EDITORIAL

1. Visits to Malaya, Sarawak, Sierra Leone and Gambia

These four visits were made in the months of October and November, 1960. The Editor finds such visits to spheres of leprosy work an inestimable privilege and of the greatest value scientifically. Even on the humble level of the clinical appearance and evolution of leprosy in one country as compared to another, there is much to learn. Even in the difficult field of classification of leprosy, we would have less confusion and fruitless argument among leprologists, after organized visits. At present, each leprologist describes and classifies leprosy as he sees it in his country, and does it faithfully enough. But for solution of the problem of an *international classification* of leprosy, we consider it an essential first step that a team of leprologists of international provenance who should be good observers and not too proud to take notes should tour the leprosy countries to report on the leprosy found and its evolution, and its response to the modern drugs, and other matters of general interest to all countries who are trying to deal with leprosy. The human side must not be forgotten, for both leprosy workers as well as patients get great encouragement from visitors from abroad who are genuinely interested in their work and their cure, respectively, and in their problems as a whole.

(*a*) *Malaya.* The Federation of Malaya has now achieved independence. We only had 5 days there but these were crammed with interest. We were on our way to Sarawak in Borneo as the main purpose of our journey to Southeast Asia from London, but in Malaya there was much to see, and there was no sloth nor tardiness in seeing it. The main focus of the visit was Kuala Lumpur which is the Federated Malayan capital in the State of Selangor. Only 10 miles away is the large leprosarium of Sungei Buloh, and some 21 miles from Kuala Lumpur is Pulau Ketam which is the site of the careful long-term BCG trial as a prophylactic against leprosy. We also met in Kuala Lumpur the Hon. the Secretary for Health, Dr. Mohammed Din Bin Ahmed, and Mr. E. J. Lawrence, who is the publicity secretary of the Malayan Leprosy Relief Association (MALRA) which is newly formed but very active and likely to be a tower of strength to leprosy work in Malaya. Dr. M. Waters kindly took us many times to Sungei Buloh leprosarium and to his leprosy Research Centre there (which is under the guidance of the Medical Research Council of U.K.) and to the site of the BCG trial against leprosy amongst a static well-controlled population. Sungei is a large leprosarium of over 1000 patients which is very beautifully situated and built and was formerly under the charge of Dr. Gordon

Ryrie, then Dr. David Molesworth, and latterly Dr. P. K. Reddy. At present it has no medical superintendent, and the Hon. Dr. Mohammed Din Bin Ahmed, Secretary for Health, assured us that the post can be considered open and applications will be welcomed by him. Dr. Bhojwani is a medical officer still working in the leprosarium, and Dr. Waters of the Leprosy Research Unit has 2 wards under his charge. At Sungei Buloh no physiotherapy is available but the reconstructive and plastic surgery for repair of deformities and stigmata of leprosy has been undertaken by Dr. Reddy and Dr. Bhojwani. Dr. Waters kindly accompanied us to visit Pulau Ketam, where we found a well-planned, well-documented, and well-supervised trial of BCG as a prophylactic against leprosy. The population is static and well-recorded. A leprosy survey there was done at the very beginning and in 5 years or so some useful data about the value of BCG may emerge. This trial impressed us as so well planned and observed over the years that it can hardly fail to yield useful results, and we congratulate Malaya and the Medical Research Council on this trial. MCFADZEAN, J. A. and BHAGWAN SINGH, R. reported on this trial in *Leprosy Review*, **31**, 3, July 1960, pp. 145–158. In the island of Pulau Ketam on the West Coast of Malaya, 3,720 persons in the age group 0–25 years were examined and the incidence of leprosy found to be 19 per thousand. Then 3,649 persons apparently free of leprosy were tuberculin-tested. Of these 3,222 were eligible for vaccination with BCG and by randomization 1,648 were vaccinated and 1,574 left as controls. The expected incidence of leprosy in the unvaccinated group over 10 years would be enough to demonstrate a level of protection of the vaccine of 50% or more. The expected incidence of leprosy in the intake of the newborn is too low to give significant results and this part of the trial has been given up. The plan is to examine for leprosy at intervals over the next 10 years the present population of 0–25 years of age. It was found that the conversion rate after BCG vaccine was lower than expected almost certainly due to a fall in the viable count of the vaccine used, itself due to tropical conditions. The authors think that in future trials the viable counts of the vaccine should be checked before use in the tropics.

The present incidence of leprosy in Malaya as a whole is unknown. There is need of a leprosy survey. Seeking to make a guess, it might be between 30 and 50 per thousand. The type of leprosy is preponderately lepromatous, of one variety or other, perhaps 70% lepromatous, and Dr. Waters has studied some cases which resemble the Lucio phenomenon. Deformities may be 25%. The task in Malaya is not only huge but they have a grave type of leprosy. Nevertheless they have priceless assets in the shape of Sungei Buloh Leprosarium, with the Leprosy Research Centre in its grounds, and the Pulau Ketam trial. One feels that a build-up of staff will set the

whole campaign going again. There is another priceless asset in the shape of the Malayan Leprosy Relief Association (MALRA) which already exists with a powerful membership and is already engaged in a publicity campaign to explain the true nature of leprosy and is interested in all sorts of support and ideas to help forward the leprosy campaign.

One feels that the Malayan leprosy work is of good quality at the base, and could readily aim at complete victory over the disease. The next stages are opening up the campaign by organizing surveys and treatments in the rural areas, restoration of full staffing, training of nationals in leprosy recognition and care, the introduction of physiotherapy, and reconstructive surgery, the use of research to try out new drugs as they become available, as well as basic research, propaganda to explain the true nature of leprosy, that it is only a disease like any other and that patients can be medically cured and surgically restored to beauty and usefulness, so that very many can be returned to civic life as useful citizens.

(*b*) *Sarawak*. We spent 2 weeks there (10–24 October), and found it a most attractive and stimulating country. There are some countries in the world which envelop the visitor in happiness, and Sarawak is high in this select group, because of the niceness of the people and their goodwill for good causes, allied to a refreshing strain of practicality. The population is 175,000 and our guess at the leprosy incidence would be the existence of 15,000 active cases of leprosy (a leprosy survey has not yet been done). The Director of Medical Services, the Hon. D. A. Baird, O.B.E., is "well up" in the experience of and understanding of leprosy, and surely an unique feature of the present Sarawak is the possession of a Governor who has *taken part in a leprosy survey* and also understands leprosy. Sir Alexander Waddell helped us in an early leprosy survey in 1938 in Malaita Island of the British Solomon Islands in the Western Pacific, and was indispensable. It was a magnificent stimulus to hear at the outset something of Dr. Baird's plans for the improvement of district or "ulu" medical work, and for the training of nationals as medical assistants, which obviously would fit in splendidly with the opening-up or widening-out of any future leprosy campaign. We also met and stayed with Mr. and Mrs. Hamish MacGregor, M.B.E., who live in a staff house at Kuching leprosarium (Rajah Sir Charles Brooke Memorial Settlement) which is 13 miles from Kuching the capital. Mr. Hamish MacGregor has been Superintendent of the Kuching Leprosarium for 11 years, and our later daily examination of the work revealed its essential soundness and the faithful steady work of Mr. and Mrs. MacGregor, Generawi bin Mok, Lau Thian Seng, Edward Chia, and Chin Jin Fok reflecting the greatest credit on them and the Sarawak Medical Department and Government, who fostered such good work. In the Rajah Sir Charles Brooke

Memorial Leprosarium, some 300 to 380 patients are treated. We had the chance of examining all the patients in the ensuing days and found that most of the patients had become cured medically, but the great number awaiting discharge, but prevented by deformities, was striking. Naturally a patient does not consider himself cured if he has a claw hand or a perforating plantar ulcer, and the introduction of active physiotherapy and reconstructive surgery will soon be arranged. The great centre of these arts is Prof. Brand's work in Vellore, and volunteers will go from Sarawak to learn his techniques. We found that in Kuching they had made themselves familiar with the potentialities of the newer drugs, had tried them out, and apprehended their advantages. There is a heavy preponderance of the lepromatous type of leprosy, and of the diffuse lepromatous in particular, and examples of the Lucio Phenomenon were not wanting (a necrotizing diffuse lepromatous variety). The tuberculoid type of leprosy provided few cases, and the lepromatous rate in the leprosarium was 90%, and probably 70% in the country as a whole. Yaws is a frequent complicating disease, also tuberculosis of the lungs. The whole picture of the leprosy was of a grave infectious disease, with strong tendency to nerve involvement and to reactions. These reactions are, however, mild on the whole. The heavy incidence of the diffuse lepromatous type should be noted. This type in very early stages may be missed in diagnosis, which emphasizes the value in any future survey or leprosy control scheme of the importance of the laboratory for smears, histology, lepromin preparation and tests. Another thing notable in the Kuching patients was the infrequency of the Borderline types, almost as if in a recent invasion by leprosy of the country (1200 A.D. for Sarawak?), the complicated intermediary types of leprosy have not had time to appear in all their delectation for argumentative leprologists. The bacterial transmission and invasion seems to remain uncomplicated for a long time, producing in a people who have low resistance on the whole a general manifestation of leprosy of the lepromatous type, and in the few who *have* resistance scanty manifestations of tuberculoid leprosy which may become borderline or lepromatous if not rapidly "cured". Another point of great interest, in view of the *González theory of the beneficial influence of thyroid depression on leprosy*, was the fact that Sarawak has goitre valleys between limestone hills, in which valleys leprosy was thought to be minimal in incidence and clinically less grave than in non-goitrous areas. In the future leprosy survey needed in Sarawak, it would be most valuable to include a close epidemiological study of the goitre areas, with special reference to the incidence and morbidity of leprosy. We did see one case at Kuching of a boy of about 12 years who had a developing goitre and leprosy, and the leprosy was a mild *tuberculoid* type.

Sarawak is soon to attempt a country-wide leprosy campaign,

aiming at eradication. The good work already done augurs success, perhaps in 10 years. As we mentioned above, we detect a strain of practicality in Sarawak peoples, and certainly they are not rigidists nor obscurantists. The Medical Department under Dr. D. A. Baird, with a wealth of excellent personnel, has already planned the training of nationals as medical assistants, and this will include training of nationals in leprosy lore under Mr. Hamish MacGregor at Kuching Leprosarium (Rajah Sir Charles Brooke Memorial). Recognising leprosy as a human disease occurring frequently in the country, they are forward-looking and open-minded, and quite ready to try to use if of value every possible good means, *even if new*. They are quite ready to get away from the conception of the modern leprosy campaign as a ponderous military operation with counter-marching and marching of big-booted parties of soldiers, and accept a conception of a Commando operation containing continued frequent, lively, and widespread attacks, recruiting and training of more soldiers (national leprosy personnel), maintenance of laboratories and research (one cannot imagine commando soldiers not being interested in new weapons, and not making intelligent trials of promising new weapons, as well as not seeking new discoveries of their own to improve the campaign and basic discoveries which will help *all* commandos). A good Commando will also take prompt steps to eliminate possible obstructions, as for example a large accumulated backlog of untreated deformities and stigmata, which can be dealt with by volunteers especially trained for the task in physiotherapy and surgery, otherwise this obstacle would cause depression and loss of hope among the *people*, and bring the campaign to a halt. These pioneer volunteers can set up schools and courses to teach other commandos. Obtaining of officers for the commandos (medical officers supervising the campaign or parts of it) has not been forgotten by Sarawak. Finally, but not least, for it should come first, a good Commando group will certainly "case the joint" and keep on "casing the joint" which means sizing up the enemy and his territory by a leprosy survey, steadily repeated. It all comes down to personnel and good soldiers. We think Sarawak already has a fine nucleus of such, and because it proposes to recruit and train many others, and arm them with weapons and tactics which they have tried out and proved in their own conditions, success is very probable in a short period of time. The total leprosy problem is moderate in scope, say some 15,000 patients with active leprosy, and the task should be compassed successfully in perhaps 2 five-year periods.

(*c*) *Sierra Leone and Gambia.* We also had the privilege, in November 1960, of a visit to *Sierra Leone* and *Gambia*. In *Sierra Leone* the leprosy situation has been surveyed, the last survey being that by C. M. Ross and helpers in 1958, who indicate that probably there are 80,000 cases in Sierra Leone, with a lepromatous incidence

of the order of 20%. This means a far milder type of leprosy than in Sarawak and Malaya. Dr. Ross advised a countrywide campaign, with adequate trained personnel, and the opening of leprosy dispensaries and the use of mobile teams and domiciliary treatments if they could be staffed. Dr. Ross pointed out that it would be wise to build a new leprosarium to act as the focus or centre of the campaign, as a site of training of nationals as leprosy assistants, of records, of research, of physiotherapy and surgery, etc. There was no intention that this new leprosarium was to be based on the former idea of institutional segregation, but accommodation for 100 patients would be provided for those requiring special care and investigation. In leprosy campaigns the possession of at least one forward-looking leprosarium has enormous advantages, not the least as being a centre of training for leprosy workers. Of course leprosy workers need field training also, but their study of leprosy recognition and care best begins in an institution where there is time for reflective study and the learning of new techniques. This idea of Dr. Ross was obviously so sound that it appealed to the Medical Department, and finance was set aside and a site chosen at *Masanga*. BELRA helped by providing workers, first Mr. and Mrs. Alan Waudby, then Mr. and Mrs. J. Boyd and Mr. R. Lowes, and very recently Mr. Alex Munro. The Colonial Office provided a medical officer, Dr. W. Bowman, who was sent to Nigeria for the study of leprosy, and on this our recent visit it was a great pleasure to find that he had returned to Sierra Leone, and had been at work since August 1960. We met him later frequently up-country, and in Freetown also had the privilege of fruitful interviews with the Minister of Health, Hon. Taplimah Ngobeh, with the Chief Medical Officer, Dr. H. M. S. Boardman, with his Deputy, Dr. A. B. Cole, with the Epidemic Disease Control Officer Dr. Neville Campbell (who has been in charge of yaws work in Sierra Leone but well understands leprosy and has given great help where he can), with Mr. R. Lowes our BELRA worker, and with Dr. F. Marti, regional representative of UNICEF, who have always afforded great practical help in leprosy campaigns. Very soon we went up-country and were with Dr. Bowman at Magburaka, from whence we visited the Masanga site, and the active leprosy dispensaries of the EUB Mission at Rotifunk (Drs. Silver and Harris), at Moyamba Hospital (Dr. P. C. Kothari, F.R.C.S., who is interested in plastic and reconstructive surgery for leprosy patients), Mabonta Clinic (Dr. Campbell and Mr. Lowes and Mr. A. S. Conteh), the leprosy clinic at Magburaka Hospital, M.C.A. Mission Clinics at Yifin and Mayoso. I heard that there were 13 clinics or centres which give treatment with DDS. Mr. Alan Waudby of BELRA, before he left had opened 130 clinics or centres which give treatment with DDS. Dr. Bowman has begun training of leprosy assistants. We visited the Masanga site and found that the early stages had run into difficulties

and these had delayed progress, but it may be expected to go ahead now and soon achieve its full and crucial place in the antileprosy campaign. With approximately 80,000 cases of leprosy, Sierra Leone has a tidy task, but it could achieve success.

In Bathurst, *Gambia*, we spoke with the acting D.M.S. (Dr. D. W. Bringam) and found that things could go ahead there, but there was some delay in obtaining a medical officer for the leprosy campaign. BELRA has already sent a worker, Mr. Mead, and he and Mrs. Mead are housed at Bansang, which may later be the centre and focus of the Gambian leprosy campaign (8,000 to 10,000 patients, many with deformities).

2. The Theory of Hypothyroidism being Favourable to Leprosy and the Action of Thyroid-Depressant Drugs against Leprosy.

Dr. ARTURO O'BYRNE GONZÁLEZ of Cali, Colombia, is the originator of this theory and has long pondered and investigated it, and has tried out methimazole-Lilly (a propyl thiouracil type of thyroid-depressant drug) against active leprosy with reported good results (shortly to be published in the International Journal of Leprosy, we hear). Dr. González has recently sent us a *Letter to the Editor* which describes his main lines of thought. The original is in Spanish, and we reproduce it in English here, considering it of great interest and importance.

Letter to the Editor from DR. ARTURO O'BYRNE GONZÁLEZ:

In 1952 and 1953 I treated a female leprosy patient who also suffered from a thyrotoxicosis of Graves-Basedow. I started her treatment with propyl-thiouracil, thinking that the treatment of her thyroid condition was more urgent than that of the leprosy. Nine months later I noted two effects of the drug, an improvement in the endocrine state and the disappearance of the leprotic macules.

Seeking a reason for the effect of the propylthiouracil on the leprosy, I emerged with the first argument, as follows:

(*a*) Iodine is harmful to the leprosy patient;

(*b*) This harmfulness of iodine has been used as a therapeutic measure (Danielssen, Muir, Schujman, Ross Innes) through a stimulation of the antigenic processes;

(*c*) Iodine bound to protein (PBI) is a normal and necessary constituent of the human body, at a normal estimated level of 5 to 8 micrograms per 100 ml. of blood;

(*d*) It is known that thiouracil and its derivatives *decrease* the proteic iodine (PBI);

(*e*) It is probable that thiouracil and its derivatives, on decreasing the proteic iodine also decrease the vitality of *M. leprae*.

These 5 points above may be amplified with some secondary arguments.

Why does the vitality of M. leprae increase in the presence of iodine?

1. We should take into account that mycobacteria are thought to be derived from algae, modified and adapted to man. The *Encyclopaedia Britannica* says: "In many respects the bacteria resemble some of the simpler plants, particularly the blue-green algae and some of the moulds, and it is largely on the basis of

this resemblance that bacteria are considered to be *simple plants* rather than animals. They are placed with the fungi, a group which includes the chlorophyll-containing blue-green algae and the non-chlorophyll yeasts and moulds".

2. "As in the case of the other algae, diverse marine Chlorophyceae (Bryopsis, and to a lesser extent Ulvaceae, Cladeophora, etc.) store up considerable quantities of iodine, though it is not as definitely localised as in some Rhodophyceae (F. E. FRITSCH, Professor of Botany in the University of London, Queen Mary's College)".

3. "Iodine is present in sea water. It occurs most abundantly in seaweeds. For a long time iodine has been recovered on a commercial scale from seaweed".

4. Hence the "iodophilia" of the mycobacteria could have phylogenetic antecedents.

Could there be some etiological similarity in lepra reaction produced by the administration of iodine and natural lepra reaction?

1. Probably so. There are various epochs in human life in which the level of proteic iodine is higher, such as during pregnancy, menstruation, puberty, the menopause, psychic stress, etc. In the same way we note the frequent aggravation of leprosy during pregnancy and menstruation, the greater incidence of malignant forms during puberty, and the frequency of lepra reactions during the menopause and during periods of stress.

2. There exist other epochs in human life in which the proteic iodine and therefore the function of the thyroid gland are low, such as during the first months of life and during old age. In the same way we note that the child of leprosy parents does not have manifestations of the disease during the first year of life, and that the old man also has not a big incidence of malign forms of leprosy.

3. "Somewhere there must be an endocrine link, lepromatous leprosy being the masculine type and tuberculoid leprosy the feminine type, with a number of patients who are not definitely either, but are, at various stages, between. The same or a related endocrine influence may be associated with higher male and lepromatous ratios which exist at present time among races whose skins are less pigmented than the Africans". (J. A. KINNEAR BROWN, Internat. J. of Lep. **27**, 3, p. 250.)

Some biochemical studies by SISTER HILARY ROSS indicate that the proteic iodine in leprosy patients under treatment is *normal*. Various other studies show "that a diet too rich in either fats or proteins or both causes an increased rate of discharge of iodine from the thyroid gland and a resultant iron deficiency. Carbohydrate diets do not produce this condition". (MCCARRISON, R. Indian J. of Med. Res., Calcutta, **7**, 433–647, 1919–20.)

It is probable that this influence of carbohydrate diet on the peoples of India and of other leprosy endemic areas may explain some questions. The areas of the civilized world where the diet is rich in either fats or proteins have a low incidence of leprosy.

Antithyroid substances are those able to suppress the formation of thyroid hormone in the normal animal and thus to diminish the proteic iodine of the blood.

There are "antithyroid foods". Some of these have a considerable antithyroid activity. The chief foods of this class, in their order of potency, are the rape or rutabaga, carrots, lettuce, turnip, peas, peaches, grapefruit, kidney beans, pears, walnuts, beets, spinach, cabbage, filberts, string beans, celery, grapes, milk. A study of these foods in relation to leprosy in various countries of the world would be most interesting.

Derivatives of aniline and of mercaptan occur among the artificial antithyroid compounds. "It was concluded earlier that the aniline compounds owe their antithyroid activity to the presence of an appropriately substituted aminobenzene grouping: $NH_2C_6H_4$ (ASTWOOD, 1944–45; TAUROG, CHAIKOFF, and FRANKLIN, 1945). ANDERSON, 1949, notes that this concept must be expanded to include methylated aniline derivatives and amino-heterocycles (MCGAVACK, "The Thyroid", 1951, p. 177). This remark of MCGAVACK causes us to ask if diamino-diphenyl-sulphone, $NH_2C_6H_4SO_2C_6H_4NH_2$, which is the chief anti-leprosy drug, is one of the antithyroid substances? We could also ask the same about Ciba 1906 which is a thiourea derivative.

There is a fact of great importance for future investigations. The majority of the compounds used at present in the treatment of leprosy and of tuberculosis

have a certain degree of antithyroid activity (Streptomycin, INH, thiosemicarbazone, PAS).

A comparative study of biochemical analysis of blood in leprosy and in hyperthyroid states leads to analogous results, very encouraging worthy of a detailed study.

From 1953 to the present time I have treated 236 individual leprosy cases with antithyroid substances. I first used those associated with DDS, in small doses. Next, greater doses were used of antithyroid drugs of the type of propylthiouracil in assocation with small doses of sulphones. In the third stage I used antithyroid drugs alone in progressively increasing doses (Tapazole, propylthiouracil).

The general results have been satisfactory in all stages of the investigation, but the order of therapeutic efficiency accords with the chronological order. The best results have been got with Tapazole-Lilly (methimazole) without combination with other antileprosy drugs. I have the impression that the addition of abundant milk to the diet improves the therapeutic effect still further.

The technique used in recent months with Tapazole was to push the dose to a maximum as soon as possible, which for an adult of average weight can be 40 to 50 mg. daily, divided into 3 or 4 doses. The possibility of intolerance must be watched, and white cell counts made whenever suitable.

I do not think that the optimum dose of Tapazole has been found yet. It must be remembered that (according to MCGAVACK) a patient of BASEDOW could become myxoedematous with a dose of 4 to 5 microcuries of radio-active iodine; on the other hand, a normal or mildly hyperthyroid subject reaches a myxoedematous state with a dose 10 *to* 15 *times greater.*

When the clinical and bacteriological improvement has been attained, the dose of Tapazole is reduced to an individual maintenance regime. In cases of febrile leprosy reaction, long in duration or strong, I have used Tapazole in very small doses (5 to 10 mg. daily), along with a moderate amount of dietary protein, with calcium gluconate, and some antimony compound. In some cases I combined Tapazole with prednisolone for a few days. Once the febrile reaction was controlled the Tapazole was continued alone, always in moderate doses.

In anergic non-reacting lepromatous cases without liver damage the dosage of Tapazole could reach the maximum in a few days. These cases yield the best results.

The most difficult leprosy cases are those in the stage of puberty. On the other hand, I think that lepromatous over 50 years of age are the easiest to treat. In general tuberculoid cases have excellent and rapid improvement.

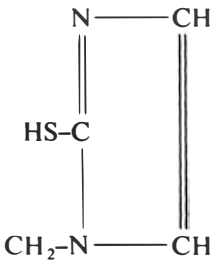
Special increase of dosage of Tapazole can be made during the time of menstruation, during pregnancy, the menopause, and periods of psychic stress.

In most of lepromatous patients treated with antithyroid preparations I note a strong pigmentation in the sites corresponding to the skin lesions of leprosy. I have tried to explain this pigmentation by the common origin of melanin and thyroxin.

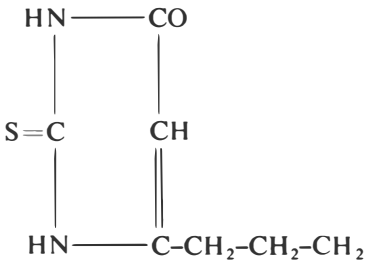
Drs. JORGE VERDAGUER and F. B. PECK, Jr., have collaborated fraternally with me in verifying this theory.

Dr. Arturo O'Byrne González,
Carrera 5a. No. 7–58,
Cali, Colombia.

Dr. JOSÉ VERDAGUER of the Lilly Research Laboratories has very kindly sent us information on the nature of Tapazole (methimazole-Lilly) and indicates that further reports on the trial of Tapazole in leprosy may be expected within the next 3 months. Tapazole has been used as an antithyroid drug for more than 10 years, and informative papers on it include that by J. CHEVALLEY, T. H. MCGAVACK, S. KENIGSBERG, and S. PEARSON, in the *J. of Clinical Endocrinology and Metabolism* 14, 8: Aug. 1954, pp. 948–960; also G. W. IRWIN, H. D. VAN VACTOR, and M. S. NORRIS, *J. of the Amer. M.A.*, **149**; 1637–40; Aug. 30, 1952. Tapazole (methimazole–Lilly) chemically is 1-methyl-2-mercapto-imidazole, and its structural formula and that of propythiouracil are as follows:—



"TAPAZOLE"



"PROPYLTHIOURACIL"

Tapazole was shown to be a potent antithyroid agent, and as little as 0.5 mg. was found to have a pronounced inhibitory effect on iodine accumulation in the normal human thyroid gland, and 5 mg. inhibited iodine uptake completely for nearly 24 hours. After dosage of 10 mg. Tapazole thrice daily the average protein-bound iodine level in the plasma fell to within normal limits and remained normal in hyperthyroid patients. The only absolute contra-indication to the use of Tapazole appears to be the presence of idiosyncracy in the form of agranulocytosis, severe leucopenia, drug fever, severe skin eruption, or other serious reaction. A history of such side-effects with antecedent use of drugs should contra-indicate Tapazole, though not necessarily if the previous drug has been an antithyroid one. The administration should be cautious, with close observation of the patient. The side effects typical of antithyroid drugs are skin rashes, urticaria, fever, granulocytopenia, and agranulocytosis.

Dosage with Tapazole is oral, and 10 to 15 mg. daily may be satisfactory for most patients as an antithyroid agent, but others may require 30 to 40 mg. daily to establish rapid and complete control. There seems to be no advantage in exceeding 60 mg. daily. A maintenance dosage may be 5 to 20 mg. daily.

Dr. O'Byrne González has very recently pointed out (Dec. 1960) that Dr. J. H. Hanks has already visualized the existence of factors which inhibit endogenous metabolic activity; and that Dr. C. T. Gray thinks that anaerobic conditions are definitely injurious to *M. leprae*; also that Dr. Pitt-Rivers in the Ciba Symposium on the thyroid gland presented some interesting data about oxygen metabolism and its variations under administration of antithyroid drugs.

This theory of antithyroid influence on leprosy is most interesting and surely should be explored more widely. We agree with O'Byrne González that a very useful part of further explorations of this question would be epidemiological studies in countries which have both endemic goitre and leprosy, of the relation between them. Such countries are Sarawak, Gambia, and Sierra Leone.

3. Transmission of the human leprosy bacillus to rats or mice placed on a special diet.

This work has been stimulated by Dr. MENY BERGEL who is Director of the Laboratory of Leprosy Research, Rosario, Argentina. This work is also of great interest and significance. Dr. Bergel informs us that in the Conference on Leprosy in the U.S. Public Health Service Hospital in Carville, La. Nov. 7–10, 1960, there were 5 papers delivered which related to this subject, namely "Inoculation of *M. leprae* in Mice on Severe Pro-oxidant diets" by MENY BERGEL; "Attempts to Infect Rats with *M. leprae*, the Rats being on a Pro-oxidant Diet" by S. S. BARKULIS, P. C. EISMAN, S. GEFTIC; "Intratesticular Inoculation of *M. leprae* in Different Species of Laboratory Animals under Special Dietary Conditions" by K. E. MASON; "A Method for the Investigation of Anti-leprotic Drugs using Pro-oxidant diets" by MENY BERGEL; "The Tocopherol-like Activity of Ciba-1906 and other Anti-leprosy Compounds in a Test System Involving Murine Trypanosomiasis" by F. C. GOBLE. Dr. Bergel says that Dr. Mason and colleagues confirm his work on the growth of *M. leprae* in rats on pro-oxidant dietary conditions.

The communications by MENY BERGEL at the recent Carville Conference on Leprosy are here summarized:—

We have shown in our laboratory that *M. leprae* grows in the testes of rats maintained on a pro-oxidant diet. We have also found that the incorporation of DDS, CIBA 6704, and CIBA 6600 into this diet at the time the animals are infected intratesticularly, suppresses the growth of the organism. These findings suggest the following method for the evaluation of compounds for anti-leprosy activity.

1. Male rats, 21 days old, are given a pro-oxidant diet which is deficient in vitamin E and contains 20% linseed oil. 0.5 parts $AgNO_3$ per 1,000 parts drinking water (distilled) is also given to the animals.

2. Thirty days later and while still receiving the pro-oxidant diet, the animals are injected in one testis with 0.1 ml. amounts of a suspension of *M. leprae* derived from a human source or from a testis of a rat previously infected and maintained on an unmedicated, pro-oxidant diet. Silver nitrate treatment is discontinued at the time of inoculation of the infection.

3. At the time of inoculation, the animals are divided into two groups: One group serves as a control group, receiving pro-oxidant diet. The other group receives the pro-oxidant diet plus the test compound. At the time of inoculation, 4 normal rats are also infected in the testis and the animals are sacrificed immediately and used as controls (starting count).

4. Four months after infection, all animals are sacrificed and the number of bacilli in the injected testes are counted.

5. Counts are also made of rats dying prior to the completion of the experiment.

6. Counts of the numbers of bacilli for each animal (in each group) are plotted. Comparison of these plottings will determine the effectiveness of the test compound in suppressing the growth of the *M. leprae*.

7. DDS, which markedly suppresses the growth of the bacillus in the testis, may be used as a reference drug.