Metyrapone Ditartrate (Metopirone) Test During
Ganglio-Pulmonary Sarcoidosis of Besnier-Boeck-Schaumann
Diagnostic and Etiopathogenic Value

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The metyrapone ditartrate (Metopirone) test was reported by Liddle and associates in the United States in 1958. It is generally used to determine the corticotropin activity of the anterior lobe of the hypophysis.

Under normal conditions, the administration of metyrapone ditartrate (Metopirone) according to a predetermined dosage provokes inhibition of the adrenal secretion of hydrocortisone which is followed, in conformance with the "feed-back" compensation mechanism, by pituitary hypersecretion of ACTH. Under this influence, the direct precursor of hydrocortisone, “S” compound is secreted in large quantity in the adrenal vein and is found in the urine in its metabolite form, tetrahydro-compound “S” (H,S). This then becomes the main constituent of urinary 17-hydroxy-corticosteroids (17-OH), the rate which increases proportionally.

The test was carried out over a three-day period. The first day, the patient received nothing and the urine was collected for verification of the urinary steroids and to determine preliminary dosage. On the second day, the subject takes, by mouth, three capsules of 250 mg of metyrapone ditartrate (Metopirone) every four hours for a total of 4.50 g. Urine of the second and third 24-hour periods verifies the secretion of 17-hydroxy-corticosteroids (Porter and Silber's method) and tetrahydro-compound “S” (Revol's method) under Metopirone effect.*

Herein we wish to show that during ganglio-pulmonary attacks of sarcoidosis, the metyrapone ditartrate (Metopirone) test reveals hyperactivity of the anterior lobe of the hypophysis which is clearly pathologic and which fluctuates in accordance with the course of the disease. In the majority of the cases in this study, evidence of good adrenal function was established by means of the ACTH test, carried out three days prior to administration of the metyrapone ditartrate (Metopirone) tablets.

**Test Results in Diseases Other Than Sarcoidosis**

We present our findings when the test was carried out on both normal subjects and on those with endocrine diseases. One of us (A. Revol) has had four years' experience in carrying out the test in collaboration with the Service de la Clinique de la Faculte de Lyon (Professor Guinet).

1. In 108 normal subjects, aged 20 to 60 years the following was observed:

—an increase in the total elimination of the 17-OH of 300 to 400 per cent of the

*After enzymatic hydrolysis of an aliquot part of the urines by Helix pomatia juice, the tetrahydroxy compound “S” is selectively and quantitatively drawn out by a mixture of eight parts of carbon tetrachloride and two parts of chloroform. The organic phase, after washing, is then used up by the Porter and Silber's reagent. Yellow coloration obtained by heating for 30 minutes at 60° produced spectrophotometer readings of 370 to 410 and 450 mg.
basic rate, but always lower than 30 mg. per 24 hours.

— a notable increase of the \( H_4S \),

partial fraction of the 17-OH, which is practically zero before metyrapone ditartrate (Metopirone), and which reaches 10 to 25 mg. per 24 hours, with an average of 15 to 20 mg.

2. In subjects with pituitary endocrine diseases the observations varied according to the hypo- or hyperactivity of the anterior hypophysal lobe.

— in antepituitary insufficiency (tumors, surgical removal, acromegaly, etc.) the increase in 17-OH is very slight under metyrapone ditartrate (Metopirone) and the elimination of the partial fraction of the 17-OH, \( H_4S \) is always lower than 5 mg. per 24 hours and frequently from 0 to 2 mg. Forty cases of this type were collected between 1961 and 1964.

— in anteriorpituitary hyperactivity syndrome (Cushing of central origin), the excretion of 17-OH and \( H_4S \) is strongly increased by metyrapone ditartrate (Metopirone). It is admitted that pathologic rates correspond to an increase in the 17-OH of about 600 per cent or 30 mg. at least and in the \( H_4S \) to 25 mg. or higher. According to Franchet' and others, 30 mg. always correspond to a pathologic rate. Increases ranging from 25 to 30 mg. are considered in an intermediate zone, somewhat less pathologic, but nevertheless abnormal, if proportionately the percentage increase of 17-OH is as high as 400 per cent in respect to the basic rate.

In this group of 155 patients tested, only five were found with antepituitary hyperactivity syndrome as compared with 40 cases of antepituitary insufficiency (eight times as many).

3. The previously reported investigations have shown us and others that Liddle's test is valid proof of pituitary hyperactivity only in the endocrine diseases corresponding to an abnormal corticotropic activity of the hypophysis. To prove the importance and the pathognomonic character of an abnormally positive test during ganglionary sar
coidosis, it is necessary also to verify that various pulmonary or mediastinal diseases did not produce abnormal changes during the metyrapone ditartrate (Metopirone) trial in non-sarcoid diseases. In the Pneumomphthiologie Department of Lyon (Prof. J. Brun), tests were carried out on 45 subjects with non-sarcoid diseases.

- Gangliopulmonary tuberculosis 25
- Pneumocooniociotic diseases 11
- Other diseases 9

In this group only one positive test was found, that in a subject with pulmonary cancer with hypercorticism.

The Test in Sarcoid Diseases

In sarcoid disease, the hypothalamic-neurohypophysary injury has been noted by us and other authors for a long time. This is evidenced by the necropsy findings of nodes in the floor of the third ventricle and the relative incidence of diabetes insipidus after sarcoidosis. For example, in 1961, Shealy and co-workers reported four cases of diabetes insipidus of sarcoid origin, in two of which there was an associated antehypophysary insufficiency underlined by a hypogonadotropic and adrenocortical hypofunction. Our own investigations, with the systematic use of the metyrapone ditartrate (Metopirone) test, have revealed, not an anteriorhypophysal insufficiency at the beginning of the disease, but a very exaggerated corticotropic hypophysal hyperactivity.

Before presenting our results, we would like to say that during sarcoidosis, the adrenals did not seem to present an autonomous syndrome of hypo- or hyperfunction. This fact was verified by systematic administration of doses of 17 hydroxycorticosteroids (reported in tables herein) and by dynamic trials with ACTH (Thorn test) which were always normal. In the interpretation of the metyrapone ditartrate (Metopirone) test we might retain only a primitive neuro-hypophysal participation.

Our 28 cases of sarcoidosis were verified by clinical evidence, ganglion or scalene node biopsy, increased quantities of gammaglobulins, the favorable response to cor-
ticotherapy, the absence of tuberculosis confirmed by negative guinea pig inoculation and negative reaction to tuberculin in nearly every case. Unfortunately the Kveim test was not systematically carried out because no antigen was available.

We present a threefold group:

(1) Recent and Non-treated Sarcoidosis.

In this group, we present 14 cases, all of pulmonary sarcoidosis, which were found either on routine x-ray examination or during investigation of some functional disturbance. In 11 cases (78.5 per cent), the metyrapone ditartrate (Metopirone) test response was perturbed following a pituitary hyperactivity. Arranged according to their radioclinical types, these cases can be divided into two groups:

(a) Isolated mediastinal ganglionic forms: (Table 1A). Of these five cases, four gave abnormally high metyrapone ditartrate (Metopirone) tests with increased elimination of the 17-hydroxyl corticosteroids (17-OH) and of the tetra-hydro-11-desoxy cortisol (H_4S). The normal response obtained in Case 5 was that of a young girl on whom the test was carried out during her menstrual period. Since cortisone therapy was initiated immediately, it was impossible to repeat the test under normal conditions.

(b) Gangliopulmonary forms: (Table 1B). These nine cases showed both mediastinal ganglionic enlargement and miliary parenchymatous infiltration. They were of recent discovery and were untreated. The metyrapone ditartrate (Metopirone) test was positive in seven cases (77.7 per cent). It must be noted that, in this group, the highest results were found for the 17-OH and H_4S elimination. In Case 6 (Table 1B) we found an unusual response which Franchet considers as symptomatic of neuro-pituitary hyperactivity, a "courbe en
dôme” with great elimination of 17-OH and H₄S during the test period and a return to normal on the third day at the end of the test. In the two cases of sarcoidosis with normal metyrapone ditartrate (Metopirone) tests, there is one response which is worthy of discussion. Indeed, if the test in Case 9 was at first normal with the elimination of 16 mg., it is shown that it progressively increased to 25 mg. with a final rate of 23.3 mg. (H₄S) when the test was repeated twice at approximately 15-day intervals. We might conclude that a certain amount of time is necessary for the evolution of a pathologic rate.

(2) Test Modifications After Cortisone Treatment of Recent Forms.

The ante-hypophyseal function study during the development of sarcoidosis has been performed by us in eight cases selected from 14 cases studied. Table 2 summarizes the results obtained at the time of these studies. This control was carried out at various times after the treatment was started and there was always an interval during which no treatment was given before the second test was carried out. Table 2 shows these various elements in detail.

In Case 7, the initial response had seemed normal and there was no modification of this response in spite of a partial x-ray clearing under cortisone treatment. In Case 5, the H₄S elimination rate remained high even though the x-ray lesions completely regressed. In Cases 1 and 8, the H₄S rate of fall was modified, whereas x-ray signs improved markedly (Case 1) or disappeared completely (Case 8).

In the other four cases, there was a closer parallel between x-ray improvement under cortisone treatment and the H₄S rate of fall after metyrapone ditartrate (Metopirone) retiral. In one patient, cortisone therapy led to a rapid and complete clearing of ganglionary lesions and in two and one-half months, the test changed from 30.8 mg. to 17.2 mg. or normal. This return to normal is not immediate when the test has been positive in the beginning.

There may be a gap between x-ray regression and normalization.

(3) Old Sarcoidosis, Stabilized and Unstabilized, Treated with Cortisone.

(a) We carried out tests on 13 patients having endothoracic sarcoidosis who were successfully treated with cortisone. All the tests carried out on this second group seemed normal according to previously established criteria. However, it is of interest that no abnormally low results were observed, causing us to suspect that there is a residual antihypophyseal insufficiency biologically demonstrable, but clinically latent, i.e., except for one case which is analyzed in detail in the etiopathogenic section.

(b) There were two cases of relapse. The first was sarcoidosis which started in 1949 as uveo-parotitis. The date of pulmonary involvement could not accurately be fixed, but it was first observed in July, 1961 when it appeared to be an already evolved form with hilar adenopathies and fibrous infiltration of both pulmonary fields. The first metyrapone ditartrate (Metopirone) test was carried out two years later in June, 1963, when the lesions were stabilized. The response was normal at 23 mg. In October, 1963, x-ray evidence of an important relapse coincided with a noticeable increase of the H₄S elimination rate under metyrapone ditartrate (Metopirone) from 23.67 mg. to 39.31 mg. Cortisone treatment was started, but the x-ray improvement was always incomplete and the biologic tests were persistently positive with the H₄S elimination remaining at 34.37 mg. after the drug.

The second relapse occurred in a patient with the gangliopulmonary form of sarcoidosis. At the beginning, the test was positive at 33.3 mg. It became normal at 17.7 mg. as the lesions regressed appreciably under cortisone treatment. However, when a slight relapse occurred because of irregularity of treatment, the rate increased to 38.34 mg.

In both cases, the x-ray findings paralleled the biologic signs. The fact that a test has become normal does not necessarily prove that the disease is cured.
(4) Uncertain or Atypical Cases:

These two atypical cases must be discussed from the diagnostic point of view.

(a) The first case was that of a patient who had worked a long time in foundries and who was found to have diffuse pulmonary fibrosis with pneumoconiotic nodes at biopsy. The first metyrapone ditartrate (Metopirone) test carried out on this patient was normal, but a second test performed one year later gave a positive response, without the presence of sarcodeosis ever having been proved. He later died of a pulmonary neoplasm.

(b) The second subject exhibited pulmonary fibrosis without any histopathologic signs of sarcodeosis. This patient had been exposed to talc dusts and while the metyrapone ditartrate (Metopirone) test was positive, the scalene node biopsy was negative. Cortisone and ACTH therapy led to substantial x-ray clearing.

These are the only cases with positive metyrapone ditartrate (Metopirone) tests for which a diagnosis of sarcodeosis could not be made. Whatever may be, they show that the test cannot be considered pathognomonic.

Discussion and Conclusions

(1) The metyrapone ditartrate (Metopirone) test becomes positive in about 80 per cent of the cases with recent sarcodeosis, while it changes to negative when the disease has been treated and stabilized. However, we have in our series three atypical cases in which pituitary hyperactivity was not shown by this test, but in which there was obviously sarcodeosis. Researchers always try to find the cause of false results thinking that perhaps some error has been made in carrying out the experiment. However, they should recognize that occasionally one encounters falsely normal results. When the total results are reviewed (Table 3), it is significant that positive metyrapone ditartrate (Metopirone) test is noted most frequently in endo-thoracic sarcodeosis. Out of 14 cases of recent gangliopulmonary sarcodeosis, 78.5 per cent of the cases were positive following a pituitary hyperactivity while only 2.2 per cent of 45 cases of diverse respiratory diseases were positive. In another department, out of a series of 45 cases of neuro-pituitary endocrine disease, only 11 per cent were positive.

We must conclude that this test has value and must be added to the already known tests in the diagnosis of sarcodeosis. Abnormally high tests are scarcely ever found during gangliopulmonary non-sarcoioid disease. Our experiments have shown that this test is not high in tuberculosis and recent studies have shown that it should usually be low. However, in spite of its value in the diagnosis of sarcodeosis, the test cannot be considered a pathognomonic one, and on the other hand, if it is normal, neither can sarcodeosis be completely ruled out (Table 4).

(2) A second fact to emphasize is that it is necessary to stop cortisone therapy at least ten days before starting the test since there is a tendency for the metyrapone di-

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<th>Table 2—Results of the Metyrapone Ditartrate (Metopirone) Test After Cortisone Treatment—(Recent Forms)</th>
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*Only the maximal values of H,S urinary elimination are given.
tartrate (Metopirone) test to normalize during the administration of this drug.

(a) In recently discovered and treated patients, there is a parallel evolution between the tendency of the test to normalize and the decrease in x-ray and clinical signs of the disease.

(b) In old and stabilized forms of the disease, the pituitary response has usually seemed normal, except for occasional serious x-ray relapses.

(3) We cannot draw too definite conclusions because of the limited experience, but it would seem that a high initial H$_S$S rate, as shown by this test, does not necessarily compromise the prognosis since we have seen important and rapid x-ray regressions in spite of the high rates (Cases 2 and 8).

(4) All these facts allow us to suggest new etiopathogenic hypotheses.

The hypersensitivity to metyrapone ditartrate (Metopirone) classically indicates a neuro-pituitary hyperactivity manifested by the release of an abnormal secretion of ACTH, which is revealed only by the test.

To date, basic rates of the 17-hydroxycortico-steroids have never been found increased in sarcoidosis patients, which excludes the hypothesis of permanent ACTH secretion.

Under these conditions, does the positivity of the test reveal a special defense reaction to an attack of a still undetermined origin, or does it evidence a direct, initial involvement of the hypothalmo-pituitary region, which may or may not evolve further to an enervation of the gland.

Favoring the second hypothesis, we have the case of a 43-year-old patient (Table 3, Case 1A) who had a positive initial test with an elimination of 35.6 mg. of H$_S$S, associated with bilateral mediastinal ganglionic involvement and bulbo-protuberancial nervous disturbances. Cortisone therapy led to a recession of the mediastinal ganglionic masses, but trice repeated tests have shown a final evolution toward an antepituitary insufficiency evidenced by a very low 17-OH (1.47 mg.) and a complete absence of the metyrapone ditartrate (Metopirone) response.

| Table 3—Complete Statistics |
|-----------------------------|-----------------|-----------------|
|                             | <N             | N               | >N               |
| 45 cases of hypothalmo-pituitary dysfunction (endocrinological Clinic of Lyon) | 88.9 per cent | 40 cases 5 cases |
| 45 cases of various non-sarcoid pulmonary diseases | 97.8 per cent | 2.2 per cent 1 case |
| 14 cases of evolutive recent sarcoidosis | 21.5 per cent | 78.5 per cent 11 cases |
| 13 cases of non-evolutive established sarcoidosis | 100 per cent |  |  

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Figures and tables are not included in the natural text representation.
However, it can also be supposed that the hyper-secretion of ACTH, revealed by this test, is in reality only the indication of more important secretory modifications yet unknown, but which could be at the origin of specific tissue reactions observed during the course of the disease and which could be released by some non-specific agent as is shown by Türiaf and Brun. In this connection it seems important to note that, in sarcoidosis with a highly positive test, the adrenal response to exogenous ACTH (Thorn test) can be lower than that provoked in the endogenous manner by metyrapone ditartrate (Metopirone). This fact does not coincide with past findings in normal subjects or in those with neuro-pituitary hyperactivity. We present as an example, the three following cases which are the most noteworthy:

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<th>Urinary 17-Hydroxy-corticosteroids</th>
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Whatever it may be, if one admits the great frequency of an intervention of the neuro-pituitary agent, it must be supposed that the effectiveness of cortisone therapy could be the result of an inhibitory action on the hypophysis. As to the eventual beneficial effects of ACTH, given in therapeutic doses, they could be accounted for as a secondary slowing effect associated with its corticotropic action. Consequently, this effectiveness appears logical, although, at first glance, it could seem incompatible if we consider the action of the hypophysis on the process of the disease.

All these considerations do nothing but postpone the solution of the etio-pathogenic problem, for there is always a mystery about the exact nature of the provocation of endocrine or other disturbances. It remains that the recognition of a pituitary hyperactivity during sarcoidosis, such as we have just cited, represents a new fact which could lead to further worthwhile research and eventually to the precise definition of the nature of the process involved.

**Summary**

The systematic study of the metyrapone ditartrate (Metopirone) test response, in an endocrinology department, permits us to establish the constant negativeness of results, except in some cases with endocrinopathies. In 120 tests, there were four positive responses indicating pituitary hyperfunction and 25 responses which revealed pituitary hypofunction.

In the Pneumo-Phthisiology Clinic of the Faculty of Lyon, where this test was carried out over a period of two years on a series of 50 non-sarcoidosis patients, all the tests were negative, as concerned a pitui-
tary hyperfunction with the exception of one case of pulmonary neoplasm.

On the contrary, in the series of cases with gangliopulmonary disease of sarcoid origin, there was a high frequency of neuro-pituitary hyperactivity symptoms related to the development of the disease in its endothoracic ganglionic, miliary or infiltrative forms.

Our findings can be summarized in the following manner:

(1) Recent untreated forms—14 cases.

The test was positive in 11 cases (78.5 per cent) at rates which were occasionally very high. The highest rate was a urinary elimination of 68.4 mg. per 24 hours of 7-OH and 64.57 mg. per 24 hours of H₂S. One of the negative cases must be ignored because the test was carried out during the subject’s menstrual period.

All the cases treated with cortisone were followed and it was observed that the test tended to normalize as the lesions diminished. The test was carried out ten days after the termination of corticotherapy.

In eight cases (75 per cent) the test returned to normal at the same time that the lesions completely regressed. In two cases in which the lesions did not completely clear, the test showed a tendency to normalize, but the stabilization was only partial.

(2) Old stabilized forms—13 cases.

In 12 completely stabilized or cured cases, the test was found normal. In the 13th case, in which the disease was of ten years’ duration, there was a pulmonary infiltrative relapse and the test was positive at 34.47 mg. of H₂S.

These findings convincingly verified can open new horizons on the disease and the effects of treatment. It is possible that cortisone acts only as an inhibitor of abnormal or excessive secretions of pituitary origin. As for the syndrome of pituitary hypofunction usually encountered in diabetes insipidus and which is contrary to the facts just reported, it is possible that it occurs secondarily, after a period of initial hyperactivity which has not yet been recognized.

Resumen

El estudio sistemático de la respuesta de la prueba con la Metopirone en un servicio de endocrinología nos ha permitido comprobar la constante negatividad de los resultados fuera de ciertas endocrinopatías caracterizadas: entre 120 resultados se han encontrado cuatro respuestas positivas indicando una hiperfunción hipofisaria cuando 25 respuestas traducían un hipofuncion hipohipofisaria.

Paralelamente, en nuestra clínica pneumo-illustrologe de la Faculté de Lyon, hemos hecho estudios sistemáticos con la prueba de Metopirone desde hace dos años: para 50 enfermos que no son sarcoidósicos, no hubo ninguna prueba positiva de hiperfunción hipofisaria, salvo en un caso tratándose de un neoplasm pulmonar.

En cambio, en el curso de los ataques gangliopulmonares de origen sarcoidósico hemos notado una gran frecuencia de signos de hiperactividad neuro hipofisaria en relación con los impulsos evolutivos de la afección en sus formas endotórácicas ganglionares, miliares o infiltrativas.

Los casos de nuestras estadísticas pueden ser clasificados de la manera siguiente:

(1) Formas recientes, todavía no tratadas: 14 casos.

La prueba fue positiva 11 veces, sea en 78.5% de los casos y el porcentaje fue a veces muy importante. El porcentaje más grande fue una eliminación urinaria de 68.4 mg por 24 horas en 17-OH y 64.57 mg por 24 horas en H₂S. En los tres casos negativos, hay uno que motiva la discusión porque la prueba se ha realizado en un periodo menstrual.

Hemos seguido todos estos enfermos que fueron tratados con corticoterapia y hemos observado que la prueba se normalizaba a medida que las lesiones retrocedían, con la precaución de practicar la prueba diez días después del paro del tratamiento. Dentro de 75 por ciento de los casos, sea dentro ocho casos, la prueba ha sido otro vez normal al mismo tiempo que las lesiones habían regresado completamente. En dos casos las lesiones no han sido completamente curadas y la prueba tuvo tendencia a normalizarse pero esta estabilización fue parcial.

(2) En las formas antiguas y estabilizadas tratándose de 12 casos completamente estabilizados o curados, la prueba se ha encontrado siempre normal. En un 13vo caso, la forma era antigua datando de diez años, pero se ha asistido a una reincidencia infiltrativa pulmonar y la prueba se ha encontrado claramente positiva a 34.37 mg en H₂S.

Estos datos particularmente probadores pueden abrir los horizontes nuevos sobre la enfermedad y los efectos del tratamiento. Es posible que la cortisona no se haga, solamente que por la acción frenadora de las secreciones anormales o exageradas de las substancias de origen hipofisario. En
cuanto a los síndromes de hipofunción hipofisaria con diabetes insipida, generalmente encontrados hasta ahora y que son opuestos a los hechos publicados antes, pueden sobrevivir secundariamente después de un periodo de hiperactividad inicial que no había todavía sido formalmente reconocida.

**Resumé**

L'étude systématique de la réponse du test au Métapironone dans un service d'endocrinologie, nous a permis de constater la constante négativité des résultats en dehors de certaines endocrinopathies caractérisées: sur 120 résultats, il a été trouvé 4 réponses positives indiquant un hyperfonctionnement hypophysaire, alors que 25 réponses traduisaient un hypo-fonctionnement hypophysaire.

Parallèlement, dans notre Clinique Pneumo-Phtisiologique de la Faculté de Lyon, nous avons fait des études systématiques avec le test au Métapironone depuis deux années: pour 50 malades non sarcoïdiques, il n'y a eu aucun test positif dans le sens d'un hyper-fonctionnement hypophysaire, sauf dans 1 cas concernant un néoplasme pulmonaire.

Par contre, au cours des atteintes ganglio-pulmonaires d'origine sarcoïdique, nous avons relevé une haute fréquence de signes d'hyperactivité neuro-hypophysaire en relation avec les poussées évolutives de l'affection dans ses formes endo-thoraciques ganglionnaires, milliaires ou infiltratives.

Les cas de notre statistique peuvent être classés de la façon suivante:

1. Formes récentes, non encore traitées: 14 cas.
   Le test a été positif 11 fois, soit dans 78,5% des cas et à des taux qui ont été parfois très importants. Le taux le plus élevé a été une élimination urinaire de 68,4 mg par 24 heures en 17-OH et 64,57 mg par 24 heures en H4S. Sur les 3 cas négatifs, il y en a un qui prête à discusion du fait que le test a été réalisé en période menstruelle.

   Nous avons suivi tous ces malades qui ont été traités par corticothérapie et nous avons observé que le test se normalisait au fur et à mesure que les lésions rétrocidéaient, en prenant la précaution de pratiquer le test dix jours après l'arrêt du traitement. Dans 75% des cas, soit dans 8 cas, le test est redevenu normal en même temps que les lésions avaient complètement régressé, dans deux cas les lésions se sont amendées incomplètement et le test a eu tendance à se normaliser, mais cette stabilisation a été partielle.

2. Dans les formes anciennes et stabilisées concernant 12 cas absolument stabilisés ou guéris, le test a été régulièrement trouvé normal. Dans un troisième cas, la forme était ancienne datant de dix ans, mais on a assisté à une récidive infiltrative pulmonaire et le test a été trouvé nettement positif à 34,47 mg en H4S.

Ces constatations particulièrement probantes peuvent ouvrir des horizons nouveaux sur la maladie et les effets du traitement. Il est possible que la cortison ne n'agisse que par action frénectrice de sécrétions anormales ou exaggerées de substances d'origine hypophysaire. Quant aux syndromes d'hypo-fonctionnement hypophysaire avec diabète insipide habituellement rencontrés jusqu'ici et qui sont à l'opposé des faits précédemment rapportés, ils peuvent survenir secondairement après une période d'hyperactivité initiale qui n'avait pas encore été formellement reconnue.

**Zusammenfassung**

Die systematische Überprüfung der Metopironon-Teste, die auf einer endokrinologischen Abteilung durchgeführt wurden, ermöglicht es, insgesamt die konstante Negativität der Ergebnisse zu begründen, abgesehen von gewissen Fällen mit endokrinen Arterien. Bei 120 Testen ergaben sich 4 positive Reaktionen, die eine Hypophysen-Überfunktion bedeuteten und 25 Reaktionen, die im Zusammenhang standen mit einer Hypophysen Unterfunktion.


Im Gegensatz dazu ergaben sich bei einer Reihe von Fällen mit knotenförmiger pulmonaler Erkrankung an Sarkoidose eine beträchtliche Häufigkeit von neuro-hypophysen Überaktivität in Beziehung mit der Krankheitsentwicklung in ihren endothorakalen Veränderungen, sei es knotenförmiger, milliaerer oder infiltrativer Art.

Unsere Ergebnisse lassen sich wie folgt zusammenfassen: (1) Frische unbehandelte Formen: 14 Fälle. Der Test war positiv in 11 Fällen (78,5%) und zwar in gelegentlich sehr hohen Ausmaßen. Der stärkste positive Ausfall bestand in einer Urinausscheidung von 68,4 mg in 24 Stunden von 17-OH und 64,57 mg in 24 Stunden von H4S. Einer von den negativen Fallen muß außer Betracht gelassen werden, der Test ausgeführt wurde, während die Patientin ihre Menstruation hatte.

Alle mit Cortison behandelten Fälle wurden nachbeobachtet und es wurde dabei festgestellt, daß der Test dazu neigte, sich eben in dem Maße zu normalisieren, wie die Herbildungen zurückgingen. Der Test wurde 10 Tage nach Abschluß der Corticoid-Behandlung ausgeführt.
In 8 Fällen (75%) normalisierte sich der Test in der gleichen Zeit, in der die Herde vollständig verschwanden. In zwei Fällen, bei denen dies nicht der Fall war, zeigte der Test eine Tendenz zur Normalisierung, jedoch war die Stabilisierung nur eine partielle.

(2) Ältere stabilisierte Formen - 13 Fälle. Bei 12 vollständig stabilisierten oder geheilten Fällen ergaben sich normale Testwerte. Bei dem 13. Fall, bei dem es sich um eine 10-jährige Krankheitsdauer handelte, stellte sich ein pulmonaler infiltrativer Rückfall ein, und der Test war mit 34.47 mg H₂S positiv.

Diese doch sehr überzeugenden Befunde vermitteln neue Gesichtspunkte über die Erkrankung und die Auswirkungen der Behandlung zu eröffnen. Es ist denkbar, daß das Cortison nur als Hemmstoff für abnorme oder excessive Sekretion hypophysen Ursprungs wirksam wird. Was das Syndrom der Hypophyse-Unterfunktion angeht, wie man für gewöhnlich beim Diabetes-insipidus anspricht, und die im Gegensatz steht zu den oben berichteten Sachverhalten, so ist es möglich, daß es sich um ein sekundäres Geschehen handelt und zwar nach einer Periode initialer Überaktivität, die nicht erkannt wurde.

### REFERENCES


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### RECONSTRUCTION OF ESOPHAGUS

The clinical applications of left colon transplants in the management of irreversible esophageal obstruction in 105 patients, and the early and late results are reviewed. The procedure permits a single-stage excision and reconstruction of the obstructed esophagus. The left-sided thoraco-abdominal approach allows a choice of two methods of restoring esophageal continuity, depending upon anatomic and pathologic considerations revealed at operation.

On the evidence revealed by this investigation, left colon interposition is preferable to esophagogastrostomy, on the score of operative risks and improved late results, in the management of benign esophageal stenosis. Esophagogastrostomy may still be the method of choice in the majority of cases of malignant obstruction.


### MYOCARDIAL REvascularization

The free omental graft operation in combination with internal mammary artery implantation would appear to approach an ideal revascularization procedure in which hundreds of new arterioles develop rapidly to bypass points of coronary artery occlusion. This bypass operation results in the formation of numerous vessels with a total blood flow that might possibly exceed the flow in normal coronary arteries. Because a large number of vessels form after this procedure, the likelihood of failure has been considerably reduced over that with other procedures.