatitis or glossitis.	Normal.
React sluggishly to direct light. Contr: poorly maintained.	Normal.	Concentric constriction. No scotoma.	Normal.	None. No dermatitis or glossitis.	Normal.
Pupillary reactions normal.	Temporal pallor more marked on left side.	Concentric constriction. No scotoma.	K.J. ++ A.J. ++	Recurrent oedema of legs for past 2 years, relieved by eating beans. No glossitis or dermatitis.	Normal.
React sluggishly to direct light. Contr: poorly maintained.	Slight temporal pallor on both sides.	Concentric constriction. No scotoma.	Normal.	Perléche present on admission but no history of glossitis, stomatitis, paraesthesiae or dermatitis.	Normal.
Reaction to direct light sluggish.	Normal.	R. normal. L. constr: nasal quadrants.	Normal.	Occasional swelling of ankles for last 2 years, relieved by eating beans. No stomatitis, glossitis, dermatitis or paraesthesiae.	Not examined
Reaction to direct light sluggish and ill maintained.	Normal.	Normal.	Normal.	Acroparaesthesiae for 2 months. No glossitis, stomatitis, dermatitis or diarrhoea.	Normal.
Reaction to direct light sluggish and poorly maintained.	Normal.	R. marked constriction. L. normal. No scotoma.	Normal.	Failure of vision more marked in right eye. No paraesthesiae, glossitis, dermatitis or diarrhoea.	Not examined
Reaction to direct light sluggish and poorly maintained.	Normal.	To white normal. To red and green markedly constr: B.S. No scotoma.	A.J. O O. Others normal.	Weakness of the extremities, palpitation and sore tongue for 5 months. No dermatitis or diarrhoea.	Normal.
Reactions normal.	Normal.	Uniformly contracted. No scotoma.	K.J. Normal. A.J. Normal.	Slight degree of angular conjunctivitis.	Normal.
Sluggish to light.	Normal.	Normal.	A.J. ++ K.J. ++	Angular conjunctivitis.	Normal.
Sluggish to light.	Normal.	Constricted. No scotoma.	K.J. present. A.J. present.	None.	Normal.

Blood picture.	X-ray Skull.	C.S.F. Kahn.	Blood Kahn.	Treatment.	Stay in Hospital.	V.A. on Discharge.
Hypochromic Anaemia.	Negative.	—	Negative.	Special diet. Yeast powder.	2½ months.	No improvement.
Normal.	Not done.	Negative.	Negative.	Dry yeast 1 drachm t.i.d. for 42 days, red rice and full Chinese diet.	48 days.	R.V.A. $\frac{6}{9}$ L.V.A. $\frac{6}{9}$ Fields slightly larger.
Normal.	Negative.	Negative.	Negative.	Yeast 14 days gr. v. t.i.d. nil. Nicotinic acid 50 mgm. b.i.d. for 7 days. Full Chinese diet.	43 days.	R.V.A. $\frac{6}{9}$ L.V.A. $\frac{6}{9}$ Fields unchanged.
Normal.	Negative.	Negative.	Negative.	Yeast 1 gm. daily 7 days nil. Nicotinic acid 50 mgm. b.i.d. 7 days. Chinese full diet.	31 days.	R.V.A. $\frac{6}{9}$ L.V.A. $\frac{6}{9}$ Fields slightly enlarged.
Hypochromic Anaemia.	Negative.	Negative.	Negative.	Nicotinic acid 50 mgm. b.i.d. for 7 days.	18 days.	R.V.A. $\frac{6}{9}$ L.V.A. $\frac{6}{9}$ Fields normal.
Normal.	Negative.	Negative.	Negative.	Nicotinic acid 50 mgm. b.i.d. for 7 days. Chinese full diet.	26 days.	R.V.A. $\frac{6}{12}$ L.V.A. $\frac{6}{12}$
Normal.	Negative.	Negative.	Negative.	Nicotinic acid 50 mgm. b.i.d. for 7 days. Chinese full diet.	19 days.	R.V.A. $\frac{6}{12}$ L.V.A. $\frac{6}{12}$
Normal.	Negative.	Negative.	Negative.	Nicotinic acid 50 mgm. b.i.d. for 7 days.	22 days.	R.V.A. $\frac{6}{12}$ L.V.A. $\frac{6}{12}$
Hypochromic Anaemia.	Not done.	Negative.	Negative.	Nicotinic acid 50 mgm. b.i.d. for 7 days. Chinese full diet.	23 days.	R.V.A. $\frac{6}{6}$ L.V.A. $\frac{6}{6}$
Normal.	Not done.	Negative.	Negative.	Nicotinic acid 50 mgm. b.i.d. for 7 days. Full Chinese diet.	23 days.	R.V.A. $\frac{6}{9}$ L.V.A. $\frac{6}{9}$ Numbness less.
Normal.	Negative.	Negative.	Negative.	Nicotinic acid 50 mgm. b.i.d. for 7 days. Chinese full diet.	18 days.	R.V.A. $\frac{6}{9}$ L.V.A. $\frac{6}{9}$ R. field full again.
Normal.	Not done.	Negative.	Negative.	Nicotinic acid 50 mgm. b.i.d. for 7 days. Chinese full diet.	11 days.	R.V.A. $\frac{6}{12}$ L.V.A. $\frac{6}{12}$ Palpitation less. Tongue much less painful.
Normal.	Not done.	Negative.	Negative.	Riboflavin 1 mgm. t.d.s. for 10 days. Full diet.	11 days.	R.V.A. 6/6 L.V.A. 6/6 Visual fields normal.
Normal.	Not done.	Negative.	Negative.	Full diet in first week. Later supplemented by riboflavin 1 mgm. t.i.d. for one week.	14 days.	R.V.A. 6/6 L.V.A. 6/6
Normal.	Not done.	Negative.	Negative.	1st week deficiency diet. 2nd week deficiency diet; riboflavin 3 mgm. daily, by mouth. 3rd week deficiency diet; thiamin 3 mgm. daily, subcutaneously. 4th week deficiency diet; Nicotinic acid 50 mgm. b.d.	Still in hospital.	1st week. Unchanged. 2nd week. Unchanged. 3rd week. Unchanged. 4th week. $\frac{6}{9}$ ptly. $\frac{6}{9}$ ptly.

effective in clearing up the muco-cutaneous lesions of pellagra, had little effect on the peripheral nervous changes produced by the disease we expected to find the drug less efficacious than yeast. These expectations were not borne out.

Nicotinic acid in a dose of 100 mgm. daily by mouth for one week exerted a marked influence on the visual defect, vision returning in some cases from less than  $\frac{6}{60}$  to  $\frac{6}{9}$  or more in one to two weeks from beginning the administration of the drug. The dosage given and the changes in visual acuity before and after can be found in the table of signs and symptoms.

The first twelve patients, with the exception of the pellagrin, were given full Chinese diet while in hospital. As the rice in this diet is red or unpolished it might be argued that the vitamin B<sub>1</sub> content of the diet or some other factor contained in it was enough to bring about a cure, and this suggestion was supported by the fact that in at least one patient (Case XIV) improvement had occurred before specific therapy was undertaken.

In an attempt to ascertain precisely which factor in the B complex was responsible for bringing about this dramatic improvement in visual acuity we applied selective therapeutic measures to the last three cases in the series. These three patients on admission had a central visual acuity of  $\frac{6}{36}$ ,  $\frac{6}{24}$  and  $\frac{6}{18}$  respectively.

Case XIII, a motor driver aged 38 was known to have had a visual acuity of  $\frac{6}{6}$  in each eye six months before admission, because he had sought treatment then for conjunctivitis. When admitted he stated that one month past his vision had been failing, and when tested the visual acuity of both eyes was found to be  $\frac{6}{36}$ . Riboflavine 1 mgm. three times a day together with full hospital Chinese diet restored vision to  $\frac{6}{6}$  in each eye in 10 days. The enlargement of the fields in this time can be seen by the charts (case XIII) in the appendix.

Case XIV, a schoolboy aged 14 had improved after one week on the full hospital diet. 1 mgm. of riboflavine was then given three times daily as a supplement to the diet and at the end of the second week visual acuity was  $\frac{6}{6}$  in both eyes.

Case XV. was a woman aged 46 who earned her living as a hawker. Her vision had been failing for six months and was reduced to  $\frac{6}{18}$

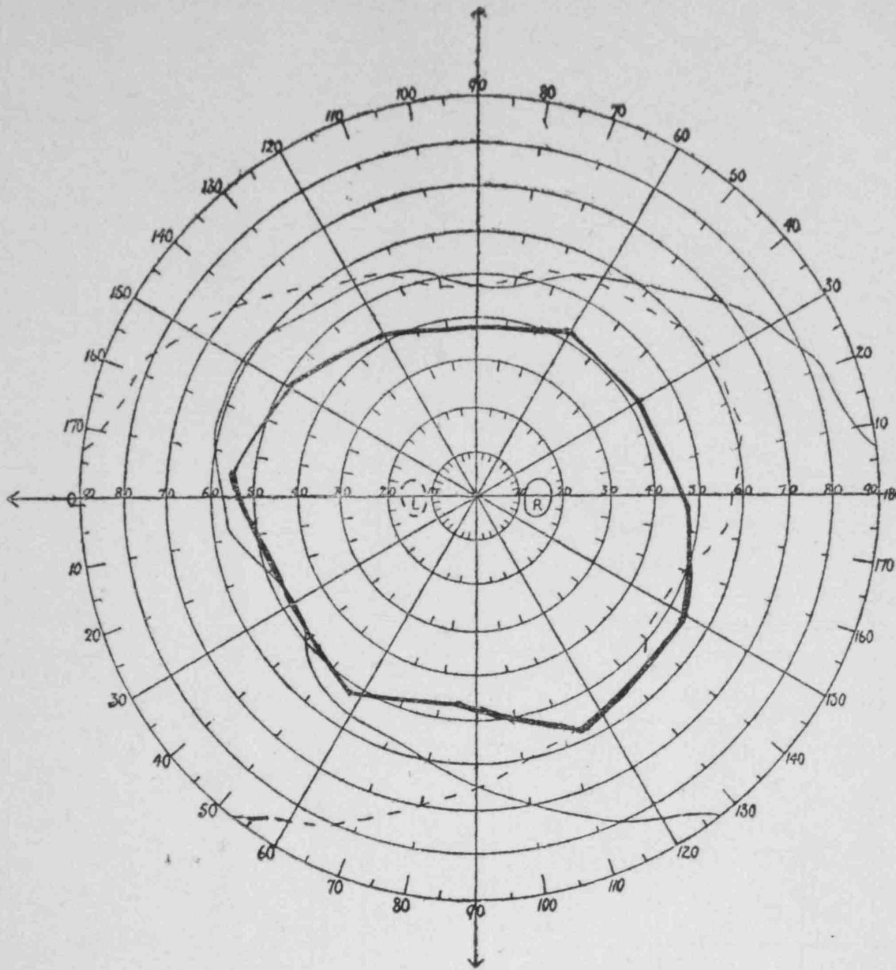


TABLE II.  
Queen Mary Hospital.—Chinese full diet.

Items.	Quantity	Protein	Fat	Carbo- hydrate	Calcium	Phosphorus	Iron	Vitamins					Calories	
								A	B <sub>1</sub>	B <sub>2</sub>	C	D		E
White Rice, 75% Rice, Red 25%	16 oz., 452.8 G.	29.5	2	348	0.7830	0.5640	0.0085	+	+					1,528
Meat	4 oz., 113.2 G.	22.8	6.9	2	0.0067	0.2632	0.0036	+	+	+	+			162
Fish	4 oz., 113.2 G.	28.5	2.5	—	0.0672	0.3456	0.0017	+			+			138
Green Vegetable	14 oz., 376.2 G.	7.1	0.8	7	0.2292	0.1478	0.0234	+	+	+	+	+		65
Dried Beans	2 oz., 56.6 G.	10.6	0.4	32	0.0435	0.0198	0.0003	+	+					174
Ground Nut Oil	2 oz., 56.6 G.	—	56.6	—	—	—	—	—	—	—	—	+		509
Total		98.5	69.2	398	1.1296	1.3404	0.0375							2,576
Deficiency Diet.—Given to Case XV.														
Rice, White	22 oz., 622.6 G.	40	2.5	483	0.3000	.7100	.0062							2,115
Green Vegetable	16 oz., 452.8 G.	8	.9	8	.2619	.1689	.0267							72
Ground Nut Oil	2 oz., 56.6 G.	—	56.6	—	—	—	—							509
Salt Fish	2 oz., 56.6 G.	14	1	—	0.3600	.0900	.0014							65
Total		62	61	491	.5979	.9689	.0343							2,760

All calculations in this table are based on "Shanghai Foods" by Read, Lee and Cheng.

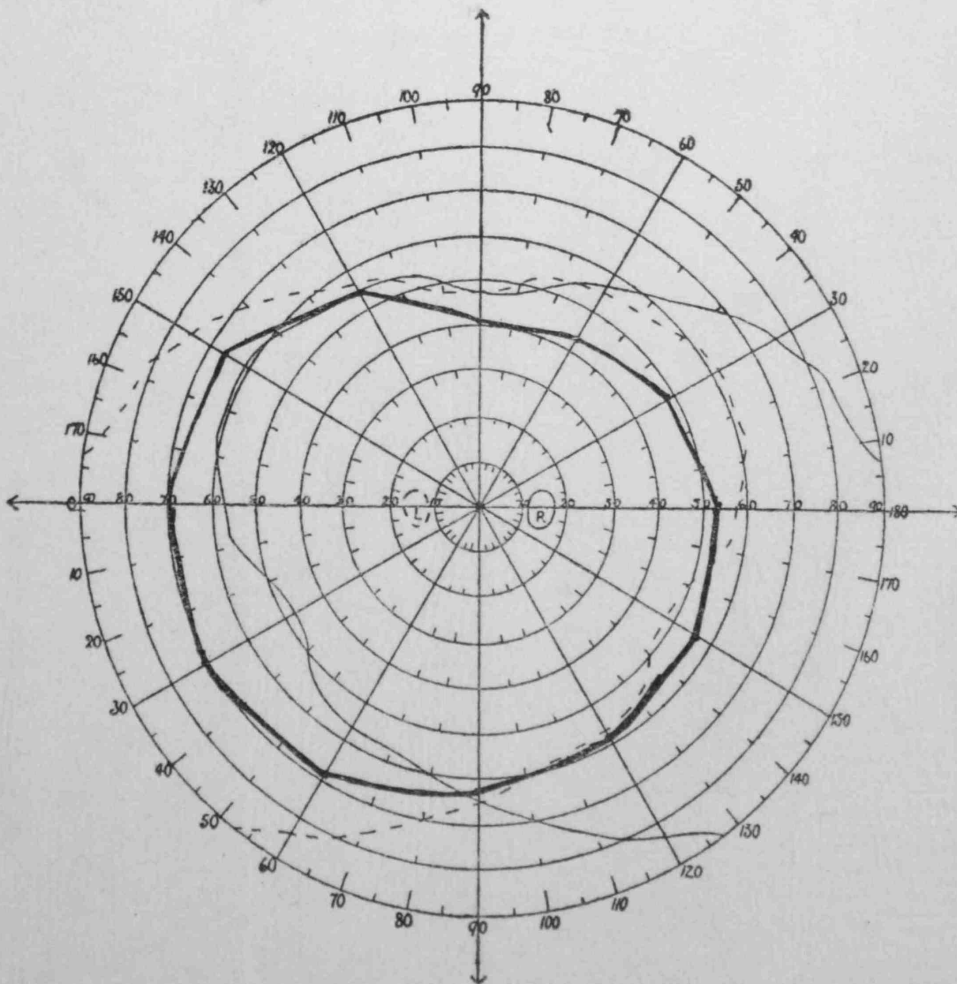
Left.



L.V.A.  $\frac{6}{60}$ .

To show the visual fields on admission. 2 mm. white object

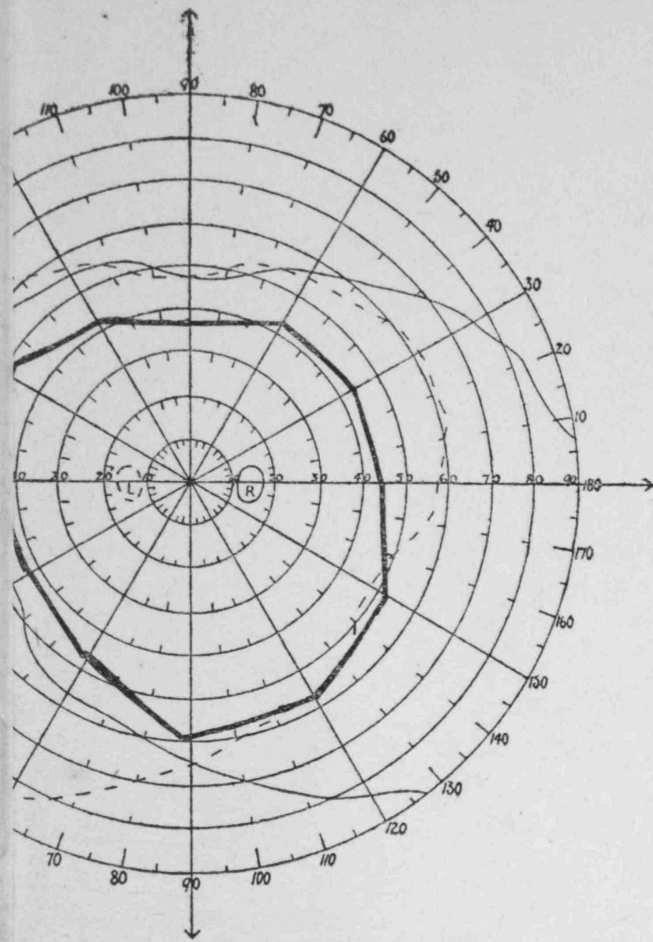
Left.



L.V.A.  $\frac{6}{9}$ .

To show fields after treatment with small daily doses of yeast for 6 weeks. Note how the fields themselves.

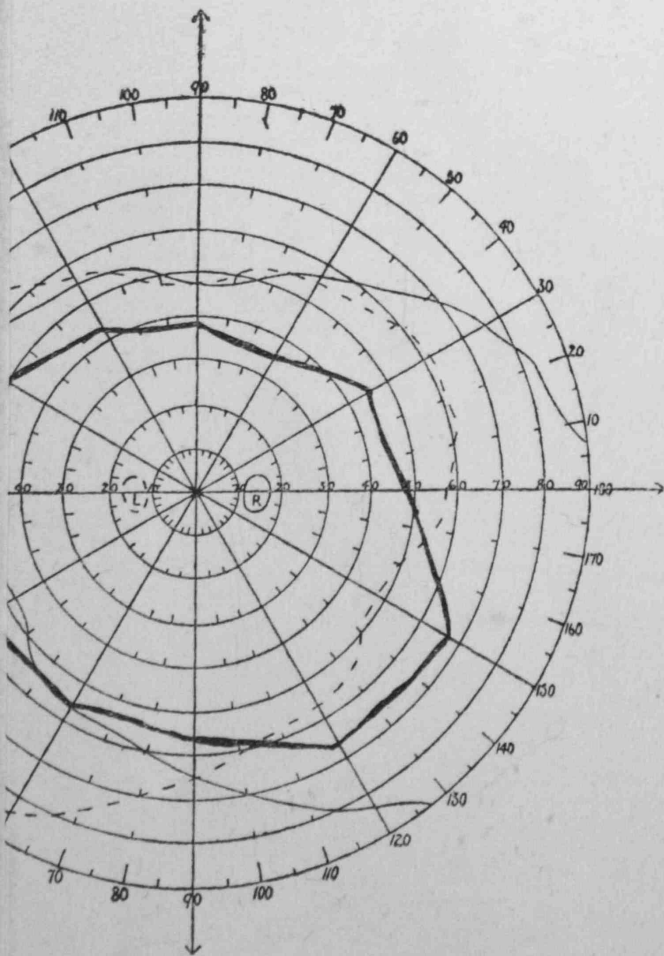
Right.



$$\text{R.V.A. } \frac{6}{60.}$$

ct. Daylight.

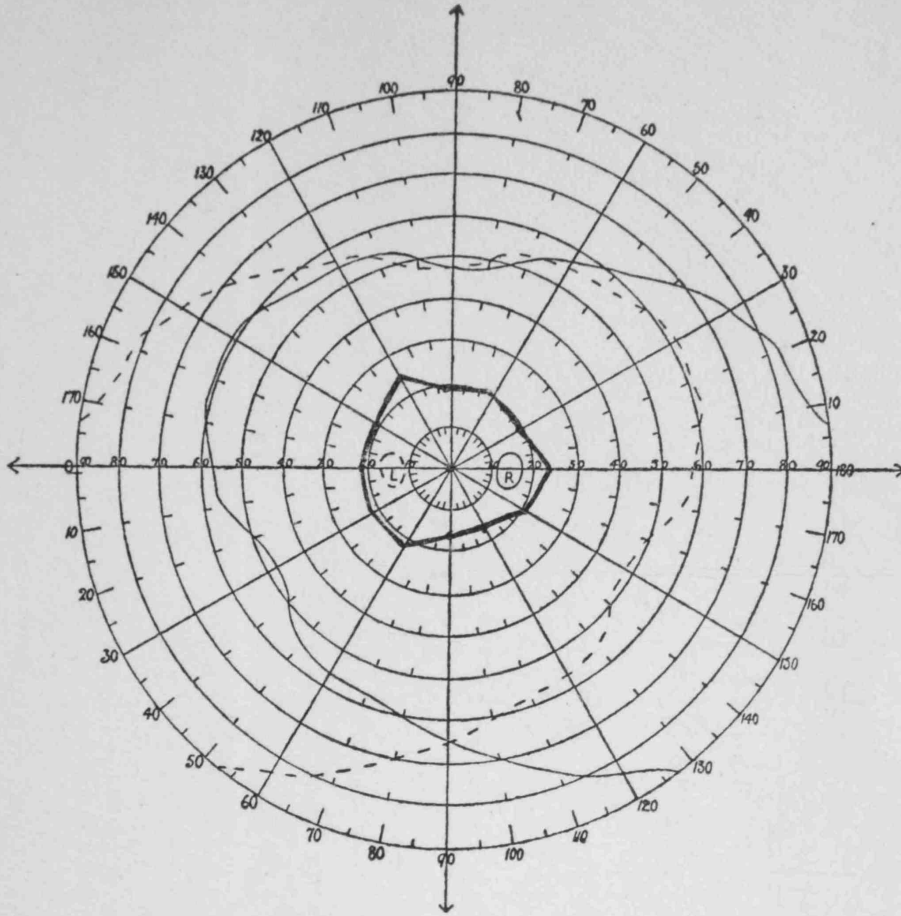
Right.



$$\text{R.V.A. } \frac{6}{9.}$$

v visual acuity improves more rapidly than

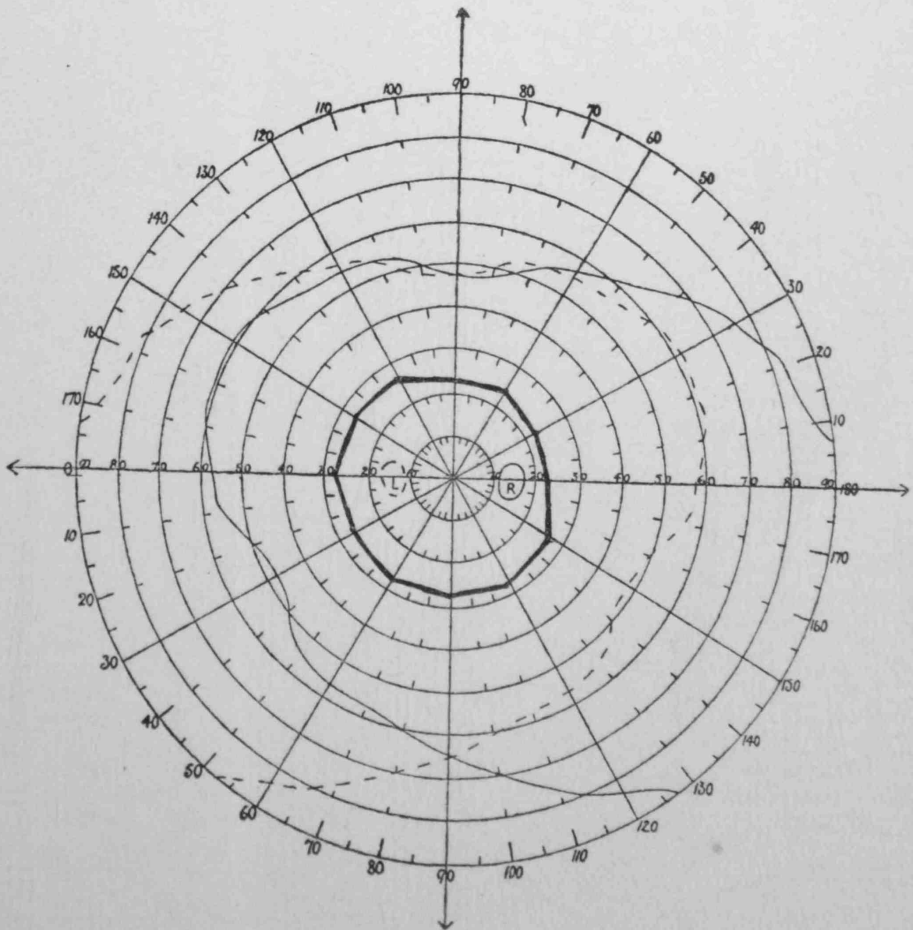
Left.



L.V.A.  $\frac{6}{60}$ .

To show the concentric constriction of the visual fields on admission. 2

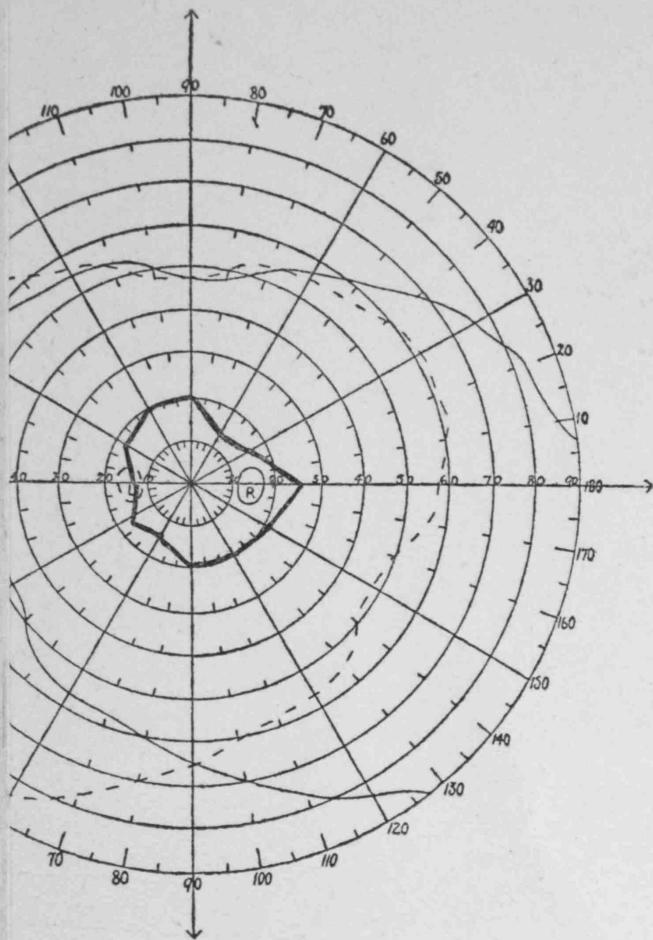
Left.



L.V.A.  $\frac{6}{6}$  ptly.

To show the fields after a week's treatment with 100 mgm. of nicotinic acid

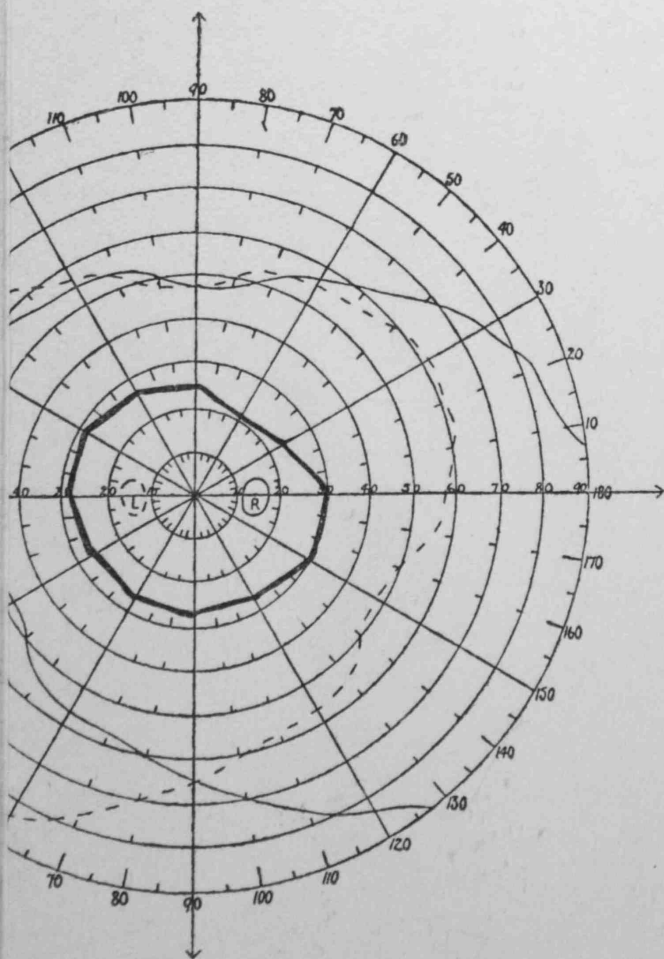
Right.



$$\text{R.V.A. } \frac{6}{60}.$$

mm. white object. Daylight.

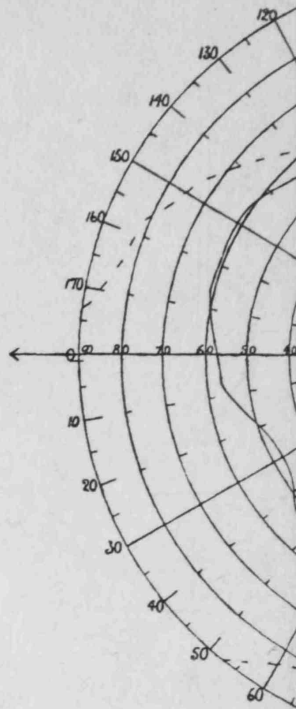
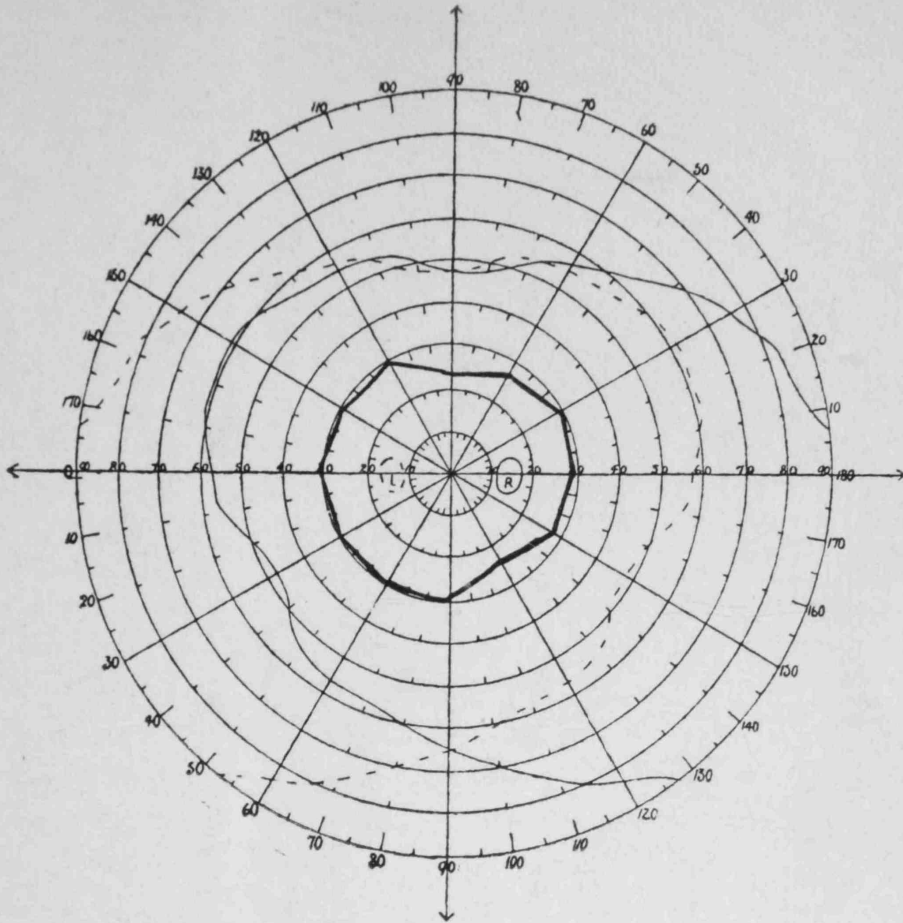
Right.



$$\text{R.V.A. } \frac{6}{6} \text{ ptly.}$$

acid daily and full Chinese diet.

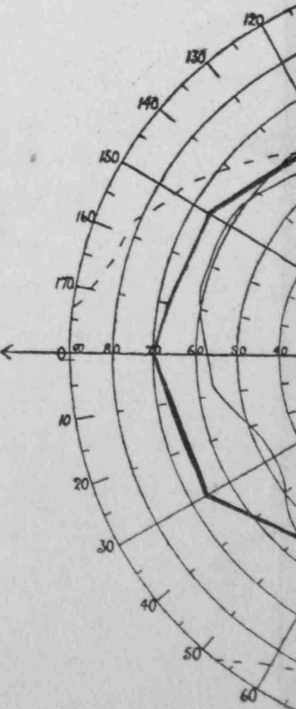
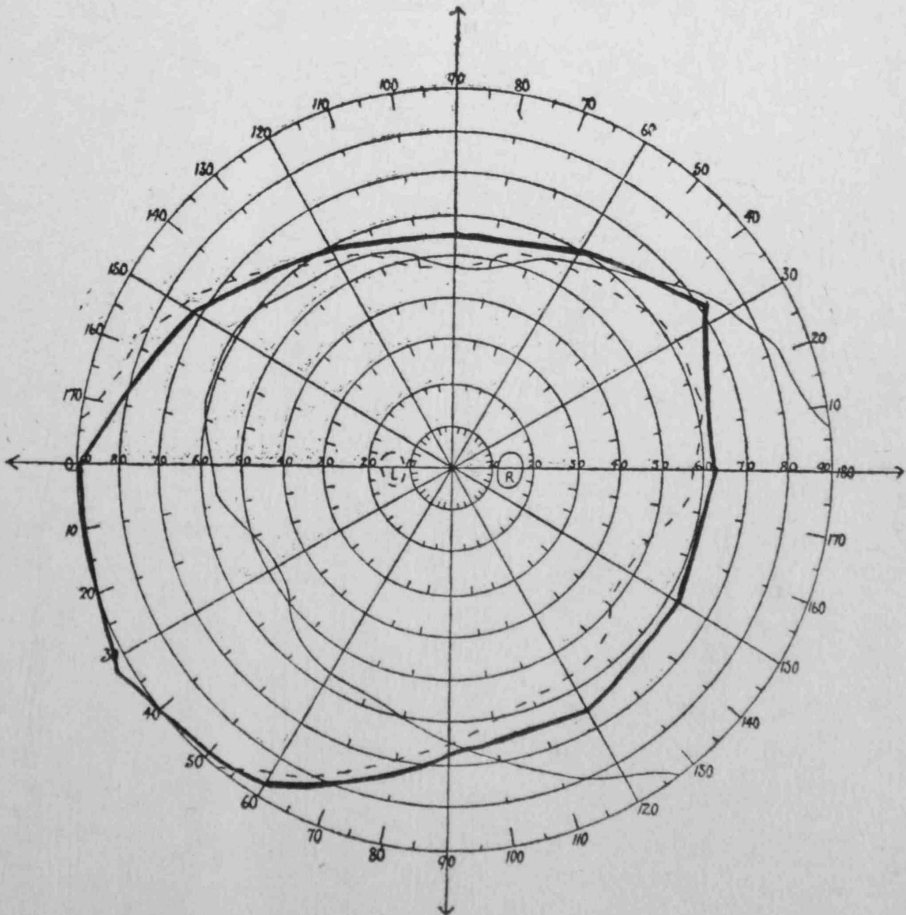
Left.



L.V.A.  $\frac{6}{36}$ .

To show the visual fields on admission, 2 mm. white object

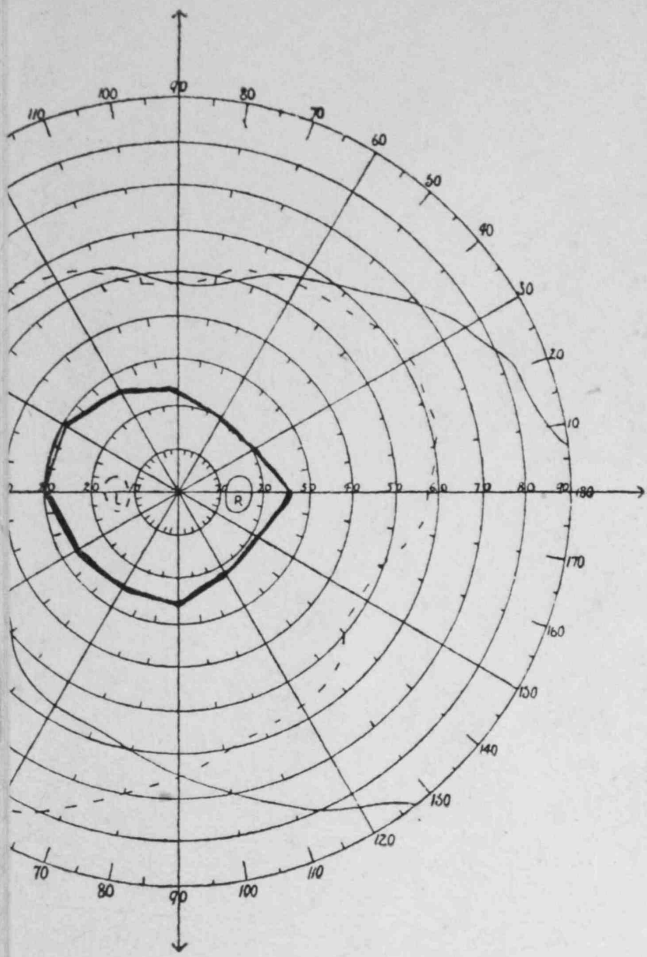
Left.



L.V.A.  $\frac{6}{6}$ .

To show fields after ten days on full Chinese diet with 3 mgm. of riboflavine in the visual acuity.

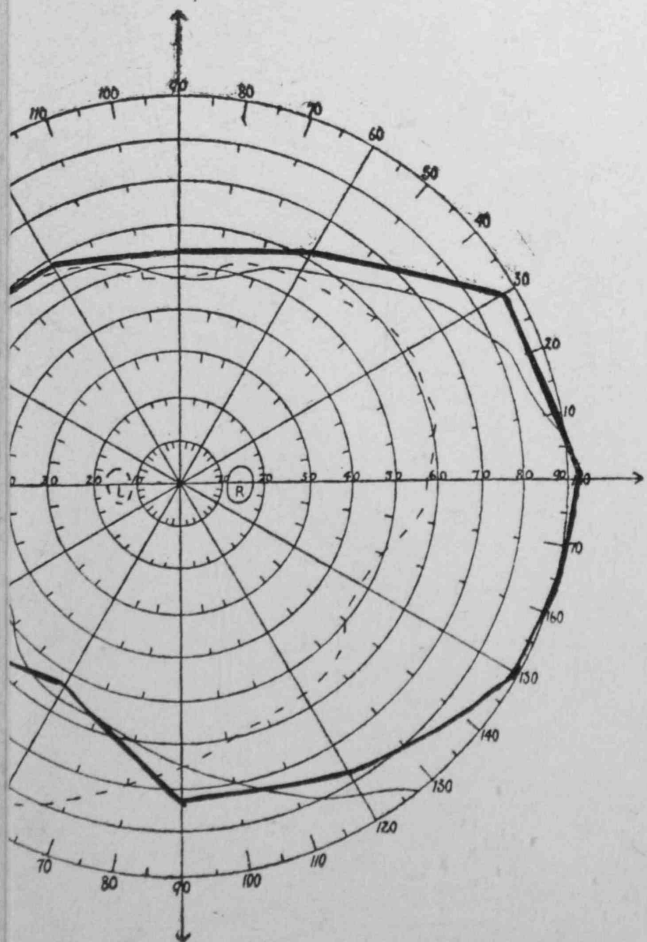
Right.



$$\text{R.V.A. } \frac{6}{36}.$$

ct, daylight.

Right.



$$\text{R.V.A. } \frac{6}{6}.$$

daily by month. Note the improvement

in each eye when she was admitted. Realising that adding known B factors to a diet whose vitamin content was adequate but unknown would not help to determine which factor was responsible for this visual defect, we kept her during her first week in hospital on a deficient diet which approximated as closely as possible to the diet she ate at home. No improvement was noted. During the second week she was given 3 mgm. of riboflavin daily while living on the same diet. Visual acuity remained unchanged. During the third week the deficient diet was supplemented by a daily injection of 3 mgm. of thiamin (Betaxin), but no improvement was noted in her vision. In the fourth week a 50 mgm. dose of nicotinic acid was exhibited twice daily, the diet remaining unchanged. At the end of this week visual acuity had risen from  $\frac{6}{18}$  ptly, to  $\frac{6}{9}$  ptly. These findings suggest that it is a lack of nicotinic acid or of one of its congeners in the diet which is responsible for the retrobulbar neuritis seen in these cases.

If these findings are substantiated it will mean that a disturbance in the second link of the co-enzyme-oxidase system may cause not merely pellagra but also retrobulbar neuritis. Although evidence of visual disturbances was not specifically sought for in many of the pellagrins seen in Kowloon this year, it must be admitted that a frank retrobulbar neuritis would not have been likely to escape notice. It is, therefore, a little difficult to explain why a disturbance of the second link should produce retrobulbar neuritis in a small percentage of patients only.

Other patients showing this type of visual defect are being treated at the moment, and the results of selective therapy in these cases will be published later.

#### DISCUSSION.

That malnutrition may cause a retrobulbar neuritis has been recognised for some time. Fitzgerald Moore (1934) described a condition in West Africa which appears to be very similar to, if not identical with, the disease described in this paper. He regarded the mouth and skin lesions as being an integral part of the syndrome and stressed the fact that they might only be seen "in an early or recurrent stage of the disease." His patients recovered when treated with marmite, but cod-liver oil and fruit juice had no curative effect on control cases.

Landor and Pallister (1935) described a condition found among the inmates of institutions in Malaya the main features of which were glossitis, angular stomatitis and scrotal eczema. Some of their patients also complained of weakness of the limbs and dimness of vision. There is little doubt that the syndrome they described is



similar to the one reported here, and they were able to show that liver, marmite and autoclaved yeast were all successful in treatment. Fitzgerald. Moore found that the ophthalmological response to treatment with marmite was very rapid, improvement being seen within three weeks, but he maintains that absolute cure is not possible, even though vision may improve to  $\frac{6}{6}$ . Whether the cases described in this paper will relapse or not is impossible to say yet, for they are still under observation.

It seems clear, even from the results obtained in so small a series as this, that the effects of nicotinic acid and of riboflavin in this condition deserve further investigation. The rapidity of the improvement in vision, the restoration of the fields to normal and the disappearance of the associated symptoms incline one irresistibly to the view that this condition is pellagrous or at any rate closely allied to pellagra. The facts which make us feel that this condition should be regarded as pellagrous are these: first, it appeared in Hong Kong shortly after pellagra proper and had never, as far as we can ascertain, been seen here before; second, the symptoms associated with some of the cases—glossitis, perlèche, acroparaesthesiae, scrotal eczema—strongly suggest a pellagrous condition; third, the response to nicotinic acid appeared to be specific and far more rapid than the response to yeast. It is for these reasons that one undoubted pellagrin has been included in this group. Why a deficiency of P.P. factor should produce retrobulbar neuritis rather than frank pellagra in certain human beings is a matter for speculation, and such speculation cannot be indulged in till the final results of selective therapy have been observed.

#### ACKNOWLEDGMENT.

We are indebted to Messrs. Burroughs Wellcome for the nicotinic acid and to Messrs. Eli Lilly and Co. for the riboflavin used in treating these patients. We are also indebted to the Dietetic Sister at the Queen Mary Hospital for her help in planning the deficient diet fed to the fifteenth patient in the series, and finally we are indebted to the Hon: D.M.S. for his permission to publish this note.

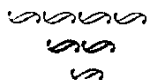
#### SUMMARY.

1. Fourteen cases of retrobulbar neuritis associated with dietetic deficiency are described.
2. One pellagrin showing optic atrophy is included in this group to stress the probably pellagrous nature of the condition.
3. Three of the cases showed temporal pallor of the optic discs and all save one showed some field defect.
4. All the cases save two showed some pupillary abnormalities.

5. Acroparaesthesiae, weakness of the extremities, palpitation, giddiness and oedema were accompanying symptoms.
6. The condition was curable slowly with dry yeast in small daily doses and with general dietetic measures. It responded much more rapidly and specifically to nicotinic acid in small daily doses over a short period of time.

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121.



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A NOTE ON THE ANATOMICAL RELATIONS OF THE LEFT  
AURICLE AND THE RECURRENT LARYNGEAL NERVE,

by

L. R. Shore,

Department of Anatomy.

This communication is prompted by the finding of certain old case notes which included observations on an interesting case of laryngeal palsy.

It may perhaps be best to present the salient clinical features first and the anatomical enquiry second.

In this paper it is proposed to revert to the old terminology of Anatomy. Whatever may be the merits of "atrium," it will be long before physicians abandon the term "auricle" or "auricular fibrillation." Curiously in the new terminology "auricle" is the equivalent of "auricular appendix."

CLINICAL NOTES.

The patient was a man of 45 years who came to Hospital complaining of shortness of breath, precordial pain and lately swelling of the lower limbs.

These disabilities had been gradually increasing for some years; indeed he had been compelled to give up heavy physical exertion for 2½ years before coming to Hospital.

The circumstance which induced him to seek advice was persistent loss of voice which had come on suddenly, in fact overnight, some five weeks previously.

*Physical Examination.* The patient was a well-built man of spare habit. There was some cyanosis and a slight icteric tinge to the skin and conjunctivae. There was some oedema about the feet and ankles.

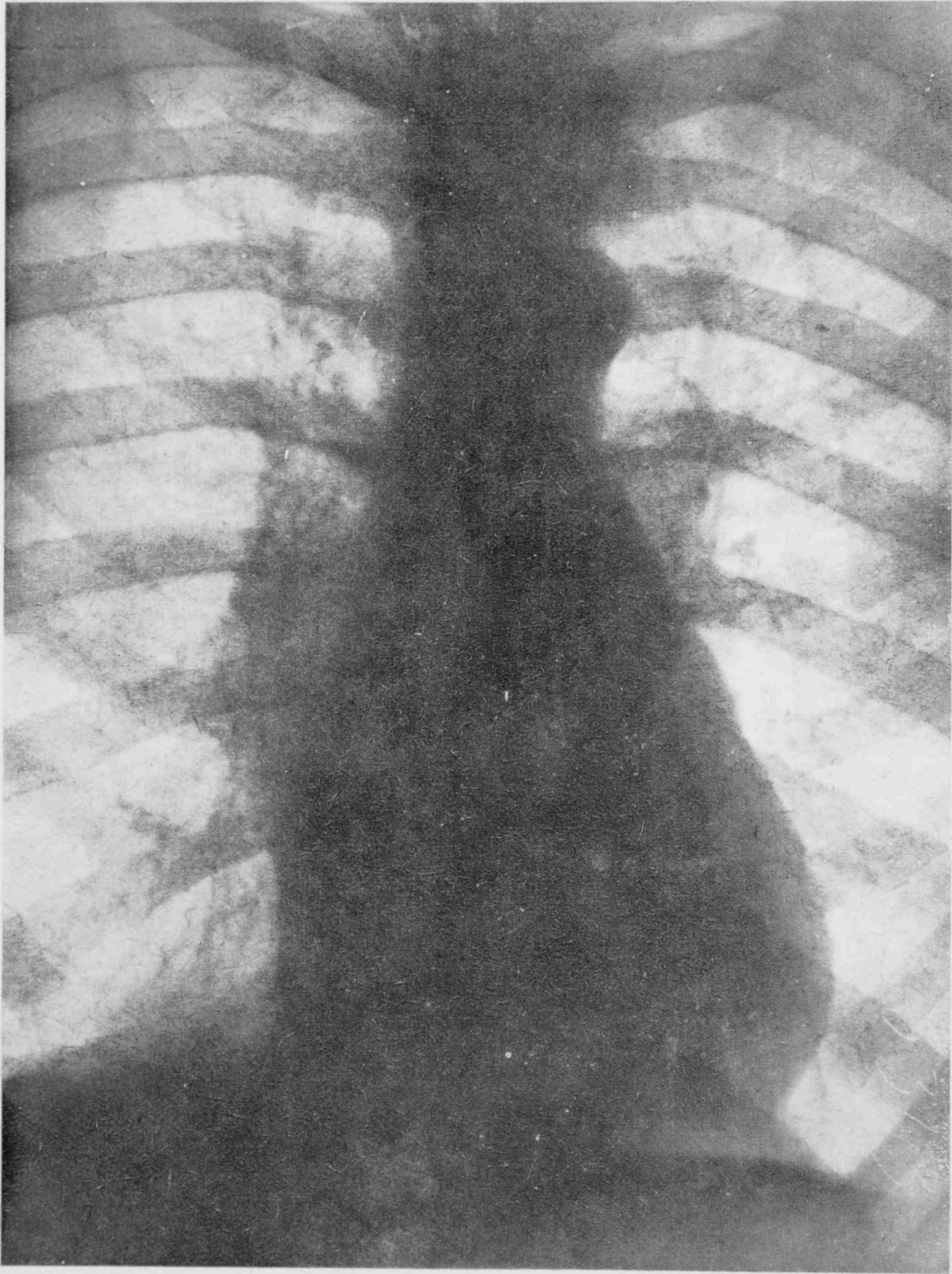
The chest was emphysematous with some bulging of the precordium and visible pulsation in the subcostal angle.

The apex of the heart was in the sixth space ½" to the left of the nipple line.

The pulse was completely irregular but of fair volume and equal on the two sides.

The frequency of the heart at the apex and at the pulse was the same—about 70 in the minute. Temperature and respiration rates were normal.

On auscultation were heard a loud systolic murmur conducted to the axilla and a diastolic murmur. The lungs were clear of adventitious sounds except for some crepitations at the right base.



*Fig 1.*  
Antero-posterior Skiagram.

Laryngoscopic examination showed an immobile left vocal cord.

A diagnosis was made of mitral stenosis with fibrillation. Enlargement of the auricle causing pressure on the left recurrent laryngeal nerve seemed at least a possible explanation of the laryngeal palsy.

A radiogram showed dilatation of the right and left auricles and of the pulmonary artery, thereby lending support to the diagnosis of mitral stenosis. A reproduction is shown in Fig: I.

Physical examination provided no signs of an aortic lesion or of aneurysm: and there was no evidence of aneurysm in either antero-posterior or in oblique radiographs of the chest.

The electro-cardiograph confirmed fibrillation.

There was no past history of rheumatic fever or of scarlet fever. The Wassermann reaction was negative.

*Clinical Course.* The patient was admitted to Hospital and kept at rest in bed. It was thought that on the balance of probabilities left recurrent nerve palsy was due to enlargement of the left auricle following on stenosis of the mitral valve.

The general condition of the patient improved with rest in bed, but the laryngeal condition remained as before.

It seemed possible that the intermittent pressure of an auricle in regular systole and diastole would be less likely to cause nerve interference than continuous pressure of a paralysed fibrillating auricle. That is to say, it was thought that fibrillation might be a determining factor in the nerve palsy. Therefore an attempt was made to interrupt fibrillation and restore the normal heart rhythm by the use of quinidine. A full course of quinidine therapy was started during the third week of rest in Hospital.

The patient showed no intolerance but the auricle proved refractory, though the drug was pushed to 45 gr. in the day. On this dosage an increased pulse rate, a deficit in the pulse rate relative to the apex rate of the heart, and nausea indicated some toxic effect.

The whole course of quinidine extended over 22 days and then was abandoned.

In the seventh week in Hospital, some two weeks after the cessation of quinidine the voice suddenly returned.

Laryngoscopic examination now showed the left vocal cord to be moving though less freely than the right.

Within a few days the patient recovered the full use of the voice. Cardiac dilatation had diminished and there was no oedema but other physical signs had not changed.

The patient left Hospital and his condition remained satisfactory with the aid of digitalis in small doses.

*Comment.* Paralysis of the left recurrent laryngeal nerve is a well recognised, if uncommon, complication of mitral stenosis.

Aneurysm had been excluded as far as physical and radiological examination can do so.

It seems most probable that pressure was the cause of the laryngeal palsy and that this pressure was exerted by the left auricle.

The recovery of function in the recurrent laryngeal nerve in the presence of continued fibrillation tends to show that fibrillation per se is not a factor.

It seems rather that the reduction in dilatation of the heart consequent upon rest is the important factor in restoration of function in the nerve.

#### ANATOMICAL NOTE.

(1). A well hardened mass of thoracic contents was removed from a cadaver. The superior mediastinum was dissected in just sufficient degree to allow of the identification of the vagus and the recurrent laryngeal nerves. With a sharp long-bladed knife a vertical section was made through the whole mass in the length of the recurrent laryngeal nerve. The plane of the nerve as it loops round the aorta is very nearly vertical.

The results of the section are shown in Fig: II, the left half of the divided mass being viewed from the median side. The knife has opened the pleural and pericardial cavities of the left side. The trachea on the left side is but grazed, the upper part of the oesophagus is opened and the right side of the descending aorta exposed.

Successively from above downwards are shown the aorta, the left pulmonary artery and the left auricle in vertical section. The recurrent laryngeal nerve leaving the vagus nerve is looping round the aorta to the left of the ligamentum arteriosum and is proceeding to the cleft between trachea and oesophagus.

It seems clear from the disposition of structures shown in this Figure that the left pulmonary artery lies between the left auricle and the recurrent laryngeal nerve below the arch of the aorta, and only by the intermediary of the left pulmonary artery can the nerve be subjected to pressure from the auricle.

Further dissections were made with the object of making an enquiry into the probable stability of the relations shown in Fig: II.

(2). A block of the mediastinum was taken from a well hardened cadaver and a horizontal section was made at such a level as to traverse the left auricle.

The lower surface of the upper part of the block of tissues is shown in Fig: IIIA, which is drawn to scale by means of the dioptograph.

In this drawing, and the others in Fig: III the reader is viewing structures from below. The top of the drawing is anterior and the bottom posterior; the reader's right represents left, and conversely.

The reader will see the fibrous pericardium, distinguished by cross lining, enclosing the left auricle, part of the right auricle with the superior vena cava, the root of the aorta near the centre and the root of the pulmonary artery on the right front. The two auricles are enclosed by one continuous sheet of serous membrane, and the aorta with the pulmonary artery by a second. The interior of the fibrous pericardium is lined with the same membrane, indicated by heavy continuous black line.

A space lies within the pericardium and is defined in front by the serous membrane that envelopes the aorta and pulmonary artery, behind by that which is applied to the anterior surfaces of the two auricles; this space is that known as the "sinus transversus" of the pericardium. In this view the sinus is of linear width or little more.

It is proposed to dissect away the left auricle and to examine the relations of the structures which lie superior to it in order to determine in particular the relative position of the left recurrent laryngeal nerve. The result is shown in Fig: IIIB.

The body of the left auricle was very easily dissected away from the superior vena cava and right auricle and from the cupola of the fibrous pericardium both above and behind, but at the places where the pulmonary veins enter it is inseparably blended with the fibrous pericardium. There was no alternative but to cut through the left auricle just where the veins enter.

Cut edges are shown in Fig: IIIB where the pulmonary veins were cut in order to remove the auricle. The heavy black line again shows the cut edge of the serous pericardium. This line follows a transverse course from the superior vena cava to the left pulmonary vein in the summit of the sinus transversus.

Behind this line is the area bare of serous membrane where the left auricle formerly made contact with the fibrous pericardium and the superior vena cava. The outlines of the bulges caused by the pulmonary artery and its two branches are shown by fine lines.

A third stage of the dissection is shown in Fig: IIIC. In this figure the main structures and landmarks are shown in plain line and the heavy lines indicating the serous pericardium are omitted.

The stem of the pulmonary artery was cut transversely as shown. This stem and its two main divisions were dissected away from

the fibrous pericardium to the place where they blended with it and then they were cut.

Now a window was cut in the pericardium as shown in Fig: C.

The thickness of this window is shown in the same cross-lining as is the fibrous pericardium elsewhere. A thickened part near the anterior edge of the window is the ligamentum arteriosum which connects the aorta to the pulmonary artery, at its bifurcation rather than by its left branch in this specimen.

The left recurrent laryngeal nerve is shown lying in the hollow of the aortic arch behind the ligamentum arteriosum, crossing transversely from left to right.

Between the pulmonary artery and the hollow of the aortic arch there is some little space whose size may be indicated by the fact that the ligamentum arteriosum in this specimen measured 7 mm. in length.

Fig: D, is a composite sketch plan and not the drawing of any single dissection. It is virtually a combination of Fig: IIIB and C, and is intended to show in plan how the arch of the aorta, the pulmonary artery and the nerve lie relative to each other.

The aorta is shown in continuous fine line and the pulmonary artery in dotted line. The area of cross hatching represents the ligamentum arteriosum, in both C and D.

The reader may infer the position of the left auricle by reference to the drawing A.

#### COMMENT.

The following points emerge clearly from drawings A, B and C.

The left auricle is fixed in front and behind by its aorta and the descending part of the arch.

On each side the left auricle is fixed by its venous tributaries which blend with the fibrous pericardium.

The pulmonary artery is fixed superior to the left auricle to the pericardium by the right and left pulmonary arteries' and more centrally by the ligamentum arteriosum.

The aorta itself is adherent where it leaves the pericardium.

The fibrous pericardium therefore is the important common factor giving as it does points of firm adherence to the aorta at its root, to the pulmonary artery at three places and to the left auricle at two places.

It is difficult to understand how the inter-relation of the six fixed points in the fibrous pericardium can be altered. That is to



say the relative positions of the aortic arch, the pulmonary artery, the left recurrent laryngeal nerve and the left auricle are likely to be very stable.

It follows that the pulmonary artery must be the means by which direct pressure reaches the recurrent laryngeal nerve from the left auricle.

It has been remarked that the space in the aortic arch which lodges the nerve is of not inconsiderable dimensions, and lodges a few small lymphatic glands in addition.

On anatomical grounds it would seem that the means by which the left recurrent laryngeal nerve might be pressed upon in the aortic arch are four.

- (1) Dilatation of the aorta.
- (2) Enlargement of lymphatic glands.
- (3) Dilatation of the pulmonary artery.
- (4) Direct pressure by the pulmonary artery transmitted from the left auricle.

In the particular case which prompted this investigation aortic dilatation was excluded. Recovery in the presence of enlarged glands would be highly improbable.

Dilatation of the pulmonary artery cannot be regarded as impossible. Pressure from the dilated left auricle represents the generally accepted view and as we have seen this explanation is compatible with the anatomical facts and with the clinical history of the case.

A combination of dilatation of the pulmonary artery and of the left auricle would most easily explain the phenomena. One would not expect spontaneous recovery and continued absence of symptoms if the pulmonary artery were primarily at fault for the pulmonary artery would scarcely tend to recover in the same measure as the more muscular auricle.

In conclusion it must be stated that the hearts from which figs. II and III were made were proved to be normal by subsequent dissection. I have never had the opportunity of making similar dissections in the presence of stenosis of the mitral valve.

Fig. II.

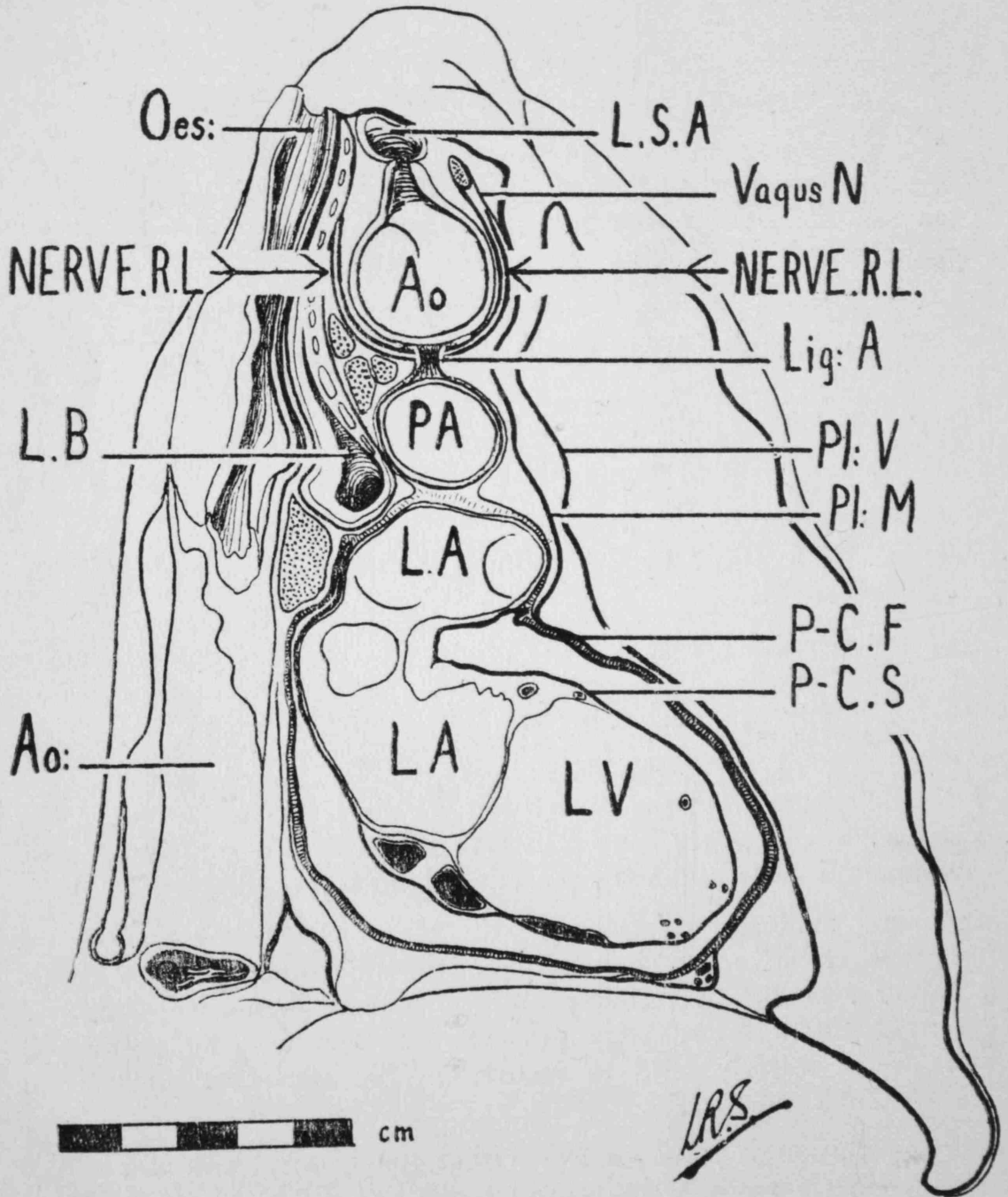


Figure II.

The structures revealed by section of the mediastinum in a plane corresponding to the loop of the left recurrent laryngeal nerve, viewed from the right.

NERVE. R. L.=left recurrent laryngeal nerve.

Ao=aorta.

L. B.=left bronchus.

PL: V=visceral pleura.

P-C. S=serous pericardium.

L.A.=left auricle.

P. A.=pulmonary artery (left branch).

Lig: A=ligamentum arteriosum.

PL: M=mediastinal pleura.

P.C. F=fibrous pericardium.

L.V.=left ventricle.

Fig. III.

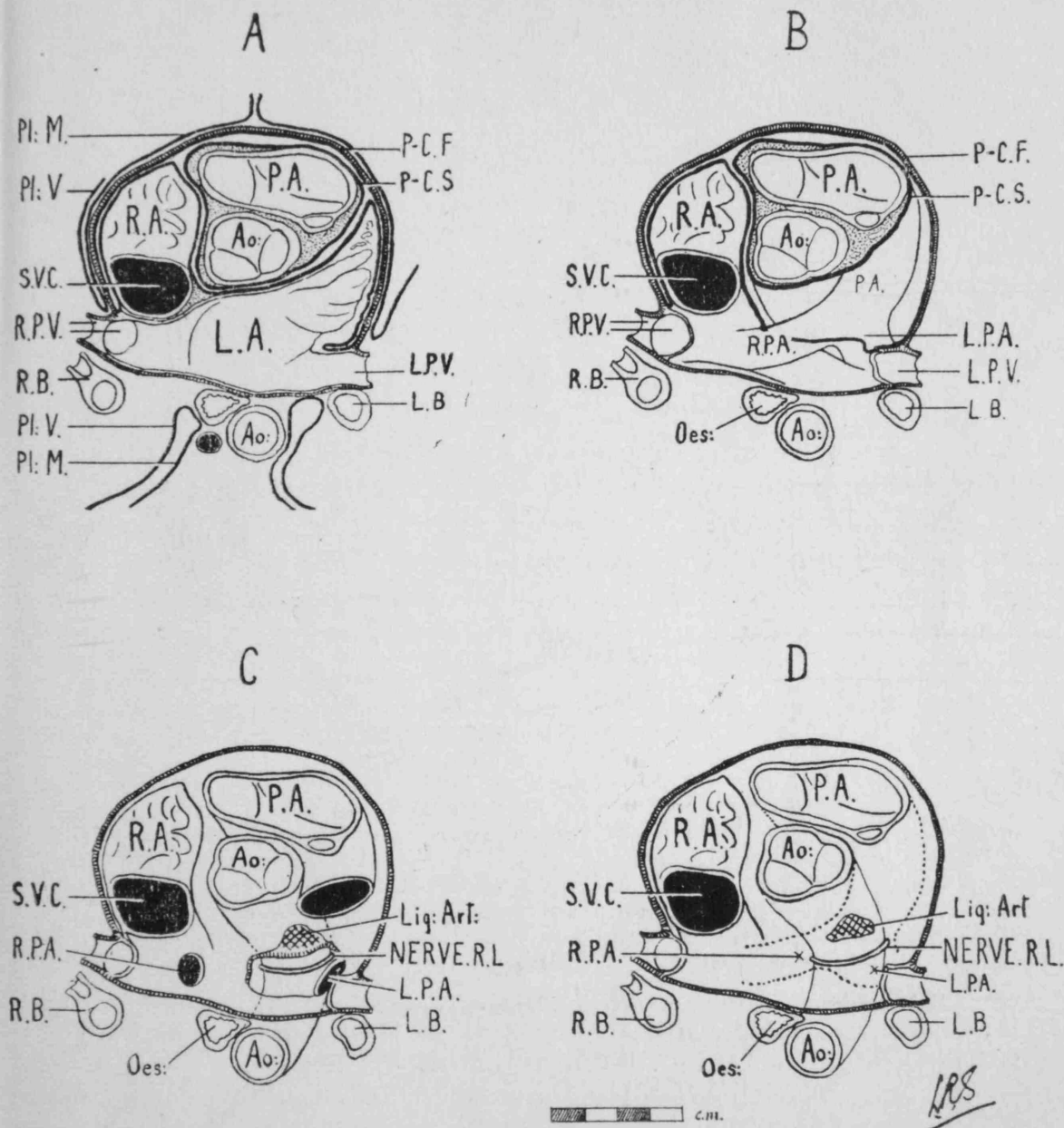


Figure III.

A section of the mediastinum has been made in a horizontal plane traversing the left auricle.

Each drawing is an inferior view. The top represents the front and the bottom the back, therefore the reader's right is the left of the specimen and vice versa.

Full explanations are in the text.

Successive dissections are shown, in B after the left auricle has been removed and in C after the pulmonary artery has been removed and a window cut in the fibrous pericardium. D is a plan formed by superimposition of C on D.

NERVE. R. L=left recurrent laryngeal nerve.

Ao=aorta. P.A.=pulmonary artery.

R.P.A. and L.P.A.=right and left pulmonary arteries.

R.P.V. and L.P.V.=right and left pulmonary veins.

R.B and L.B=right and left bronchus.

Lig: Art=ligamentum arteriosum.

Pl. V and Pl. M=visceral and mediastinal pleura.

P-C. F=fibrous pericardium.

P-C. S=serous pericardium.

## PROGRESSIVE MUSCULAR ATROPHY AND BULBAR PALSY TREATED WITH VITAMIN E PREPARATIONS,

by

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### INTRODUCTION.

In view of the interest which has recently been aroused by the influence of preparations containing vitamin E on certain tract degenerations of the nervous system, a brief note on two patients treated with vitamin E during the last six months may have some value.

One of these patients was a European woman who showed the classical picture of early progressive muscular atrophy; the other was a Chinese woman who presented an equally typical picture of moderately advanced bulbar palsy. The interval between the onset of symptoms and the beginning of treatment was approximately two months in the first case, six months in the second. The first patient responded dramatically to vitamin E therapy whereas the second one made no perceptible response to such treatment.

### CASE HISTORIES.

*Case 1.* G.H.A. a European of 57, living with her husband in Hong Kong, complained of tingling in the finger tips of the left hand in March 1940. This tingling had been present almost continuously since onset and a fortnight before she was seen on May the 24th 1940 she noticed that the whole left arm was feeling heavy, uncomfortable and "achy." At the same time she noticed flickering movements in the ball of the left thumb. These flickering movements have become more marked and the ball of the thumb has wasted perceptibly. She has tired very readily and has been conscious of palpitation for the last two weeks.

There were no other symptoms. She had had no recent illnesses of any sort, no fever, no gastro-intestinal or urinary symptoms, no visual disturbances and no history of trauma. She thought there had been some recent loss of weight.

On examination the patient looked pale and ill. The lungs, heart and abdomen were normal. The cranial nerves were normal throughout. Not a trace of facial asymmetry could be detected and the fundi and tympana showed normal appearances.

The left biceps, triceps, supinator and knee jerks were more active than the right. The ankle jerks were unobtainable even with reinforcement. The left abdominal reflexes tired more readily than the right, but the plantar responses were both flexor. The left arm and left leg were slightly weaker throughout than the right, the difference being more marked in the arms. There was obvious guttering of the interosseal spaces, and flattening of the thenar eminence on the left side, but the most striking feature was the presence of coarse almost continuous fibrillation in the left thenar eminence, the fibrillation being gross enough to displace the thumb slightly at each twitch. Coupled with these changes in the intrinsic muscles of the left hand was a moderate degree of left forearm and shoulder girdle weakness. No fibrillation was noted anywhere save in the left thenar eminence.

The paresis was a flaccid one, and the difference between the two arms amounted to no more than  $\frac{1}{4}$ ". There was no difference between the two legs on measurement, and the trunk musculature appeared to be normal and equal on the two sides. No sensory disturbance could be made out on objective testing. The blood W.R. reaction was negative, but it was not possible to make more detailed biochemical investigations.

A diagnosis of progressive muscular atrophy was made and treatment with Zygon (wheat germ oil) was begun two days later. One teaspoonful of the oil was taken once daily.

The patient was seen one month later. She looked very much better and said that she had noted a marked subjective improvement within ten days of beginning treatment. The first symptoms to disappear were the feeling of general tiredness and the palpitation. The fibrillation lessened during the first fortnight of treatment and had completely disappeared during the last ten days. On examination no fibrillation was noted. The intrinsic muscles of the left hand were all stronger to the tests applied though no visible change had occurred in the wasted interosseal and thenar muscles. Her signs were those she had shown on the first examination but of her subjective improvement and of the actual gain in power of the whole left arm there could be no doubt.

She was seen again three months later. By this time the hands were symmetrical in appearance. No trace of atrophy or fibrillation could be detected in any of the intrinsic muscles of the left hand, although muscle testing showed that they were still weaker than those of the right. The ankle jerks were still absent on both sides. This means to say that both objective and subjective improvement had occurred during five months treatment with a vitamin E preparation. The subjective improvement, loss of the sense of languor, disappearance of palpitation and fatiguability, was noted much earlier than the changes in the atrophic muscles, a phenomenon precisely similar to that seen in cases of beri-beri treated with vitamin B<sub>1</sub>.

*Case 2.* S.L.S. a Chinese woman aged 50 came to Out-patients on August 1st, 1940, complaining that for the past six months water had regurgitated through her nostrils when she swallowed. For the same period she had noticed difficulty in speaking and some weakness of the left facial musculature and tongue. She had been unable to swallow saliva normally for five months, and during the last four months her left hand and arm had been growing weaker. She had had an unspecified fever six months before these symptoms appeared, but apart from this her past history had been uneventful. There was no family history of nervous disease of any kind.

On examination the woman presented the typical picture of moderately advanced bulbar palsy. The face was expressionless and on attempting to innervate the facial musculature it was obvious that the whole of the left half of the face was weaker than the right. The mouth at rest was wide and whistling was impossible. Drooling of saliva was marked, and on examining the tongue it was found to be small for the size of the mouth. Fibrillation was evident throughout the tongue and the patient remarked that it had grown smaller since the onset of the disease.

The voice had a nasal element and speech was reduced to a moaning semi-articulate sound which made it very difficult to understand what she was saying. On admission she was only able to swallow solid and semi-solid food as nasal regurgitation was marked and mastication had become difficult owing to her inability to keep food between the teeth when eating.

The neck musculature was not perceptibly wasted and there was no weakness or limitation of head movements. Nor was any atrophy detected in the erectores spinae or trunk musculature.

Coupled with these signs there was obvious wasting and weakness of the intrinsic muscles of the left hand and arm and the left arm jerks were exaggerated. The knee jerks were present and equal but the left ankle jerk was absent. The plantar responses were both flexor and there was no sphincter disturbance or sensory loss. The blood and cerebrospinal fluid Kahn tests were negative, and beyond a slight pleocytosis of 14 cells per cu.mm. in the cerebrospinal fluid the other biochemical investigations revealed nothing of import.

A diagnosis of bulbar palsy was made and treatment was begun at once with a vitamin E preparation called Viteolin. 18 mgms. of  $\alpha$  tocopherol were given by mouth each day and it seemed at first as though she improved slightly. Swallowing became a little less difficult and the tongue could be protruded a few millimetres farther, but the improvement was unfortunately short-lived and after four weeks of treatment it was clear that her condition was deteriorating. Despite an increase in

the dose of  $\alpha$ -tocopherol to 36 mgm. daily and the simultaneous exhibition of vitamin B<sub>1</sub> parenterally she continued to grow worse and atrophy appeared in the muscles of the right hand nine weeks after her admission.

One is forced to conclude that in this case the motor cells involved in the pathological process may have been destroyed because of vitamin privation in the six months between the onset of symptoms and the beginning of treatment. This supposition accords with the results of experimental work which has shown that if treatment with vitamin E be begun early enough in animals who are developing nervous changes through lack of it, the changes may be not only arrested but reversed.

#### DISCUSSION.

Since 1928 it has been known that deprivation of vitamin E causes atrophies and paralyzes in young rats. These early observations were made on young animals in the course of experimental work on sterility but some years later Ringsted reported that chronic avitaminosis E produced paresis in older rats (1935) and Lipshutz in 1936 described various tract degenerations in the nervous system resulting from vitamin E privation. Further work was carried out on older rats and in 1938 Einarson and Ringsted published a monograph on the effects of vitamin E privation on the nervous system and somatic musculature of old rats. They showed that deprivation of the vitamin caused degenerative changes in the anterior horn cells, the pyramidal tracts and the posterior columns, and they suggested that there was an analogy between these conditions and progressive muscular atrophy and amyotrophic lateral sclerosis in man. They also suggested that the muscular dystrophies and tabes dorsalis might in some way be connected with vitamin E deficiencies.

The two important pathological changes observed by them were degeneration of the proximal parts of the posterior roots and of the anterior horn cells of the lumbar region of the spinal cord, and primary muscular degeneration. Later work seems to show that it is the muscular system in young animals and the nervous system in old which are most sensitive to deprivation of vitamin E. It is noteworthy that neither of these patients showed any sensory loss and objective sensory loss is not a constant feature in the picture of progressive muscular atrophy of any type. However cases of amyotrophic lateral sclerosis showing definite signs of posterior column involvement have been described. (Wechsler 1936).

The exact connection between these muscle paralyzes and nervous degenerations and the anti-sterility factor in wheat germ oil was not understood, and Einarson and Ringsted suggested that a second factor might be present in wheat germ oil which was concerned with maintaining the functional integrity of various tracts in the nervous system. In 1940 Evans and his co-workers were able to confirm this suggestion by showing that whole wheat germ oil contained both  $\alpha$  and  $\beta$  tocopherols and that absence of the  $\alpha$  tocopherol was probably concerned in the production of the atrophies and nervous degenerations.

Bicknell (1940) adduced evidence showing that vitamin E deficiency might occur in normal human diets. He pointed out that the vitamin E of the ordinary English diet was contained in egg yolk, animal fats and flesh, milk from pasture-fed cows, vegetable oils and some fruit. Rancidity, cold storage and pasteurisation he suggests may all destroy vitamin E, and as green leaves, another rich source of the vitamin, are never eaten in large quantities many people probably exist on the verge of vitamin E deficiency. An effort was made to obtain a dietary history in each of these cases. Case I lived on a moderately well balanced European diet, as far as such a diet is obtainable in Hong Kong, and apart from a dislike for milk showed no pronounced food fads. Case II lived on Chinese food and as she came from a moderately well-to-do family was unlikely to have suffered from any marked vitamin deficiency. The first patient gave no history of antecedent dyspepsia of any kind, but the second one had had "gastritis" seven years before her illness began and sometimes suffered from hunger pains and abdominal pain after food. It is possible that in her case mal-absorption may have been present despite an adequate supply of vitamin E in her food.

Bicknell reports successful results in the treatment of the muscular dystrophies and amyotrophic lateral sclerosis by administering vitamin E. Wechsler (1940) also reports encouraging results in two cases of amyotrophic lateral sclerosis. This paper records the results obtained by the use of whole wheat germ oil in a patient suffering from progressive muscular atrophy, and the ineffectiveness of the same preparation in another patient suffering from bulbar palsy.

#### ACKNOWLEDGMENT.

I am greatly indebted to Dr. G. D. R. Black for allowing me to make use of notes on one of his cases in writing this report.

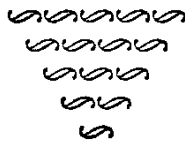
#### SUMMARY.

1. Brief clinical descriptions are given of a case of progressive muscular atrophy and a case of bulbar palsy.
2. Vitamin E ( $\alpha$  tocopherol) was given by mouth and the results of treatment are reported.

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## THE WINTER COMFORT ZONE FOR SHANGHAI SEDENTARY WORKERS,

by

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### INTRODUCTION.

Chiefly due to the introduction of new methods of heating buildings human comfort in relation to environmental warmth has been a matter of investigation in different countries for the last two decades. The comfort zone of a normal person in any particular environment is that atmospheric condition under which the human body is able to maintain a normal balance between the production and loss of heat without the individual being conscious of undue effort on the part of the heat regulating mechanism. While the heat loss from the human body depends mainly on the physical environment, this is modified by the degree of adaptation of the individual to climate and season by clothing and other general living conditions. The degree of muscular activity of an individual is the primary factor affecting metabolism which in turn determines the zone of warmth comfort. The need for research to provide a standard of environmental warmth to fit the physiological requirements of our body as well as for the efficiency and economy of certain types of work is apparent. This paper presents some of the results that have been carried out to define the winter comfort zone for persons doing sedentary or very light work in Shanghai in terms of various physical factors which make up the thermal environment.

### EXPERIMENTAL.

This series of observations was carried out from November 14 to April 4 on the first floor of the main building of the Henry Lester Institute of Medical Research in Shanghai. The walls of the building are made of stone and concrete, and the partitions of different laboratories within are made of light aerocrete and are non-structural. The general heating system of the building is the hot water radiator type. Four laboratories, three of the dimension twenty-four by eighteen feet and one thirty by eighteen feet, of which two had windows facing south and the others facing north, were engaged for the observations. During the peak of the cold weather an extra electric radiator was installed in one of the rooms facing north.

Eight healthy male members of the Chinese Staff of the Institute engaged in research took part in this study. Their ages ranged between 20 to 50 years. Four were born in North, two in Central and two in South China. All had lived in Shanghai for more than

three years. The clothing worn by the subjects were essentially of European style, consisting of cotton underwear, cotton shirt, woollen suit and a laboratory gown. Two to five heat sensation votes from each environment were recorded according to the method and scale of Crowden and Lee (1940), each subject having been in his room about one hour.

In assessing the reliability of different scales of warmth as indices of comfort due allowance has to be made for the variation of personal opinion as to what conditions of warmth are comfortable. Objectively a more accurate estimate is obtained by the so-called method of correlation, by which for the derivation of the comfort zone and the most comfortable conditions of warmth, the constants in regression equations were calculated according to the following formula:—

$Y = a + bX$  where  $Y$  is the average heat sensation,  $X$  is the measure of environmental warmth and  $a$  and  $b$  are constants.

From these equations have been calculated the temperatures, and cooling power corresponding to average heat sensations of 'neutral' (= 0, on the numerical scale) and 'comfortably warm' (= +1) and 'comfortably cool' (= -1). The best conditions of warmth have been taken to be those yielding an average sensation of 'neutral' (neither warm nor cool), and the range of conditions at which the average sensations were from 'comfortably warm' to 'comfortably cool' have been taken as the limit of comfort zone.

The instruments for measuring the warmth of the environment employed were as follows:—The whirling psychrometer was taken to measure dry-bulb and wet-bulb temperatures of the air, from the difference between these readings dew point temperatures were calculated from hygrometric tables.

The kata-thermometer, which was devised by Hill, is a measure of the rate of heat loss from the bulb itself. It is influenced by the temperature and velocity of the air as well as by radiation from the surroundings. Cooling power is known as the quotient of a factor of the instrument which is proportional to the total amount of heat in millicalories lost per sq. cm. divided by the number of seconds taken in cooling from 100° to 95° F. The dry kata cooling power combines the heat losses due to radiation and convection. There is a relationship between air velocity and cooling power, and so the kata-thermometer is a valuable instrument for use in measuring air currents.

Equivalent temperature is a scale which measures a combination of the effects of radiation and of the temperature and velocity of the air. The mean temperature of the surroundings is a measure of the mean radiation intensity from the surroundings of an enclosure and

is estimated from globe thermometer readings, air temperature and air velocity. They are all derived from the alignment charts of Bedford and Warner (1934). The globe thermometer is a simple instrument, consisting of a blackened, hollow, copper sphere, 6 inches in diameter, containing an ordinary thermometer with its bulb at the center of the sphere; it was introduced by Vernon (1930). Its temperature depends entirely on the environment, lying between the temperature of the air and the mean temperature of the surrounding objects. The reading is influenced by the amount of air movement. Its readings are used for measuring radiant heat.

"Effective temperature scale" is a combined measure of air temperature, humidity and air velocity and can be read off from a chart (Yaglou and Miller, 1925). It has been widely applied in America but this scale makes no allowance for radiant heat.

The resultant thermometer, which Missenard (1935) has recently introduced, is a small globe thermometer ( $3\frac{1}{2}$  inches in diameter) with about one-third of its area covered with moist gauze. This instrument can only be used in calm air, where the air velocity does not exceed 40 feet per minute. It takes into consideration the air temperature, humidity, air velocity and radiant heat, and its readings are a resultant of these factors.

#### RESULTS.

##### (1). *Observed conditions of comfort in relation to Dry-bulb Temperature.*

A total of 1,514 heat sensation votes were recorded, ranging from 'too cold' (-5) to 'warm' (+2) according to the heat sensation scale.

Table I shows the percentage of persons who were comfortable at different dry-bulb temperatures when the latter was recorded at a height of about 4 feet from the floor.

Over a temperature range from  $64^{\circ}$  to  $70^{\circ}$  F., more than half of the sensation votes were comfortable, while over 90 per cent. of the votes were between comfortably cool and comfortably warm. It is reasonable to deduce from this that about  $67^{\circ}$  F. is a suitable air temperature for sedentary workers with a maximum comfortable range between  $64$  and  $70^{\circ}$  F.

##### (2). *The Range of Warmth Conditions Studied.*

The range of air temperature covered in this enquiry, together with the range and variation of other instrumental readings are shown in Table II.

It appeared that there is little difference between the air temperature and wall temperature of these rooms as were shown by the

closeness of the means and ranges of dry-bulb temperatures, globe thermometer temperatures and mean temperatures of surroundings, though the surroundings were slightly warmer than the air. Under the conditions of the present study, as an instrument to record environmental warmth, the resultant thermometer gave readings resembling effective temperatures both in their range and mean value. The environmental conditions covered the widest range when expressed in terms of equivalent temperatures.

(3). *Heat Sensations in Relation to Physical Measurements.*

The coefficients correlating the sensations recorded with the objective measurements of warmth, together with their standard errors, are set out in Table III. Of the scales of warmth considered, dry-bulb temperature gives the highest correlation with heat sensation votes, but resultant thermometer readings, globe thermometer readings, equivalent temperatures and effective temperatures follow closely. In fact, under the conditions studied the correlations of these five scales with heat sensation votes do not differ significantly. The correlation between heat sensation votes and the mean temperature of the surroundings, dry kata cooling power, wet-bulb temperature and dew-point temperature are all significant, and indicate a definite relationship between the numerical scale of heat sensations and the thermal measurements concerned. In order to test the significance of the difference between two correlation coefficients, the differences and standard errors of differences between pairs of correlation coefficient are calculated. It is significant if the difference between them is more than twice its standard error. This test has been applied to the first seven coefficients shown in Table III, and Table IV gives the differences and their standard errors. Differences which are now more than twice the standard errors are underlined.

(4). *Comfort Zone and Best Conditions of Warmth.*

It is seen from Table IV which is computed from the regression equations the constants of which are tabulated in Table V, that comparatively wide variations in warmth conditions can be tolerated without serious discomfort.

The comfort zone in winter at Shanghai in terms of dry-bulb, which is a good instrument for measuring warmth of environment when the air temperature does not differ much from the wall temperature and with doors and windows closed, lies between  $62.4^{\circ}$  and  $73.1^{\circ}$  F., a range of more than ten degrees F.

In terms of effective temperature scale, the comfort zone extends from  $59.2^{\circ}$  to  $68.5^{\circ}$  F. It covers even a wider range when radiation temperatures and air movement are considered together with air temperature, as shown by the measure of equivalent temperature scale. The comfort zone is limited to within two and half units in terms of dry Kata cooling power.

The most comfortable condition, that is, the comfort line, in terms of dry-bulb temperatures is obtained at  $67.8^{\circ}$  F., for which condition more than half of the sensation votes are 'neutral' and over 90 per cent. are between 'comfortably warm' and 'comfortably cool.' This line lies at about  $64^{\circ}$  F. effective temperature or  $67^{\circ}$  F. equivalent temperature. In terms of Kata cooling power it is 4.7.

#### DISCUSSION.

In calm air conditions, when the windows and doors are closed in winter, such as are usually met with indoors, and using a hot-water heating system, air movements rarely exceed twenty feet per minute, and so dry-bulb temperature readings are a good measure of environmental warmth. Other factors such as radiation, humidity and air movement seem to play a minor part in the determination of comfort sensations indoors in winter, as has been shown by the comparison between sensations and different warmth measures in the present study.

Complicated scales such as effective temperature and equivalent temperature do not surpass the simple dry-bulb instrument in estimating the winter indoor warmth under conditions as specified in the present study. Elaborate instruments such as the globe thermometer and the resultant thermometer do not show any better association with the heat sensations than the dry-bulb. The inferiority of Kata cooling power as a measure of warmth is in agreement with Bedford's conclusion (1936).

It has been found that the comfort zone covers from  $59.2^{\circ}$  to  $68.5^{\circ}$  F. effective temperature. Other workers have observed a comfort zone of similar wide range though at slightly different levels. Thus, Yaglou and Drinker (1928) found a comfort zone of  $63^{\circ}$  to  $71^{\circ}$  F. the effective temperature for Americans living in the northern States during the winter season. Partridge and MacLean (1935) give  $61.5^{\circ}$  to  $71.5^{\circ}$  F. as the effective temperature for Canadians, Bedford (1936) gives  $53.7^{\circ}$  to  $67.8^{\circ}$  F. as the effective temperature for light industrial workers in England.

Our effective temperature line lies at  $64^{\circ}$  F., which is about  $2^{\circ}$  F. below that of the Americans and about  $3^{\circ}$  F. above that of the British. This difference might be due to acclimatization as the British prefer a cooler indoor air, while Americans have their buildings heated at rather a higher level. It is most unlikely that the difference is due to the effect of clothing and activity for special attention has been paid to these aspects of the subject. The most desirable cooling power was found to be at 4.7 which indicated that persons doing laboratory work prefer a calmer air than those engaged in light industrial operations, for which it was reported to be 6.1 (Bedford, 1936).

## SUMMARY.

The winter comfort zone for sedentary workers in Shanghai has been determined by a study of eight males, twenty to fifty years of age.

A total of 1,514 observations were made, and treated statistically. Correlations between heat sensations and physical measurements of the environment have been made. Both the comfort zone and the most comfortable condition were given in terms of different measures of warmth. Their significance has been discussed in the light of published data.

The comfort zone lies between  $62.4^{\circ}$  and  $73.1^{\circ}$  F. dry-bulb temperature and between  $59.2^{\circ}$  and  $68.5^{\circ}$  F. effective temperature.

The author wishes to express his cordial thanks to his colleagues who so kindly cooperated to render this investigation possible.

TABLE I.

Observed Conditions of Comfort (neither warm nor cool)  
in relation to dry-bulb temperature.

Dry-bulb Temperature F.	Number of observations	Percentage of Persons	
		Comfortable	Comfortable cool to comfortably warm
54-55.9	36	—	6
56-57.9	80	—	17
58-59.9	128	4	36
60-61.9	280	18	68
62-63.9	336	37	83
64-65.9	302	52	90
66-67.9	203	54	95
68-69.9	133	68	98
70-71.9	12	83	100

TABLE II.  
The Range of Warmth Conditions Studied.

<i>Instrumental Reading</i>	<i>Range</i>	<i>Mean</i>	<i>Standard deviation</i>
Dry-bulb Temperatures .....	50 - 72° F.	63.2° F.	3.52° F.
Globe Thermometer Temperatures .....	52 - 74° F.	63.7° F.	3.99° F.
Equivalent Temperatures .....	45 - 72° F.	61.0° F.	4.75° F.
Effective Temperatures .....	50 - 69° F.	60.0° F.	2.93° F.
Mean Temperatures of Surroundings .....	50 - 75° F.	64.1° F.	4.23° F.
Dry Kata Cooling power .....	8.5 - 3.5	5.7	0.74
Wet-bulb Temperatures .....	42 - 69° F.	53.3° F.	3.75° F.
Resultant thermometer Temperatures .....	50 - 70° F.	60.5° F.	3.53° F.
Dew point Temperatures .....	24 - 64° F.	42.2° F.	6.97° F.

TABLE III.

Correlation between Heat Sensation and Physical Measurements.

<i>Heat Sensation Correlated with</i>	<i>Correlation Coefficient (r)</i>
Dry-bulb Temperatures .....	+ 0.669 ± 0.014*
Resultant Thermometer Temperatures .....	+ 0.650 ± 0.015
Globe Thermometer Temperatures	+ 0.641 ± 0.015
Equivalent Temperatures .....	+ 0.639 ± 0.015
Effective Temperatures .....	+ 0.637 ± 0.015
Mean Temperatures of Surroundings .....	+ 0.618 ± 0.016
Dry Kata cooling power .....	- 0.590 ± 0.17
Wet-bulb Temperatures .....	+ 0.505 ± 0.019
Dew point Temperatures .....	+ 0.340 ± 0.023

\* Standard error is calculated by the formula:

S.E. =  $1 - r^2 / \sqrt{n - 1}$ , where  $r$  is the correlation coefficient and  $n$  is the number of observations.

TABLE IV.

Differences and standard errors of differences between correlations of Heat sensations with environmental conditions.

<i>Heat sensations correlated with</i>	<i>Differences, and standard errors of differences, from correlations of heat sensations with</i>					
	<i>Dry-bulb Temperature</i>	<i>Resultant Thermometer Temperature</i>	<i>Globe Thermometer Temperature</i>	<i>Equivalent Temperature</i>	<i>Effective Temperature</i>	<i>Mean Temperature Surroundings</i>
Resultant Thermometer Temperature .....	0.019 ± 0.020					
Globe Thermometer Temperature .....	0.028 ± 0.020	0.009 ± 0.021				
Equivalent Temperature .....	0.030 ± 0.020	0.011 ± 0.021	0.002 ± 0.021			
Effective Temperature .....	0.032 ± 0.020	0.013 ± 0.021	0.004 ± 0.021	0.002 ± 0.021		
Mean Temperature of Surroundings .....	<u>*0.051 ± 0.021</u>	0.032 ± 0.022	0.023 ± 0.022	0.021 ± 0.022	0.019 ± 0.022	
Dry Kata cooling power .....	0.079 ± 0.022	0.060 ± 0.023	0.051 ± 0.023	0.049 ± 0.023	0.047 ± 0.023	0.028 ± 0.023

\* When the difference between two correlations is greater than twice the standard error of the difference, they are *underlined* as being significant.



TABLE V.  
 Constants in regression equations of Heat Sensation  
 votes on Warmth Conditions.

Physical Measurements	Constants <sup>a</sup>	
	a	b
Dry-bulb Temperature .....	- 12.67	+ 0.187
Globe Thermometer Temperature .....	- 10.93	+ 0.158
Resultant Thermometer Temperature .....	- 12.61	+ 0.180
Equivalent Temperature .....	- 8.92	+ 0.132
Effective Temperature .....	- 13.67	+ 0.214
Mean Temperature of Surroundings .....	- 10.07	+ 0.144
Dry Kata Cooling power .....	+ 3.66	+ 0.784
Wet-bulb Temperature .....	- 7.90	+ 0.133
Dew point Temperature .....	- 2.87	+ 0.048

\* *b* is the regression coefficient, i.e. the amount of change that will on an average take place in one characteristic when the other characteristic changes by one unit and is equal to:

Correlation Coefficient X  $\frac{\text{Standard deviation of Heat sensation}}{\text{Standard deviation of the physical measures}}$   
 (See Table III)

*a* is the constant obtained after the grouping of the other numerical values in  $Y = a + bX$ .

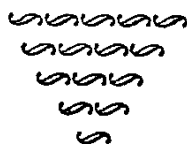
TABLE VI.

The most comfortable conditions, and the Limit of Comfort Zone, for men doing very light work.

Physical Measure	The most comfortable conditions	Limit of Comfort Zone	
		Lower	Upper
Dry-bulb Temperature .....	67.8° F.	62.4° F.	73.1° F.
Resultant Thermometer Temperature .....	70.0° F.	64.4° F.	75.6° F.
Globe Thermometer Temperature .....	69.1° F.	62.7° F.	75.3° F.
Equivalent Temperature .....	67.3° F.	59.8° F.	74.9° F.
Effective Temperature .....	63.9° F.	59.2° F.	68.5° F.
Mean Temperature of Surroundings .....	70.0° F.	63.1° F.	77.0° F.
Dry Kata Cooling power .....	4.7	5.9	3.4
Wet-bulb Temperature .....	59.6° F.	52.0° F.	67.1° F.

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# UNIVERSITY OF HONG KONG.



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Master of Surgery . . . . .	M.S.

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The Academic Year which commences in September is divided into three sessions :—

First session . . . . .	September to December
Second session . . . . .	January to March.
Third session . . . . .	April and May.

The next session opens on *Tuesday, April 1st, 1941.*

**Medical School Buildings.**—The buildings of the Medical School are :—

- School of Anatomy, erected in 1913.
- School of Physiology, erected in 1917.
- School of Pathology, erected in 1919.
- School of Tropical Medicine, erected in 1919.
- School of Surgery, erected in 1934.

**Appointments.**—Appointments as House Physicians, House Surgeons, and House Obstetricians, and Clinical Assistants, are available at the Queen Mary Hospital for students when they have passed their final examination. These appointments afford unrivalled opportunities for clinical experience.

**Scholarships.**—A number of scholarships are tenable at the University. Scholarships open for competition and awarded annually are :—

1. Ng Li Hing Scholarship for Anatomy.
2. Chan Kai Ming Scholarship for Anatomy, Physiology, General Pathology and Pharmacology.
3. Blake Scholarship for Ophthalmology.

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The Dean,  
Faculty of Medicine.

# HONG KONG UNIVERSITY MEDICAL SOCIETY.

## CONSTITUTION.

### Article 1—Name and Object of the Society.

- (a)—The society shall be called the Hong Kong University Medical Society.  
(b)—The object of the society shall be to hold meetings at which papers shall be read, or discussions held, on medical and general subjects; and to foster a spirit of comradeship and professional unity among its members.  
(c)—The society shall produce a journal at least once a year, to be called *The Caduceus* as a record of the proceedings of the Society, and for the publication of original articles in medical science.

### Article 2—Membership.

- (a)—All undergraduates, graduates, past and present members of the teaching staff of the Medical Faculty of the Hong Kong University, local medical practitioners, members of the army and naval medical service, shall be eligible for membership of the society.  
(b)—Other persons may be elected associate members at the discretion of the Executive Committee.

### Article 3—Officers.

There shall be a Patron, a President, Vice-Presidents, a Chairman of Committee, an Honorary Secretary, and a Graduate Honorary Treasurer.

### Article 4—The Executive Committee.

The management of the society shall be vested in an Executive Committee consisting of the Chairman, the Honorary Secretary, the Graduate Hon. Treasurer, six undergraduate representatives, and a graduate representative, all of whom shall be elected annually by members of the society. Five members shall form a quorum.

### Article 5—The Journal.

- (a)—There shall be a Caduceus Finance Committee.  
(b)—The Caduceus shall be controlled by the Caduceus Finance Committee to be appointed by the Society annually. It shall consist of:—

The President  
The Chairman  
The Secretary  
The Treasurer  
The Editor

of the Executive Committee.

One of the Associate Editors.

A member of the Medical Professional Staff.

A junior member of the Medical Teaching Staff.

### Article 6—Amendments of Constitution.

No alteration of this Constitution, nor any addition thereto, shall be made except at a general meeting of which not less than seven days notice shall be given.

## BYE-LAWS.

1.—Election of Officers and Members of the Executive Committee.

(a) The officers and members of the Executive Committee shall be elected by ballot at the first general meeting of the academic year. Vacancies occurring between such meetings may be filled by the Committee.

(b) The six undergraduate representatives, one for each year, are to be elected by the members of the year represented.

2.—Representation on the University Union Council.

The Chairman of the Committee and the Hon. Secretary shall be the society's representatives on the University Union Council.

3.—Conduct of Meetings.

The President, a Vice-President, or the Chairman of the Executive Committee shall preside at general meetings; or in their absence, a Chairman may be elected from among the members present.

4.—Subscriptions.

(a) Members shall pay an annual subscription of \$5/- payable at the commencement of the academic year.

(b) That the subscription for Life Membership be \$30/-.

(c) Post graduates who have before 1935, paid their subscription to the sum of \$30/- shall be Life Members.

5.—Amendment of Bye-laws.

No alteration of these bye-laws, nor any addition thereto, shall be made except at a general meeting of which not less than seven days' notice shall be given.



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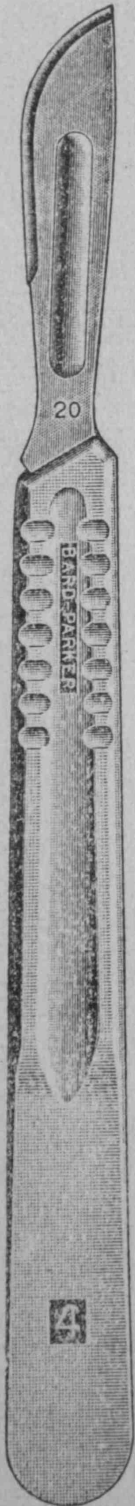
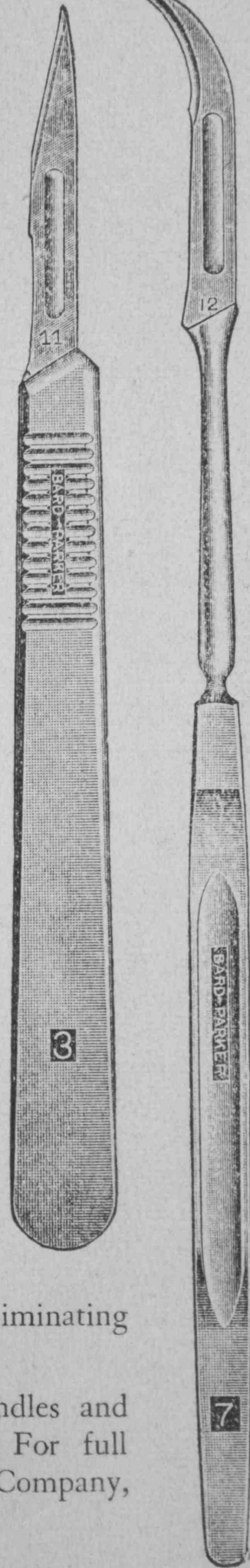
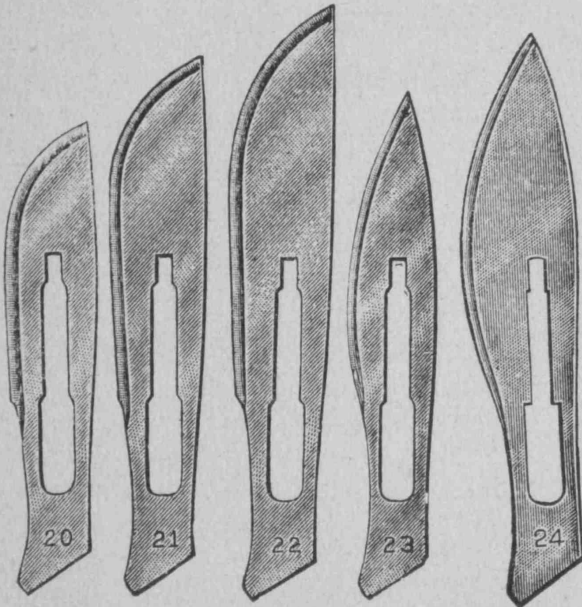
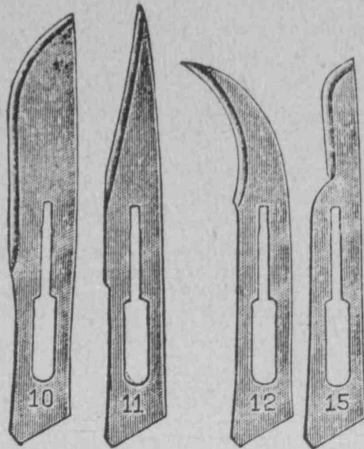
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