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University of Minnesota

Cutaneous Tuberculosis

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INDEX

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I.

UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS

February 8 - February 15, 1947

No. 144

Saturday, February 8

7:45 - 8:50 Orthopedics Conference; Wallace H. Cole and Staff; Station 21, U. H.

9:00 - 9:50 Surgery-Roentgenology Conference; O. H. Wangensteen, L. G. Rigler, and Staff; Todd Amphitheater, U. H.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; M-515, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:00 - 12:50 Obstetrics and Gynecology Grand Rounds; J. L. McKelvey and Staff; Station 44, U. H.

11:00 - 12:20 Anatomy Seminar; Eperimental Cytology of the Central Nervous System; J. F. Hartmann; Harvey Cushing, surgeon and anatomist; J. Gordon Scannell; 226 I. A.

Monday, February 10

9:00 - 9:50 Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H.

9:00 - 10:50 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; Interns' Quarters, U. H.

11:00 - 11:50 Roentgenology-Medicine Conference; Veterans' Hospital.

11:00 - 11:50 Physical Medicine Conference; Club Feet; Douglas Linsey; W-200 U. H.

12:15 - 1:15 Obstetrics and Gynecology Journal Club; M-435, U. H.

12:30 - 1:20 Pathology Seminar; Studies on the Pathogenesis of encephalitis; Berry Campbell; 104 I. A.

12:15 - 1:30 Pediatrics Seminar; Irvine McQuarrie and Staff; 6th Floor Seminar Room, Eustis Amphitheater, U. H.

12:00 - 12:50 Physiology Seminar; Some Effects of Potassium Ions; S. A. Corson; 214 M. H.

4:00 - 4:50 School of Public Health Seminar

8:00 - Clinical Research Club; Clinical Use of tetra-ethyl ammonium chloride; Russell Wilson; A method of venography; Davitt Felder; Eustis Amphitheater, U. H.

Tuesday, February 11

9:00 - 9:50 Roentgenology-Pediatrics Conference; L. G. Rigler, I. McQuarrie and Staff; Eustis Amphitheater, U. H.

10:30 - 11:20 Surgery Seminar; John R. Paine; Small Conference Room, Bldg. I, Veterans' Hospital.

12:30 - 1:20 Pathology Conference; Autopsies; Pathology Staff; 102 I. A.

2:00 - 2:50 Dermatology and Syphilology; H. E. Michelson and Staff; Veterans' Hospital, Bldg. III.

3:15 - 4:15 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U.H.

3:30 - 4:20 Clinical Pathological Conference; Veterans' Hospital.

3:45 - 4:50 Pediatrics Staff Rounds; I. McQuarrie and Staff; W-205, U. H.

4:00 - 4:50 Surgery-Physiology Conference; Use of radioactive isotopes in surgery; David State and Robert Lisson; Eustis Amphitheater, U. H.

5:00 - 5:50 Roentgenology Diagnosis Conference; General Hospital.

Wednesday, February 12 -- Holiday

4:00 - 6:00 Medicine and Pediatrics Infectious Disease Rounds; W-205, U. H.

Rounds will be held.

Thursday, February 13

8:30 - 9:20 Surgery Grand Rounds; John R. Paine and Staff; Veterans' Hospital.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; Todd Amphitheater, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:20 Roentgenology-Surgery Conference; Staff; Veterans' Hospital.

12:00 - 12:50 Physiological Chemistry Seminar; Chemical Fractionation of Steroids; Saul Cohen; 214 M. H.

4:30 - 5:20 Ophthalmology Ward Rounds; Erling Hansen and Staff; E-534, U. H.

4:30 - 5:20 Bacteriology Seminar; Staff; 214 M. H.

5:00 - 5:50 Roentgenology Seminar; Emptying of gallbladder; Joseph S. Summers; M-515 U. H.

Friday, February 14

9:00 - 9:50 Medicine Grand Rounds; C J. Watson and Staff; Todd Amphitheater, U.H.

9:00 - 9:50 Pediatric Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:20 Medicine Grand Rounds; Staff; Veterans' Hospital.

10:30 - 12:20 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Otolaryngology Department; U. H.

11:30 - 1:00 University of Minnesota Hospitals General Staff Meeting; Acute Poliomyelitis; Clifford C. Grulee, Jr. and Theodore C. Panos; New Powell Hall Amphitheater.

1:00 - 1:50 Dermatology and Syphilology; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.

1:00 - 2:50 Roentgenology-Neurosurgery Conference; H. O. Peterson, W. T. Peyton and Staff; Todd Amphitheater, U. H.

Saturday, February 15

7:45 - 8:50 Orthopedics Conference; Wallace H. Cole and Staff; Station 21, U. H.

9:00 - 9:50 Surgery-Roentgenology Conference; O. H. Wangensteen, L. G. Rigler, and Staff; Todd Amphitheater, U. H.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; M-515, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:00 - 12:50 Obstetrics and Gynecology Grand Rounds; J. L. McKelvey and Staff; Station 44, U H.

11:00 - 12:20 Anatomy Seminar; Antibodies and the adrenal cortex; Arthur Kirschbaum; Ceroid pigment; Marthella Frantz; 226 I. A.

II. VITAMIN D_2 IN THE TREATMENT OF CUTANEOUS TUBERCULOSIS

John R. Haserick

Introduction

Lupus Vulgaris and other types of cutaneous tuberculosis have apparently been successfully treated with large doses of vitamin D_2 (calciferol). Independent investigations by Charpy[1], in France, Dowling and Frosser Thomas[2] in England, and Fanielle in Belgium have shown excellent results with this method of treatment. This is a report on the cases so treated at the University of Minnesota Hospitals and in private practice by local dermatologists.

Lupus Vulgaris

According to the classification of Michelson and Laymon[4], lupus vulgaris is the one form of cutaneous tuberculosis which is chronic and progressive without necessarily being associated with serious systemic tuberculosis. Its importance lies in its relation to the other forms of cutaneous tuberculosis, most of which tend to heal spontaneously. Self healing is especially typical of (1) the cutaneous primary complex (tuberculous chancre), (2) the tuberculosis cutis verrucosus, (3) the necrotic papular, and (4) lichenoid tuberculids, but is also seen in the more slowly healing, (5) erythema induratum, and (6) scrofuloderma.

However, untreated lupus vulgaris is almost a perfect balance between the organism and resistance of the host, and because of this extreme chronocity spontaneous healing is rare and it will remain active for decades. The patient can thus act as his own control in new therapeutic trials. Pathologically, lupus vulgaris consists of typical non-caseating tubercles in the corium. Not infrequently tubercle bacilli are demonstrable in the sections, and guinea pig inoculations commonly produce tuberculosis.

Historical Background

In 1848 Emery[5] treated 74 patients with lupus vulgaris by daily administering as much as a liter of cod liver oil, now known to contain approximately eighty-five international units of vitamin D per gram. Improvement was noted, but the unpalatability of such large amounts of cod-liver oil made the method impracticable.

Basing his experiments on the observation by Henri and Baroni[6] in 1910 that the tubercle becillus loses acid-fastness after a few minutes radiation with a quartz lamp, Malmström[7], in 1925, irradiated cod liver oil. He injected extracts into tuberculous lesions, and reported prompt healing. Villaret, Justin-Besancon and Fauvert[8], in 1926, used irradiated cholesterol up to 500 cc. intrapleurally in purulent tuberculous empyema. They considered their results to be promising but not as spectacular as those of Malmström. They suggested the oral use of irradiated oils as a valuable aid with which to build up the patient's general health.

Working with white rats, which are ordinarily immune to tuberculosis, Grant, Suyenaga and Stegeman[9] decreased the calcium and vitamin D in the diet, rendering the rats susceptible to acid-fast infection. On the other hand, rats which received adequate diets before and after inoculation with the tubercle bacillus were immune to four to ten times the usual doses. In 1935 Steiner, Greene and Kramer[10] reported that rachitic rabbits showed no greater incidence or any more extensive tuberculosis following inoculation of virulent acid-fast bacilli than did control rabbits.

In 1930 Levaditi and Po[11] in France and Spies[12] in America independently reported increased calcification of tubercles in guinea pigs treated with irradiated ergosterol. Levaditi and Po[13] demonstrated that dead as well as the living tubercle bacilli provoked this response and postulated that the calcium deposition was the result of intracellular calcium metabolic changes and not phagocytosis of loose calcium. The tuberculous processes seemed to have a more special affinity for the calcium than normal tissue.

Trevorrow, de Savitsch, Black and Lewis[14], reporting on experimental tuberculosis of rabbits and guinea pigs, stated that 92-94% of the groups treated with viosterol alone, with viosterol and tuberculin combined, and with prolonged sunlight irradiation without tuberculin showed calcification of the lesions, whereas 25% of the tuberculin controls and 14% of the untreated controls showed similar calcification. However, the viosterol treated rabbits expired earlier, presumably due to toxicity from the vitamin D. Reed, Stuck and Streck[15] quote Capocacoia (1934) as finding no beneficial effect in guinea pig and rabbit tuberculosis with sub-toxic doses of vitamin D.

In 1928, Bamberger and Spranger[16] found improvement in forty infected guinea pigs, and then applied the drug to children with various forms of tuberculosis. Improvement in the local processes was constantly noted, but toxic symptoms prevented prolonged use. Sub-toxic doses showed no change in the tuberculous processes. Later, their drug (the old Vigantol of the I. G. Farben Co.) was found to have a high toxisterol content, necessitating further purification.

Crimm[17], in 1932, produced hypercalcemia, with irradiated ergosterol in pulmonary tuberculosis. He felt that "activated ergosterol may favor fibrosis and hasten absorption of tuberculous infiltration". He found that adult cases of pulmonary tuberculosis tolerated a hypercalcemia of 15 mgs%, and was the first to suggest the use of intravenous sodium bicarbonate to control toxic symptoms.

In 1945 Levinson[18], reporting on 500 cases of tuberculous meningitis seen at Cook County Hospital, Chicago, stated that only three recovered. Two of these had received massive doses of vitamin D and calcium.

Gounelle and Bachet[19] reported in 1946 on five cases of pulmonary tuberculosis treated with massive and prolonged doses of vitamin D_2. Usually the chest x-ray became worse during the first week, followed by a gradual improvement. They were impressed with the lack of progression to an expected fatal outcome in cases with serious bilateral tuberculosis which were beyond aid through thoracoplasty, although cavities did not fill up and the fibrous lesions did not change.

Cutaneous tuberculosis and vitamin D_2

Fanielle[3] used irradiated ergosterol in the treatment of human tuberculosis and after twelve years of observations concluded that it was of distinct value. In 1942 he reported favorable results in 4 cases of lupus vulgaris, 2 cases of ulcerated tuberculosis and 1 case of varrucous cutaneous tuberculosis. These findings were confirmed by Alechinsky[20] who reported the cure of several cases by the same method.

Credit for focussing medical attention on this subject, however, is usually given in the French, English and Spanish literature to Charpy of France. In 1943 he[1a] reported 27 cures of lupus vulgaris treated with calciferol in a glycero-alcoholic solution (sterogyl). About two-thirds required additional destructive therapy to complete the cure. Charpy noted that the results were rapid with a definite change in the first week. Surrounding lymphangitis and adenitis were quickly reduced, but the cutaneous nodules were more resistant and often required cauterization. He supplemented the vitamin D_2 with the calcium contained in 1-2 liters of milk daily.

Using the "Charpy method", Gougerot and Gaullier[21] obtained cures in 20 out of 35 cases. There was no change in four. They attributed their relative lack of success to the fact that their patients were hospitalized for other diseases and had less resistance. Huriez and Leborgne[22] reported excellent results in 7 of 15 cases of lupus vulgaris. Four were very much improved and four were failures, three of which were attributable to bad social conditions.

Similar results have been reported by Garrie[23], Bureau, Yves and Barriere[24], and Vachon[25]. Also using the Charpy-Fanielle method, Meyer, Gaulier and Desgrez[26] followed 148 or 300 cases of lupus vulgaris at the Finsen Institute of which over 75% were greatly improved, but nearly all required addi-

tional local care. They did not observe a single serious case of vitamin D intoxication.

Working independently in England Dowling and Prosser Thomas[2] began treating lupus vulgaris with calciferol in 1943. They reported 18 of 32 cases as cured, 9 much improved, and 5 not greatly improved. Using the method of Dowling and Prosser Thomas, MacCrae[27] reported cures in 14 of 20 cases of lupus vulgaris. The average duration of the disease before treatment in MacCrae's cases was 19 years. During treatment he noted a reaction during the first 2-3 weeks, particularly that "the patches became angrier and isolated nodules more scarlet, with an increased tuberculin reaction and sedimentation rate". A steady improvement was usually noted following this reaction. Bell[28] in 1946 reported cures without reaction in two children with tuberculous adenitis.

Vitamin D_2 (Calciferol)

In 1938 Bills[29] pointed out that at least ten different compounds have anti-rachitic qualities, and therefore merit the name vitamin D. Only two, vitamin D_2 (calciferol) and D_3 (7-dehydrocholesterol) are known to be of prime importance to medicine. When ergosterol is irradiated with ultra-violet light, calciferol is one of the products, as shown by Bills' modification of a scheme given by Setz:

Ergosterol
↓ UVL
Lumisterol (not anti-rachitic)
↓ UVL
Tachysterol (not anti-rachitic)
↓ UVL
Calciferol (vitamin D_2--anti-rachitic)
↓ UVL
Toxisterol (doubtful anti-rachitic activity, but with toxic properties)
↙ ↘
Suprasterol I Suprasterol II

In 1939 Reed, Stuck and Steck[35] emphasized that many reports on toxic reactions to vitamin D in the period from 1928-1930 were probably due to the high concentration of toxisterol. To prevent reactions from vitamin D_2 and to obtain the best clinical result in the treatment of cutaneous tuberculosis, most investigators insist that it be in its most refined form, and in an alcoholic solution. Marsh[31] stated that the synthetic calciferol preparations made in England are less toxic than the natural vitamin D_3 found in fish liver oils, whereas the calciferol prepared by irradiating ergosterol was often incompletely purified and contained toxisterol. Charpy[1] found that vitamin D_2 in an oily base did not give consistent results. Mayoux[32] stated that vitamin D_2 in oil was "constantly ineffective" while excellent results were obtained with vitamin D_2 in an alcoholic solution.

Dosage

The Charpy method, used extensively on the continent, consists of the oral administration of 600,000 units of vitamin D_2 in a glycero-alcoholic solution as follows: Three times during the first week, twice weekly for the next three weeks, and once each week during the following four months. Charpy considers a high calcium intake a necessary adjunct to calciferol therapy. His patients received from one to two liters of milk daily, or if this was impracticable, 0.5 gm. of calcium gluconate daily by mouth for twenty days of each month.

Dowling and Prosser Thomas varied their dosage scheme according to the patient. The maximum daily dose was 150,000 units; this was reduced to 100,000 units daily after varying periods and further reduction to 50,000 units was sometimes made. They did not find supplemental calcium to be of additional value.

Our treatment at the University of Minnesota Hospitals combined the French and English methods. At first we used viosterol in oil in a dosage of 150,000 units daily. An adequate intake of calcium was assured by having the patients drink at least one quart of milk daily. More recently we have changed to a solution of vitamin D_2 in propylene glycol (Drisdol)* which was especially prepared for us in a form containing 50,000 units of vitamin D_2 per cubic centimeter. As propylene glycol is water soluble and more readily miscible with the gastric contents, it is felt that more beneficial results might be obtained with this vehicle. Therefore we now use (between 1000-2000 units per kilogram of body weight per day) vitamin D in propylene glycol. The toxic dose is about 20,000 units per kilogram of body weight per day.[35]

Reactions

In spite of improvement in vitamin D preparations, reports on vitamin D intoxication continue to appear in the literature. The symptoms commonly noted are anorexia, nausea, malaise, post-auricular headache and urinary frequency. In 1946 Covey and Whitlock[33] reported 5 cases of intoxication, two of the patients having arteriosclerosis and hypertension, which are usually considered to be contraindications to massive vitamin D therapy. Bauer and Freyberg[34] listed six reports on vitamin D toxicity, on six different types of vitamin D preparations. Steck, Deutsch, Reed and Stuck[30] reported that of 773 humans (adults) treated with over 100,000 units of vitamin D daily 8% had symptoms of intoxication. The duration of treatment varied from 87 days to two years. There were no deaths.

Reed[36] and Bicknell and Prescott[37] emphasized that symptoms of intoxication did not always go with hypercalcemia. Both animal and human experiments have demonstrated toxicity without hypercalcemia and hypercalcemia without toxicity.

Enormous doses of vitamin D have been used in the treatment of chronic arthritis and psoriasis. Wyatt, Hicks and Thompson[38] used 300,000 units daily in arthritis, and Ceder and Zon[39] a similar amount in psoriasis, noting a progressive hypercalcemia. Farley[40] used up to 1,000,000 units daily in arthritis, and stated that toxic symptoms seldom developed if the dose remained under 400,000 units.

We feel that reactions to vitamin D_2 in the treatment of cutaneous tuberculosis fall into two groups. The first is the local flare-up, likened to the Herxheimer reactions of syphilis, seen at the site of the disease. The second group is more purely a vitamin D_2 intoxication. Dowling and Prosser Thomas, in surveying the literature, found that a sense of well being and a good appetite appeared often to be a prelude to later symptoms of intoxication. Mental depression and headache may also be early symptoms. Excessive doses may mobilize phosphorus and calcium, producing metastatic calcification of soft tissues, particularly of the renal tubules and arterioles.

In our patients very few toxic symptoms were noted. A local flare-up was noted once. In two patients anorexia and mild transitory mental depression were seen.

Mode of action.

The exact action of calciferol on cutaneous tuberculosis is unknown. Two attempts to determine the bacteriocidal action of vitamin D have resulted in conflicting results. In 1937 Steenken and Baldwin[41] added 100-400 units to cultures of the tubercle bacillus (H_{37} strain), and, after a period of growth, inoculated guinea pigs with the suspension. Tuberculosis usually resulted. On the other hand, in 1946, Raab[42] showed a complete absence of growth of tubercle bacilli in cultures to which calciferol in propylene glycol had been added. Controls using the propylene glycol alone showed unchecked growth.

In support of the theory of a direct action on the bacillus is the not too infrequent local reaction seen immediately after starting treatment. This

* Kindly furnished by the Winthrop Chemical Company.

is similar to the Herxheimer reaction of syphilis, and apparently occurs up in to 20% of the treated cases. The reaction was so marked in one of our cases of scrofuloderma (Case of Dr. E. T. Ceder) that it was necessary to stop treatment. A case of lupus vulgaris was presented at the Chicago Dermatologic Society in December, 1946, in which tuberculids appeared during treatment, indicative of an allergic response to therapy.

Prosser Thomas[43] reported that local treatment of lupus vulgaris with calciferol had no effect.

The calcifying action of vitamin D_2 may be the responsible factor in the improvement, this has not been verified nor entirely disproved. However, Charpy and Dowling have not been able to correlate hypercalcemia with clinical response. They had a number of patients who improved rapidly with no change in the calcium levels. Vachon and Feroldi[44] reported the post treatment histologic studies on Charpy's patients. He found no evidence of local calcium deposits, and, only rarely, cure in the histologic sense. A general increase in fibrosis was noted which had a "suffocating" effect on the tubercles. Mayoux and Martin[45], studying 70 post-treatment biopsies found that anatomic cure occurred several months after clinical cures. At no time was calcium demonstrated in their post-treatment sections. A change in the tuberculin reaction was noted by Charpy[16] who felt that this was further evidence for a direct action on the bacillus. He noted a change from strongly positive mantoux reaction to negative in 2 of 11 cases tested after treatment with vitamin D_2.

Distribution of vitamin D_2 in the body would seem important if its effect were to be noted in the various organs infected with tuberculosis. In 1939 Vollmer[46] administered 1,000,000 units of vitamin D in $3\frac{1}{2}$ days to a dying infant. After death the various organs were bio-assayed for the presence of vitamin D. He found that the major portion was storied in the brain, liver and skin. No appreciable amounts were found in the lungs, spleen or bones. Windorfer[47], reported a similar experiment in 1938. He found that most of the vitamin D was stored in the brain and kidney.

Case Reports

We have administered vitamin D to 9 patients with cutaneous tuberculosis. They have been under observation for a period varying from two to nine months. The small number of patients and the short period of observation makes this no more than a preliminary report. Three cases of lupus vulgaris, 4 cases of erythema induratum, 1 case of papulo-necrotic tuberculid, and 1 with scrofuloderma, are included in the study. All with the exception of the papulo-necrotic tuberculid and the scrofuloderma were old cases which had resisted previous treatment.

Case #1.

, male, weight 150 pounds, 25 years of age. First treated at Dermatology Out-Patient Department in June, 1939. Lupus vulgaris on the left cheek since 4 years of age. Biopsy confirmed diagnosis. Chest x-ray revealed an old healed fibrotic lesion. The lupus vulgaris was previously treated with cautery, starch injections and ultra violet light. Temporary improvement was noted in August 1939 following a blistering dose of ultra violet light. Vitamin D started May 6, 1946, using 150,000 units of vitamin D with 2 quarts of milk daily. Improvement was noted in June, and marked improvement in September 1946.

Case 2.

. (Case of Dr. Robert Priest and Dr. Carl W. Laymon) 60 years of age. She was seen first on 6-5-42 with obstruction of the left nostril for 2 months, with left epiphora. A rough, granular overgrowth of tissue was noted on the spetum and lateral wall of nose. Biopsy was made 6-8-42 and reported as tuberculosis of the skin (lupus vulgaris) by Dr. E. T. Bell. Chest plage negative. Seen again on 6-10-46 with progression of lesion to upper lip. Vitamin D_2 (calciferol) started 8-7-46, using Charpy method. On 9-11-46 lesion was smaller. On 10-21-46 there was

marked improvement. Dr. Priest reported on 11-15-46 that she "seemed to be completely healed".

Case 3.

(Case of Dr. John F. Madden), male, 48 years of age. Lupus vulgaris of the buttocks for 31 years. Several plastic operations. Cervical abscess at 9 years of age. Biopsy May 7, 1945 was tuberculosis of the skin (E. T. Bell), Mantoux positive. Chest x-ray negative. Previous treatment consisted of ultra violet light, penicillin, and tyrothricin. Vitamin D (calciferol in propylene glycol) began 10-12-46. Improvement noted in two weeks. Almost completely changed to scar tissue in two months. Post-treatment biopsy showed scar tissue and no evidence of tuberculosis.

Case 4.

(Case of Dr. Henry E. Michelson) female, 30 years of age. Papulo-necrotic tuberculid of right cheek for one year. No previous treatment. Mantoux strongly positive. Chest x-ray revealed a calcified scar. Calciferol in propylene glycol started in November, 1946. Improvement noted in 2 weeks on 150,000 units of vitamin D_2 daily. Her blood calcium level was 15 mgs.% in six weeks, and therapy was stopped. No recurrence noted in one month.

Case 5.

(Case of E. T. Ceder). Female, 50 years of age. Scrofuloderma, right neck, for 2 years. During first week of calciferol therapy, the adenitis and drainage increased markedly and it was necessary to stop therapy.

Cases 6, 7, 8, 9. (Cases of Dr. H. E. Michelson)

These four cases were all females with erythema induratum. Response to vitamin D_2 was immediate in all four cases. One case relapsed after the treatment was stopped. Duration of treatment in this case was only 4 weeks.

Summary

The literature concerning the use of vitamin D in cutaneous tuberculosis is reviewed.

A modification of the methods suggested by Charpy, Dowling and Fanielle was used in 9 cases. Our series is neither large enough, nor has sufficient time elapsed for any conclusions to be drawn, other than to state that vitamin D therapy was definitely helpful, with one exception, in all cases.

The use of propylene glycol as a vehicle for calciferol is suggested. (Drisdol).

It is emphasized that in addition to the usual reactions to vitamin D, Herxheimer-like reactions are often noted at the site of the disease, indicating a possible direct effect on the tubercle bacillus.

References

1. (a) Charpy, M.J.:
Technique de traitement du lupus tuberculeux.
Ann. de dermat. et syph. 11-12: 331 (Nov.-Dec.) '43.
Ibid. p. 340.

(b) Charpy, M. J.
I. Nouveaux essais therapeutiques du lupus tuberculeux.
II. Au sujet du traitment du lupus tuberculeux.
III. Les reactions tuberculiniques apres traitement des lupus tuberculeux.
Ann.de dermat.et syph. 3-4: 110 (Mar.-Apr.) '44.

(c) Charpy, M. J.
A propos du traitement du lupus tuberculeux. Une question de priorite.
Ann.de dermat. et syph., 11-12: 317 (Nov.-Dec.) '45.

(d) Charpy, M. J.
Le traitement des lupus tuberculeux et des tuberculoses cutanees per la vitamine D:

Technique personelle.
L'Union Medicale du Canada,
75:553 (May) '46.

(e) Charpy, M. J.
Le traitement des tuberculoses cutanees par la vitamine D_2 a hautes doses.
Ann. de dermat.et syph. 5-6:
310 (May-June) '46. (This article is the most extensive and contains a complete bibliography).

2. (a) Dowling, G. B., and Prosser Thomas, E. W.
Lupus vulgaris treated with calciferol.
Proc.Roy.Soc.Med.,39: 96 (Dec.) '45.

(b) Dowling, G. B. and Prosser Thomas, E. W.
Treatment of lupus vulgaris with calciferol.
Brit.J.Dermat.(Mar.-Apr.) '46.

(c) Dowling, G. B.
New Remedy for Lupus, Lancet,
1: 590 (April 20) '46.

(d) Dowling, G B., and Prosser Thomas, E. W.
Treatment of Lupus Vulgaris with Calciferol.
Lancet 1: 919 (June 22) '46.

3. Fanielle, M. G.
Le traitement des affections d'origine tuberculeuse par l'ergosterol irradie associe a la calcitherapie.
Scalpel 95: 539 (Dec.) '42.

4. Michelson, H. E., and Laymon, C. W.
Classification of Tuberculosis of the Skin.
Arch.Dermat. & Syph. 52: 108 (Aug.)'45.

5. Emery, M.
Sur l'emploi de l'huile de foie de morue a haute dose dans le traitement du lupus.
Bull. gen.de therap.med.et chir.,
35: 373, 1848.

6. Grant, A. H., Suyenaga, B., and Stegeman, D. E.
The Effect of Rachitic Diets on Experimental Tuberculosis in White Rats. I. Calcium and Vitamin D Deficiencies as Factors in Lowering Resistance.
Am.Rev.Tuberc.16: 628, '27.

10. Steiner, M., Greene, M. R., and Kramer, B.
The Effects of Vitamin D Deficiency on Experimental Tuberculosis in Rabbits.
Am.Rev.Tuberc.35: 640, '35.

11. Levaditi, C., and Po, Li Yuan.
Etude experimentale de la calcification des lesions tuberculeuses sous l'influence de l'ergosterol irradie.
Bull.Acad.de med. 103:502, '30.
Same title,
Presse med. 38: 1720 (Dec.17) '30 -- essentially the same article with better illustrations.

12. Spies, T. D.
The Calcification of Tubercles by means of Irradiated Ergosterol.
Am.J.Path.6: 337 (May) '30.

13. Levaditi, C. and Po, Li Yuan.
L'action calcificante de l'ergosterol irradie sur les lesions tuberculeuses provoquees par des bacilles prealablemen tues,
Compt. rend. Soc. de biol., 106:
169, '31.

14. Trevorrow, V. E., de Savitsch, E. C., Black, W. C., and Lewis, R. C.
Effects of Prolonged viosterol administration and of artificial Sunlight Irradiation on Experimental Tuberculosis in Rabbits.
Proc.Soc.Exper.Biol.& Med., 31:802,
'34.

15. Capocaccia, M.
Sull'azdone calcificante dell'ergosterina irradiata nella tuberculosi sperimentale.
Ann.d.Lst Maragliano p. la cura d. tuberc. 4: 275, '34. Quoted by Reed, Stuck and Streck[35].

16. Bamberger and Spranger.
Vigantol bei Tuberkulösen Kindern.
Deutsche.med Wchnschr. 27:1116
(July 6), '28.

17. Crimm., Paul D.
Vitamin Therapy in Pulmonary Tuberculosis.
Am.Rev.Tuberc., 26:112 (Aug.) '32.

18. Levinson.
Tuberculosis Meningitis.
Am.J.Dis.Child.69: 62 (Jan.) '45.
(Society transactions).

19. Gounelle, H. and Bachet, M.
Action favorable de la vitamine D_2 a doses elevees et prolongees sur une tuberculose evolutive non justiciable de la collagsotherapie.
Bull.Soc.med.d.hop.(Paris) 62:247, '46.

20. Alechinsky, A.
La methode de Fanielle dans le traitement des tuberculoses cutanees.
Bruxelles-med. 25:838, '45.

21. Gougerot, H. and Gaullier.
Traitement de Charpy dans les tuberculoses cutanees.
Ann.de dermat. et syph. 7-8: 210 (July-Aug.) '44.

22. Huriez, Cl., and Leborgne, J.
Action de la vitamine D a doses massives dans le traitement des tuberculoses cutanees.
Ann.de dermat.et syph. 7-8: 211, (July-Aug.) 1944.

23. Garrie, M.
Apropos de traitement du lupus tuberculeux par la methode de Charpy,
Ann.de dermat.et syph. 11-12: 313 (Nov.-Dec.) '44.

24. Bureau, Y., and Barriere.
Resultats obtenus par la vitamine D_2 (methode de Charpy) dans le traitement de la tuberculose cutanee et de certaines dermatoses.
Ann.de dermat.et syph.7-8: 196 (July-Aug.) '45.

25. Vachon, Rene.
Le traitement du lupus tuberculeux par la methode de Charpy.
Ann.de dermat.et syph.2:91 (Feb.)'46.

26. Meyer, Jean, Gaulier and Desgrez:
Le vitamine-calcitherapie dans le traitement du lupus au laboratoire de Finsen
Ann.de.dermat.et syph.5:348 (May-June) '46.

27. McCrae, D. E.
Calciferol in Tuberculous Conditions.
Lancet 2:528 (Oct.12)'46.

28. Bell, Anthony
Calciferol for Tuberculous adenitis
Lancet 2:808 (Nov.30) '46.

29. Bills, C. E.
The Chemistry of Vitamin D.
J.A.M.A. 110:2150 (June 25) '38.

30. Steck, I.E., Deutsch, H., Stuck, H.C. and Reed, C. I.
Further Studies on Intoxication with Vitamin D.
Ann.Int.Med.10: 951 (Jan.) '37.

31. Marsh, J. T.
Letter to Lancet, p.109 (Jan.19) '46.

32. Mayoux, R.
Le traitement du lupus endonasal par la methode de Charpy,
Ann.d'oto-laryng. (Paris) 12:409, '45

33. Covey, G. W. and Whitlock, H. H.
Intoxication Resulting from the Administration of Massive Doses of Vitamin D.
Ann. Int.Med.25:508 (Sept.) '46.

34. Bauer, J. M. and Freyberg, R. H.
Vitamin D Intoxication with Metastatic Calcification.
J.A.M.A. 130:1208 (Apr.27) '46.

35. Reed, C. J., Stuck, H. C., and Steck, I.E.
Vitamin D: Chemistry, Physiology, Pharmacology, Pathology, Experimental and Clinical Investigation.
Chicago, University of Chicago Press, '39.

36. Reed, C. I.
The Vitamins, A Symposium, p.535.
Chicago A.M.A. 1939.

37. Bicknell, F. and Prescott, F.
The Vitamins in Medicine.
London, William Heinemann, Ltd.

38. Wyatt, B. L., Hicks, R. A., and Thompson, H. E.
Massive Doses of Vitamin D in the Treatment of Proliferative Arthritis.
Ann.Int.Med.10:534 (Oct.) '36.

39. Ceder, E. T. and Zon, Leo
Treatment of Psoriasis with Massive Doses of Crystalline Vitamin D and Irradiated Ergosterol: A Preliminary Report.
Pub.Health Rep. 52:1590 (Nov.5) '37.

40. Farley, R. T.
Management of Arthritis.
Ill.M.J. 71:64 (Jan.) '37.

41. Steenken, W., Jr., and Baldwin, E. R.
The Effect of Irradiated Milk Compared with Vitamin D oils on inhalation Tuberculosis of Guinea Pigs.
Proc.Soc.Exper.Biol. & Med., 37: 348, '37.

42. Raab, Walter.
Vitamin D--Its Bacteriocidal Action.
Dis. of Chest, (Sept.-Oct.) p. 409, '46.

43. Prosser Thomas, E. W.
In discussion on Marre, I. R.
Effect of Calciferol on Lupus Vulgaris.
Proc.Roy.Soc.Med.Vol.XL, p.10-12, (Nov.) '46.

44. Vachon, R. and Feroldi, J.
Le traitement du lupus tuberculeux pear la methode de Charpy.
Les resultats anatomiques, Ann.de dermat. et syph. 9-10: 241 (Sept.-Oct.) '45.

45. Mayoux and Martin, Cited by Charpy, M. J.
Le traitement des tuberculoses cutanees par la vitamine D_2 a hautes doses.
Ann.de dermat.et syph. 5-6: 319 (May-June) '46.

46. Vollmer, H.
Distribution of Vitamin D in the body after administration of Massive Doses.
Am.J.Dis.Child. 57:343, '39.

47. Windorfer, A.
Über die Vitamin D Resorption bei Verabreichrung Hober Doser,
Klin.Wchnschr. 17:228, '38.

III. GOSSIP

This weekend I will be in Chicago to attend the midwinter meetings of the Council on Medical Education and Hospitals and allied groups. This has become one of the largest meetings of the year to be devoted exclusively to problems of medical economics and medical service. Tomorrow, I will address the radiologists on the subject of selecting graduate students in Radiology. Inasmuch as I have never selected one, it seems most inappropriate for me to tell them how it should be done, but I have watched the master mind L. G. Rigler do it, so I will tell about what I have learned from him. Radiologists seem to spring from those whose interests were in Internal Medicine and those who were interested in physics or electrical engineering. In the past it has been a field which has been recommended to those who have a physical disability even though the work is heavy and confining. Some graduate students in radiology came over from pathology. In the average case, the student was impressed by some radiologist he knew and when the opportunity was given him to secure training he accepted it. Some of the best graduate students in any field are those who have been invited to take training. Poorest candidates are those who are not able to put their financial houses in order before they start; and shoppers, i.e., those who will take any kind of a fellowship, just to be taking one. The need for radiologists is great. There is a great shortage. It has been estimated that we can absorb one for every 25,000 people. Even though every doctor dabbles in radiology, an expert in the field is an asset in any group. Older radiologists who have built enormous practices will be replaced by many well-trained young radiologists with smaller practices who work together through their associations and societies. Dr. Rigler imbues his men with a teaching and investigative spirit as well as a service viewpoint. The average doctor, before he studied medicine, imagined himself either as a physician sitting at the bedside of his patient, or a surgeon standing beside his operating table. We can broaden his view to include studying a patient or treating disease by means of the x-ray, and more graduate students will go into radiology... On Sunday I will speak to the Federation of American Boards on Basic Science Training. Minnesota, Northwestern, Washington and Pennsylvania will tell of their Basic Science courses while others will discuss the need for such courses and still others will estimate how much credit should be given to them. Our course apparently is turning out a group of men who are acquiring studious habits. They now realize that medicine is broader than the specialty which they had in mind when they started advanced training. They are being transferred into better doctors which automatically will make them better specialists as they will be able to appreciate the service which men render in other fields. So-called Basic Science courses include the study of those phases of anatomy, physiology, biochemistry, bacteriology, and pharmacology and pathology which apply to the specialty, or they consist of time spent in one fundamental department, i.e., anatomy, pathology, etc., without any special relation to the specialty or they consist of satisfying the curiosity of a clinician through reading (this seems rather weak to me); or in the case of our group, a systematic review of anatomy, pathology, physiology, etc. of each system of the body, and the clinical application. If this is followed by special studies in a particular field of interest and constant association during the period of training with other departments including the fundamental group, a good specialist will be the result. Unfortunately many of our specialists are technicians, not doctors.... I was out at a greenhouse (as we called them in the country) one day last week, and I noticed a great deal of rat poison on the shelves. I learned that rats like flowers and that this particular concern had lost nearly 2000 carnations because the rats liked the buds. When ordinary methods failed, the concern sprinkled poisoned carnation buds about,' which the rats promptly ate and died. Since then they have learned that cats are a better method....I never take a trip that I do not experience the reaction of John Sherman, music critic of the Minneapolis Star who speaks of the funny feeling of suddenly becoming Mr. Anonymous. If going some distance it is rare to run across somehone you know..