destruction is much slower, and a difference between the 2 vitamins is apparent. The half-life period of vitamin D_2 during this phase is 2.7 days, while the half-life period for vitamin D_3 is 3.9 days. The destruction of vitamin D_2 is, therefore, proceeding at a rate exceeding that of vitamin D_3 by approximately 50%.

Summary. The metabolism of large (hypercalcemic) dosages of vitamins D_2 and D_3 has been studied in the chick. The chick evidently does not absorb vitamin D_2 as well as it does vitamin D_3, at least in the doses given; a larger proportion of it is found in the feces, and less is found in the carcasses. The amounts of vitamin D_3 found in carcasses and feces account for all of the dosage given, but about 35% of the vitamin D_2 cannot be accounted for. Analysis of the data indicated that there are two phases of inactivation of the vitamins. In the first both are inactivated at about the same rate, but in the second phase the rate of destruction of vitamin D_2 is about 50% greater. The generally more rapid inactivation of vitamin D_2 in the tissues may have a bearing on the fact that it is less effective in the chick than is vitamin D_3.

14933

Supplemental Use of Ergotamine in Eliciting Transient Disturbances of Rhythm in Acute Rheumatic Fever.

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The diagnosis of acute rheumatic fever has frequently been found, among soldiers, to be less dependent on the elicitation of significant cardiac murmurs than on the registration of transient aberrations in sequential electrocardiographic curves.[1] For the most part, these aberrations have consisted of various types of disturbances in rhythm due to a temporary hypervagotonic state excited by the acute rheumatic process.[1,2] However, in a significant number of instances, such electrocardiographic alterations, presumably because of their very brief duration[1] may never be apparent even in repeated tracings. Therefore, in an attempt to improve the usefulness of the electrocardiograph in such circumstances, the author undertook a clinical study in which this diagnostic aid was employed, following the administration of a sympatholytic preparation such as ergotamine tartrate (Gynergen). The results obtained by this method would seem to justify this brief preliminary report concerning the utility of such a simple supplementary procedure.

Material and Method. The observations were made in a random group of 8 soldiers suffering from acute migratory polyarthritis. In most instances no clinical evidence of cardiac disease was discernible. A routine electrocardiogram, in all cases, was obtained with the patient in the recumbent position shortly after his admission to the hospital. If the tracing revealed no significant changes, a control curve was obtained immediately preceding the intravenous administration of 0.5 mg of ergotamine tartrate, followed by comparable sequential records at 30 and 60 min intervals after the exhibition of the drug. Each of the 8 patients was under close medical surveillance during the convalescent stage of his illness and in 5 of them, a similar type of study was repeated after the usual manifestations of activity of the infection had disappeared.

Results. In each of the 8 patients, the initial electrocardiogram, before the administration of the ergotamine tartrate, was within normal limits. In 6 of the cases, comparative tracings obtained after the exhibition of this drug revealed significant disturbances in rhythm of a type usually associated with acute rheumatic fever, and consisted of first degree A-V heart block in 4 instances, second degree

1 Wendkos, M. H., and Noll, J., *Med. Clin. N. A.*, 1944, **2**, 124.

2 Wendkos, M. H., unpublished data.

TABLE I.

Case No.	Age	Date	Electrocardiographic response to ergotamine	Remarks
1	24	2-14-44	Second degree A-V heart block with dropped beats	Rapid sedimentation time. Joint pains present.
1	24	3-25	Some slowing of sinus rate	Normal sedimentation time. Joint pains absent.
2	21	1-24	Nodal rhythm with first degree A-V heart block	Rapid sedimentation time. Acute polyarthritis.
2	21	3-1	Some slowing of sinus rate	Normal sedimentation time. Joint pains absent.
3	19	12-10-43	First degree A-V heart block (PR—0.28)	Rapid sedimentation time. Acute polyarthritis.
3	19	3-10	Some slowing of sinus rate	Normal sedimentation time. Joint symptoms absent.
4	21	3-12-44	First degree A-V heart block (PR—0.40)	Rapid sedimentation time. Joint pains both shoulders.
4	21	3-23	Some slowing of sinus rate	Sedimentation time reduced. Joint pains absent.
5	19	3-12	First degree A-V heart block (PR—0.32)	Sedimentation time rapid. Acute polyarthritis.
5	19	3-18	Some slowing of sinus rate	Sedimentation time reduced. Arthritis completely disappeared.
6	34	1-3	First degree A-V heart block (PR—0.30)	Sedimentation time rapid. Acute polyarthritis, some persistent deformity, swelling in small joints of hand.

A-V heart block with dropped beats in one instance, and nodal rhythm with first degree A-V heart block in another (Table I). These ergotamine-induced changes were of brief duration and generally disappeared within 60 min after the drug was administered. The maximum effect usually was noted within 30 min after its use. No untoward reactions except for occasional and transient nausea and headache were observed. In the 5 individuals in whom this testing method was employed for comparative purposes after the active phase of the disease had disappeared, the effect was similar to that which occurs in the normal subject (Fig. 1) and consisted of a slight slowing of the sinus rate (Table I). This response was in marked contrast to the significant disturbances of rhythm which had been provoked by the ergotamine during the early stage of the acute rheumatic process. This phenomenon is well illustrated in a typical instance by Fig. 2 and 3.

Illustrative Case. A 24-year-old white male was admitted to the hospital because of aching in various joints of his body. He first became ill one month previously, the onset of the illness being acute and characterized by chills, fever and sore throat. Four days later he developed redness and swelling in both hands and in both feet. These arthritic symptoms, as well as the chills and fever, subsided 3 days later. However, after an interval of well-being for several days, he developed stiffness and pain in the lower back, both knees, both elbows, both wrists, and the fingers of both hands. The stiffness and pain in these joints became progressively more severe so he was eventually admitted to the medical ward with a tentative diagnosis of rheumatoid arthritis. The patient gave no history of antecedent rheumatic infection, and aside from seasonal attacks of hay fever, he had always been in good health. The physical examination, including careful attention to the heart, revealed no significant pathology. Passive movement in all the joints was unrestricted, and no arthritic swelling or redness was noted. The day following his hospital admission, the erythrocyte sedimentation rate was estimated to be 78 mm in one hour (normal—15 mm), and his electrocardiogram was not significantly altered (Fig. 2A).

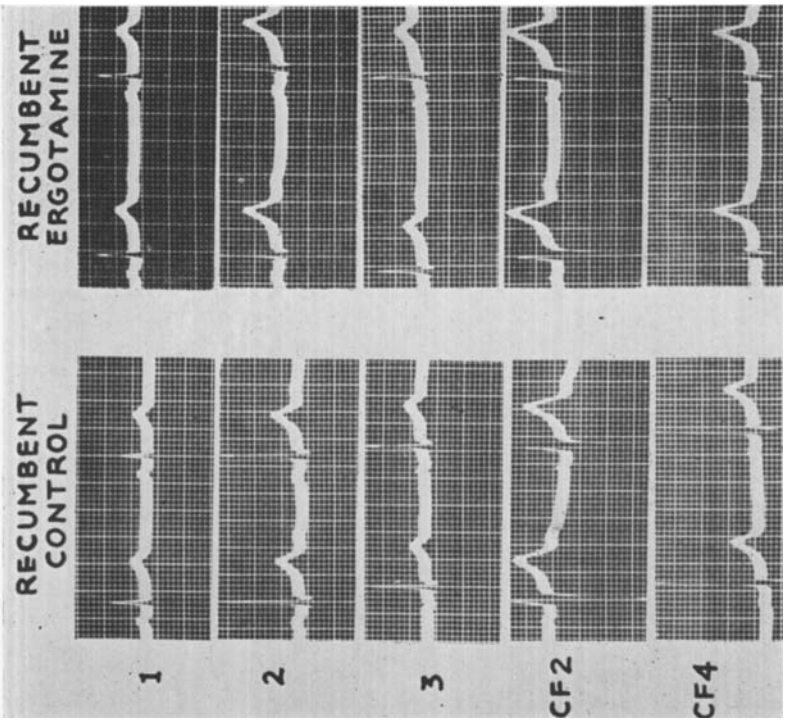


FIG. 1.
The electrocardiographic registration of the parasympathetic mimetic effect of ergotamine tartrate in a normal subject: The response is characterized by a slowing of the sinus rate and by a slight increase in amplitude of the T waves in each lead.

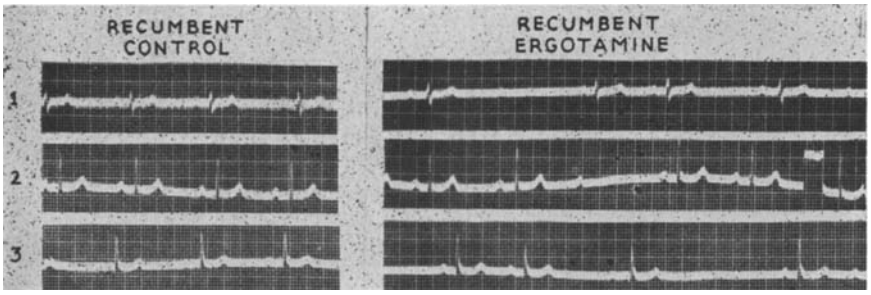
However, at that time, following the administration of ergotamine tartrate, a second degree A-V heart block with dropped beats was induced (Fig. 2B). His subsequent clinical course was uneventful and within 6 weeks his sedimentation time had dropped to normal and his joint symptoms had improved. During his entire period of hospitalization, no abnormalities of the heart were revealed in the repeated clinical examinations, and several electrocardiograms obtained at weekly intervals demonstrated no aberrations. During the convalescent stage of his illness, after all collateral evidences of persistent activity of the infection had disappeared, the procedure employing ergotamine tartrate was repeated, and no effect except for some slowing of the sinus rate was apparent (Fig. 3).

Discussion. Autonomic imbalance with vagal preponderance undoubtedly is an important component of the disturbed physiology associated with the acute rheumatic state, because it has been conclusively demonstrated that a parasympatholytic drug such as atropine can temporarily abolish the first degree A-V heart block[1,3,4] and other types of rhythm disturbances[2] which are the chief electrocardiographic expressions of the disease. However, since characteristic features of these disturbances in rhythm are their inconstancy and transient nature, it is likely that a spontaneous variation occurs in the intensity of discharge of the exaggerated cholinergic stimuli in the early stages of rheumatic fever, it being implied that the subordination of a hypervagotonic state below a certain critical level will prevent the registration of the usual electrocardiographic representations of such vegetative dysfunction. Under circumstances in which this "latent" phase of vagal preponderance conceivably is present in individuals suffering from acute rheumatism, the suppression of activity of the normal antagonist of the vagus by the use of a sympatholytic preparation such as ergotamine tartrate[5] would be expected to provoke, in their electrocardiograms, vagal effects, akin to, but not necessarily identical with, the precordial lead T wave alterations

3 Bruenn, H. G., *Am. Heart J.*, 1937, **13**, 413.

4 Keith, J. D., *Quart. J. Med.*, 1938, **7**, 29.

5 Goodman, L., and Gilman, A., *The Pharmacological Basis of Therapeutics*, New York, Macmillan Company, 1941.



A FIG. 2. B

The electrocardiographic registration of the parasympatheticomimetic effect of ergotamine tartrate in an individual during the early active phase of acute rheumatic fever: The effect primarily is upon the A-V node, resulting in the development of a second-degree heart block.

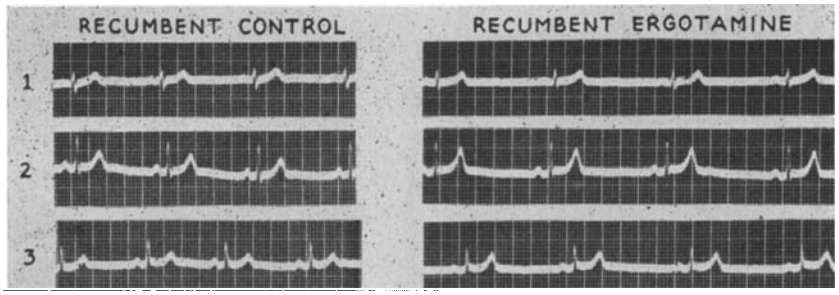


FIG. 3.

The electrocardiographic registration of the parasympatheticomimetic effect of ergotamine tartrate in the same individual as in Fig. 2, during the subacute phase of rheumatic fever: The effect is similar to that which occurs in a normal subject. (See Fig. 1.)

produced by this drug in emotionally unstable individuals, when a "latent" stage of "cholinergia" exists.[2,6] Actually when the initial record was normal significant disturbances in rhythm were usually elicited by this method in the relatively few cases of acute rheumatic infection in which it was employed. (Table I)

Even though the series is small, the results seem to be significant inasmuch as studies, which are based on experiments in large numbers of individuals in whom no imbalance of the autonomic nervous system would be expected to occur, have demonstrated[2,7,8] that the only physiological effects of ergotamine tartrate upon the human electrocardiogram consist of a slowing of the sinus rate and a slight increase in the amplitude of the T waves (Fig. 1). Since this effect is not unlike that which occurs in an individual who is in the subacute stage of a rheumatic infection (Fig. 3) in contrast to the response to the same agent in the same subject when collateral evidences of active infection existed (Fig. 2), it is probably reasonable to suppose that this testing method, besides assisting in the diagnosis of acute rheumatic fever, may also be found useful in helping to decide when recovery is beginning to occur.

Conclusions. 1. It is suggested, from a limited experience with the method, that the supplemental administration of ergotamine tartrate may be useful in increasing the precision of the electrocardiograph as a diagnostic aid in acute rheumatic fever. 2. It is considered that the rationale of this procedure depends on the elevation of a subordinated or "latent" hypervagotonia by a suppression of activity of the normal antagonist of the vagus, so that "cholinergigenic" disturbances in rhythm are thus made manifest in the electrocardiogram. 3. The procedure is simple, can be standardized easily and is without any harmful effects.

[6] Wendkos, M. H., *Am. Heart J.*, 1944, **28**, 549.

[7] Nordenfeldt, O., *Acta. med. Scandinav.*, 1941, Supp., CXIX.

[8] Hartwell, A. S., Burrett, J. B., Graybiel, A., and White, P. D., *J. Clin. Invest.*, 1942, **31**, 409.