TRIAMCINOLONE THERAPY IN RHEUMATOID ARTHRITIS

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The introduction of cortisone as an anti-inflammatory agent stimulated the search for newer steroids with greater anti-rheumatic effect, but with fewer associated side-reactions. Shortly afterwards, hydrocortisone became available, and, although its anti-rheumatic effect was slightly greater, undesirable physiological responses were more or less similar. Fried and Sabo (1953) synthesized a corticosteroid analogue with a halogen atom at the 9 carbon position of the steroid nucleus called 9- α -fluoro-hydrocortisone. It was very much more potent than hydrocortisone, about ten times greater in anti-inflammatory effect, and with approximately 125 times the mineralocorticoid action (Liddle, Richard, and Tomkins, 1956; Boland, 1955). Marked sodium retention with this halogenated derivative precluded its application for practical use as an antiphlogistic agent in the treatment of rheumatoid arthritis, but it was of some value for patients with Addison's disease where the exaggerated mineralocorticoid effect was desirable.

In 1955, a very important chemical structural change resulted in the formulation of prednisone and prednisolone (Herzog, Nobile, Tolksdorf, Charney, Hershberg, Perlman, and Pechet, 1955) when a double bond was inserted between carbon atoms 1 and 2 of cortisone and hydrocortisone, respectively. These newer compounds were equally potent; they were approximately four times as great as their predecessors in glucocorticoid effect, whereas the mineralocorticoid action was diminished. In the usual maintenance dosages for treatment of rheumatoid arthritis, for example, electrolyte changes induced by these delta-1 analogues of cortisone and hydrocortisone proved no problem in clinical management of patients. However, other undesirable physiological reactions still occurred. In the hands of some investigators (Bunim, Pechet, and Bollet, 1955; Bollet, Black, and Bunim, 1955; Boland, 1956), complications with these latter

steroids, such as peptic ulceration, have been reported with even greater frequency.

In 1955 and 1956 a series of methylated corticosteroids were synthesized. Boland and Liddle (1957) reported that one of these, 6-methyl-prednisolone (Medrol), differed in no essential way from prednisolone itself. The sodium-retaining and potassium-losing activities of this compound were thought to be slightly less than those of prednisolone, but this was not definitely established. The hormone appeared to be at least as powerful as prednisolone in producing nitrogen-wasting; 41 patients with rheumatoid arthritis who received the drug at initial therapy showed no significant difference in degree or character of improvement from that anticipated with prednisone or prednisolone. Dosages were alike. Although the authors stated that their study was not sufficiently extensive properly to evaluate the complications of this new compound, they thought that most of the adverse reactions seen with the older preparations were also observed with 6-methyl-prednisolone.

Bernstein, Lenhard, Allen, Heller, Littell, Stolar, Feldman, and Blank (1956) synthesized a new preparation, by adding a 16- α -hydroxyl group to the 9- α -fluoro-prednisolone structure, and triamcinolone (16- α -hydroxyl-9- α -fluoro-prednisolone) was formulated. This compound eliminated the marked sodium-retaining potency of the previous analogue without diminution of glucocorticoid activity. Animal investigations (Perrine, Bell, Bortle, Heyder, Ross, and Ringler. In the press) revealed that triamcinolone was ten to forty times more active than hydrocortisone and three to twelve times more active than prednisolone in inducing glycogen deposition in fasted adrenalectomized rats. Diuretic and natriuretic potency exceeding that of prednisolone or hydrocortisone was also demonstrated in both adrenalectomized and normal animals. No hypertensive effect was observed in

rats. Haematological responses were similar to those noted with other steroids. The anti-inflammatory activity in inhibiting granuloma formation in rats was about ten times that of hydrocortisone.

Human metabolic studies (Hellman, Zumoff, Schwartz, Gallagher, Berntsen, and Freyberg, 1957; Freyberg, Berntsen, and Hellman, 1958) showed that triamcinolone caused a sodium diuresis, but no increased potassium excretion. The latter has been shown with long-term treatment and in acute metabolic studies with dosages as high as 30 mg. Preliminary information on calcium and phosphorus excretion and on nitrogen balance revealed relatively negligible changes in patients receiving 12 to 24 mg. of hormone daily. On very high doses, that is, over 50 mg. daily, losses of calcium, phosphorus, and nitrogen did take place. However, no general conclusions could be drawn on the influence of triamcinolone on nitrogen balance. A lesser tendency to cause peptic ulceration than other steroids was suggested by the preliminary findings of these investigators.

The encouraging animal and human studies on triamcinolone, particularly the possibility of decreased ulcerogenic effect and the lack of adverse mineralo-corticoid response, warranted further evaluation of this preparation. Our experiences with triamcinolone therapy in fifty patients with rheumatoid arthritis are reported below.

Procedure

The general plan for administering triamcinolone* was similar to that employed with other anti-inflammatory steroids; that is, an initial suppressive dose was followed by gradual reduction to maintenance levels. Those patients receiving other steroids were switched to triamcinolone, with the same dose. Individuals not previously on such therapy were started on triamcinolone in total daily doses varying from 6 to 30 mg. Adjustments in dosages were made in small amounts, usually by 2 to 4 mg. and preferably at weekly intervals, until maintenance levels were attained. Early in the treatment with triamcinolone, when relatively large doses may have been administered, the dose was lowered more rapidly. After maintenance values were established, prednisone was substituted in many patients for comparative purposes. In a similar manner, the acetate and free alcohol forms of triamcinolone were compared by substituting one for the other, but without the patient's knowledge. The free alcohol form of triamcinolone was used for the major part of the study.

Other forms of therapy were continued without alteration. Most patients were simultaneously treated with gold salts and salicylates.

At each visit the patient's joints were evaluated subjectively for pain, stiffness, and range of motion, and objectively for the degree of synovitis as demonstrated by the amount of heat, swelling, capsular thickening, fluid, tenderness, and range of motion. These were estimated and recorded as a composite percentage value, 100 per cent. indicating maximum improvement.

The duration of observation varied, but it was continued for more than a year in fifteen subjects; 34 cases were studied for more than 6 months, and only six for less than 2 months.

Clinical evidence of toxicity was sought at each visit. Observations were made of moon facies, hirsutism, ecchymoses, blood pressure changes, body weight, and particularly of gastro-intestinal disturbances. Other possible complications were also recorded.

Laboratory procedures included urine analysis, complete blood count, and erythrocyte sedimentation rate (Westergren), at least once monthly and more frequently when the patient was first placed on a new medication. Electrolyte determinations for sodium, potassium, and chloride, and fasting blood sugars were done throughout the study.

Gastric analyses were performed serially on fourteen patients according to the technique of Kirsner and Ford (1955). Histalog in a dose of 0.5 mg./kg. body weight was used to stimulate the gastric mucosa. Eight specimens of gastric juice were obtained at 15-minute intervals during the test, four before histalog stimulation, and four afterwards. Volume, concentration in clinical units of free acidity, and mg. hydrochloric acid were determined for each specimen. A total of 38 gastric analyses were done. Barium meals were performed serially during therapy in twelve of the above patients, and also in twelve others. Nine patients had gastric mucosal biopsies using the Wood's technique (Joske, Finckh, and Wood, 1955).

Results

The free alcohol and acetate forms of triamcinolone were compared in eighteen individuals. No significant difference was demonstrated between these preparations in anti-inflammatory response. The dosages used for each were generally the same, only an occasional patient requiring a slightly higher dose of one drug or the other. A limited supply of the acetate derivative did not permit long-term comparisons of side-reactions, but no disparities were noted during the short period of observation.

The initial higher dosage of triamcinolone was lowered to maintenance levels without difficulty. The maintenance dose averaged 7.9 mg., but there were wide variations from 2 to 24 mg. daily.

The anti-inflammatory response to triamcinolone was very satisfactory. All but four patients demonstrated significant improvement (i.e. greater than 50 per cent.). In only one instance was there no anti-inflammatory response. The alleviation of

* The triamcinolone used in this study was supplied as Aristocort by Lederle Laboratories Division, American Cyanamid Company, Pearl River, N.Y.

rheumatic manifestations was similar to that observed with other steroids as regards rapidity, degree, and duration of improvement. A few patients still preferred triamcinolone to prednisone or prednisolone for its anti-rheumatic effect, although there was no objective evidence to corroborate this impression. The dose of triamcinolone was approximately 80 per cent. that of these latter compounds as evaluated in fifteen patients.

White blood cell counts increased during therapy in the majority of instances. The erythrocyte sedimentation rates diminished in the same way as with earlier steroids. The urine analyses were normal. The electrolyte determinations of sodium, potassium, and chloride (performed 43 times in seventeen patients at various times during the study) revealed no significant alterations. Acute studies were not done with initial dosages. The fasting blood sugar was unchanged in twenty patients on whom a total of 61 tests were made. In several cases there were four, five, or six determinations of the fasting blood sugar. In three individuals, fasting sugars were elevated on one occasion, but subsequent re-checking revealed normal values. Diabetes did not result in any subjects.

Many adverse physiological reactions occurred (Table I), particularly moon facies and buffalo humping which developed in 24 patients. Ecchymoses were recorded in sixteen. Hirsutism was prominent and was associated with moon facies in twelve patients. It was not possible to compare these side-effects exactly with those of previous steroids in these patients because the duration of observation with the other hormones was not sufficiently long.

An initial weight loss of 2 lb. or more during the first week's therapy occurred in sixteen of 37

patients checked. In two of these the loss was considered coincidental because of similar variations in past weeks on other medications. Nineteen of this group had originally been switched from prednisone or prednisolone to triamcinolone, with seven demonstrating a like diminution in weight. Weight loss of 2 lb. or more occurred in nineteen subjects over the entire period of study. Loss of 10 lb. or more occurred in seven cases (maximum 27 lb.). In fifteen patients after triamcinolone therapy for varying periods, prednisone was substituted for intervals of a few days to 1 month. Seven of this group then showed an increase in weight of 2 lb. or more. Nine patients gained weight during triamcinolone therapy.

Increased appetite occurred in eleven patients and anorexia in ten, with two of the former group later developing anorexia. Other gastro-intestinal symptoms (bloating, excess gas, nausea, epigastric burning, etc.) were observed in fifteen subjects. One patient had much bloating while taking prednisone, but this was less marked with triamcinolone. Another had had a disturbingly increased appetite while taking the earlier steroids, and found triamcinolone more satisfactory because the appetite returned to normal.

The effect of triamcinolone on gastric-juice production was studied in fourteen patients (8 male and 6 female). Three patients were evaluated during therapy extending over approximately a year, and a fourth patient for over 200 days. Control histalog gastric analyses were performed in thirteen individuals, ten during a period of no steroid therapy, and three during prednisone administration. One patient had no control analysis. The results are summarized in Table II (opposite), showing volume, concentration in clinical units, and total mg. hydrochloric acid. The four specimens before histalog stimulation and the four following are totalled and listed under the Basal and Histalog columns respectively. The figures suggest a slight trend towards an increase in gastric juice or hydrochloric acid formation in five or six cases in the post-histalog period, but no consistent alteration was produced. The various gastric analyses performed during triamcinolone administration revealed no constant change when compared with the prednisone or no steroid control periods. Nor was there any difference in the effect of the acetate and free alcohol forms of triamcinolone in this limited trial. The results were very variable from patient to patient and even on different occasions in the same individual.

TABLE I

HORMONAL EFFECTS OF TRIAMCINOLONE THERAPY IN FIFTY PATIENTS WITH RHEUMATOID ARTHRITIS

Reaction	Number of Patients
Moon Facies	24
Final Weight Loss	19
Ecchymoses	16
Nausea, Gas, Bloating, Epigastric Distress ..	15
Initial Weight Loss	14
Hirsutism	11
Increased Appetite	11
Anorexia	10
Weight Gain	9
Muscle Cramps	7
Flushes	6
Erythema	3
Dizziness	3
Acne	3
Headache	2
Weakness	2
Gastric Ulcer	1
Osteoporosis and Fracture	1

* Case 14 (Table II) did not have rheumatoid arthritis.

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TABLE II
RESULTS OF GASTRIC ANALYSES DURING TRIAMCINOLONE THERAPY
IN PATIENTS WITH RHEUMATOID ARTHRITIS

Patient No.	Sex	Age (yrs)	Date	Drug†	Average Total Daily Dose (mg.)	Duration of Therapy (days)	Basal*			Histalog*		
							Vol. (ml.)	Cl.U.	Output† (mg.)	Vol. (ml.)	Cl.U.	Output† (mg.)
1	F	64	3.4.57	Pred	8	740	65	0	0	49	0	0
			23.4.57	Tdac	4	8	37	0	0	76	6.3	2.19
			21.5.57	Tdac	6	25	54	0	0	48	0	0
			26.3.58	TOH	4	340	92	0	0	83	8	22.6
2	F	62	1.4.57	Pred	13	150	39	17.0	24.2	77	56	158.1
			16.4.57	Tdac	12	8	52	40.5	76.8	51	92	335.8
			17.5.57	Tdac	10	30	50	24.0	15.94	83	89	150.1
			18.6.57	TOH	10	72	25	8.5	4.0	61	63.5	83
3	M	67	8.5.57	Pred	15	23	—	4	—	—	25	—
			5.11.57	TOH	5	43	127	49.0	229	145	74	309.0
			2.5.58	TOH	6	221	—	5	—	—	0	—
4	F	54	10.4.57	Tdac	8	51	—	32	—	—	98	—
			24.4.57	Tdac	8	61	61	89	127.5	145	112.5	215.8
			24.5.57	Pred	10	18	36	14	6.5	57	0	0
			19.3.58	TOH	10	390	34	14	7.8	124	76.0	110.7
5	F	63	25.4.57	None	—	—	12.5	11.5	5.4	43	29	48.6
			10.6.57	Tdac	8	14	47	0	0	40	0	0
			11.2.58	TOH	8	273	53	4.5	—	99	40	144.5
6	F	58	29.3.57	None	—	—	74	12	37.0	115	63.0	182.4
			12.4.57	Tdac	12	11	45	21	52.0	226	67.0	809.0
			3.5.57	Tdac	12	32	54	0	0	61	0	0
7	M	62	17.2.58	None	—	—	92	30	18.7	143	41	312.0
			16.4.58	TOH	8	56	83	25	186	164	76	1,040.0
8	F	50	15.1.58	None	—	—	75	—	—	99	25	209.0
			4.3.58	TOH	16	28	30	5	23	222	14	301.0
9	M	45	22.1.58	None	—	—	72	35	174	175	57	437.5
			20.2.58	TOH	16	25	84	26	150	272	65	625
10	M	45	10.12.57	None	—	—	48	0	0	178	57	273
			23.12.57	TOH	8	5	63	0	0	128	38	413
11	F	56	18.2.58	None	—	—	25	0	0	45	51	86
			8.4.58	TOH	8	49	35	20	18	73	46	124
12	M	53	22.1.58	None	—	—	98	0	0	83	4	12.4
			17.2.58	TOH	16	14	165	4	24	163	17	99.7
13	M	35	15.3.58	None	—	—	228	0	0	145	0	0
			26.3.58	TOH	16	12	126	0	0	106	4	11.7
14	M	80	19.1.58	None	—	—	70	37	95.6	194	49	468
			28.1.58	TOH	8	12	—	—	—	239	60	502

* These values are the combined figures for the four specimens before and after histalog stimulation respectively.

† Output equals Volume × Clinical Units × 0.00365 × 10.

‡ Pred = Prednisone acetate.

Tdac = Triamcinolone diacetate.

TOH = Triamcinolone (alcohol).

Roentgenograms of the upper gastro-intestinal tract were performed in 24 patients during triamcinolone therapy, including twelve of the above group. Approximately half also had control films.

Patient 1 (Table III, overleaf) developed a peptic ulcer located on the lesser curvature of the stomach which appeared after 9 months on maintenance doses averaging 9 mg. daily. The ulcer healed without difficulty while steroid therapy was continued as before, and antacids, an ulcer diet, sedation, and anticholinergics were added to the regime. Patient

13 (Table III), who had an asymptomatic "scarred duodenal bulb" on the control barium meal, revealed no change with a repeat examination 3½ months later. Patient 14 (Table III), who had a scarred duodenal bulb before the study, showed no evidence of this subsequently. Patient 18 (Table III) had two gastric ulcers from prednisone therapy when he was switched to maintenance doses of triamcinolone with the addition of the anti-ulcer regime mentioned above; the ulcers healed within 10 weeks as established by gastroscopy, x-ray

TABLE III

CORRELATION OF DURATION OF TREATMENT AND DOSE
OF TRIAMCINOLONE WITH BARIUM MEALS IN
24 PATIENTS WITH RHEUMATOID ARTHRITIS

Patient No.	Duration of Therapy at Time of Last Barium Meal (days)	Average Daily Maintenance Dose (mg.)	Results of X Ray
1	435	8	Gastric ulcer after 9 months; subsequently healed
2	178	6	Negative
3	525	9	Negative
4	198	9	Negative
5	154	11	Negative
6	316	9	Negative
7	333	4	Negative
8	260	5	Diverticulum of stomach
9	400	16	Negative
10	460	8	Negative
11	383	6	Negative
12	159	6	Negative
13	109	6	Scarred duodenal bulb in control; no subsequent change
14	198	7	Scarred duodenal bulb in control; negative subsequently
15	367	3	Negative
16	283	8	Negative
17	185	22	Negative
18	105	8	Gastric ulcers with prednisone; healed during triamcinolone therapy
19	305	14	Negative
20	93	12	Negative
21	103	12	Negative
22	77	8	Negative
23	80	9	Negative
24	106	9	Negative

examination, and clinical evaluation of symptoms. Patient 8 (Table III), who had severe rheumatoid arthritis with a gastric diverticulum, had a gastrointestinal haemorrhage after receiving triamcinolone for 8 months in doses averaging 5 mg. daily. The site of bleeding was not established despite x-ray studies and gastroscopy, but the haemorrhage ceased spontaneously in a few days, and triamcinolone was restarted after temporarily discontinuing its use.

Table III correlates the average maintenance dose and the duration of therapy with the results of the last barium meal. In most instances, x-rays were obtained after 6 months' treatment.

Gastric mucosal biopsies were taken in nine patients. Eight had both control biopsies and repeat procedures after 2 weeks of triamcinolone therapy in dosages averaging 12 mg. daily. The ninth was the patient with the gastric diverticulum and bleeding in whom a biopsy was performed after the source of haemorrhage was not elucidated by x-ray and gastroscopy. This biopsy was also non-revealing. None of the sections showed any significant difference from the controls when examined with the haematoxylin-eosin stain. One

patient had chronic gastritis in both the control and follow-up.

Muscle cramps occurred in seven patients, three of whom had had similar episodes before this therapy. Erythema of the face and chest was noted in three cases, and flushes in six. All of the latter patients were in the menopausal age group or older. Headaches occurred in two, one of whom had taken prednisone without similar difficulty. Weakness was also present during prednisone administration in one out of two patients with this complaint. Acne, which had been present as a result of previous prednisone treatment in two cases, gradually disappeared on triamcinolone. In both these instances the dose of triamcinolone was lower than the earlier steroid dose. Mild acne developed in three other cases. Osteoporosis with fracture of a lumbar vertebra occurred in one individual. Episodes of severe lower back pain in two additional subjects did not prove to be due to osteoporosis or fracture on x-ray examination. There were no elevations of blood pressure. Neither psychosis nor euphoria was observed.

Several findings, possibly related to triamcinolone therapy but more likely coincidental occurrences, are listed in Table IV. Alopecia in each of the two instances happened in elderly women and was localized to the scalp where its distribution was generalized. One patient had three episodes of syncope after 8 months of therapy with maintenance doses averaging 22 mg. daily. No similar experiences had occurred before or since, although the medication was continued for an additional 2 months. Superficial thrombophlebitis was found in three patients; this was evanescent and disappeared within 1 to 2 weeks, and no serious complications resulted. Three patients developed herpes zoster. Blanching of the fingers became a prominent finding after 3 months of triamcinolone therapy to a 25-year-old white female who was maintained on doses averaging 8-12 mg. daily; the Raynaud's phenomena grew progressively worse in the ensuing 2 months, while the steroid dosage was gradually reduced to nothing. Gangrene developed at the tip of one

TABLE IV
QUESTIONABLE HORMONAL EFFECTS OF TRIAMCINOLONE IN FIFTY RHEUMATOID PATIENTS

Reaction	Number of Patients
Superficial Thrombophlebitis	3
Herpes Zoster	3
Alopecia	2
Syncope	1
Periarteritis with Raynaud's Phenomenon	1

finger, and a muscle and skin biopsy from a clinically uninvolved area revealed a marked inflammatory reaction in the blood vessels of both tissues indicative of a periarteritis. The walls of small arteries, arterioles, and capillaries were infiltrated with polymorphonuclear leucocytes and lymphocytes, and in some areas showed necrosis. It could not be determined whether this was a primary reaction or secondary to steroid therapy.

Triamcinolone was discontinued after varying periods of treatment in seventeen patients for the reasons listed in Table V. In six this was necessitated by complications; patient contact was lost in seven; and the treatment was no longer needed in four. The one death which occurred was unrelated.

TABLE V
REASONS FOR DISCONTINUATION OF
TRIAMCINOLONE THERAPY

Cause	Number of Patients
Loss of Contact with Patient	7
No Further Need for Steroid	4
Osteoporosis with Fracture	1
Inadequate Improvement	1
Deceased	1
Anorexia and Weight Loss	1
Periarteritis	1
Gastro-Intestinal Haemorrhage	1

Discussion

Triamcinolone was found to be a very effective anti-rheumatic agent. The anti-inflammatory effect was slightly greater than that of prednisone or prednisolone in a dosage ratio of approximately 4 to 5. In a few patients triamcinolone was preferred to the latter drugs. The acetate and free alcohol forms of triamcinolone were interchangeable without noticeable effect.

Many undesirable side-effects of triamcinolone therapy were comparable to those of other anti-inflammatory glucocorticosteroids. Moon facies, hirsutism, and ecchymoses seemed to be at least as prevalent as with the older preparations. Gastro-intestinal complaints of nausea, gas, bloating, anorexia, or epigastric distress were not unusual. Anorexia which would be a disadvantage in most instances could also serve a useful purpose by aiding weight reduction in obese cases. In addition, patients with a disturbingly increased appetite from previous steroids might find this lack of stimulation of appetite a very desirable feature. Such was the case in one patient. It should be mentioned that increased appetite occurred about as often as anorexia, and that weight gain was not infrequent. The latter could be attributed to the stimulation of

appetite or to the increased sense of well-being which fostered better eating. Weight gain was not due to fluid retention.

Of great interest was the weight loss which occurred in some individuals. The initial loss might be explained by depletion of fluids due to sodium diuresis which was previously demonstrated with triamcinolone (Hellman and others, 1957; Freyberg and others, 1958). Explanation of weight loss progressing with long-term therapy was not clear; continuing diuresis was not likely. Anorexia which was a problem in several patients might have been partially responsible because of decreased food intake. For those individuals without anorexia, nitrogen wasting secondary to steroid therapy would appear to be the likely explanation, although adequate proof was lacking at this time. Early metabolic studies showed no nitrogen loss (Hellman and others, 1957), but later investigations (Freyberg and others, 1958), utilizing large doses of steroid indicated that catabolism did occur. The one instance of osteoporosis with fracture in this series, and the relative infrequency of this occurrence in other reports, suggested that factors other than negative nitrogen balance might play a part. However, it should be realized that x-ray evidence of negative nitrogen balance as demonstrated by demineralization of bone does not appear early, and that the studies thus far reported have been of relatively short duration for this manifestation. Chronic dehydration (Freyberg and others, 1958) and negative electrolyte balance (Curd and Spurr, 1958) have been proposed as additional factors in this weight loss.

The possibility of a decreased ulcerogenic potential for triamcinolone requires further observation for affirmation. Development of a gastric ulcer in only one of 24 patients examined roentgenographically supports other encouraging reports in this regard (Hellman and others, 1957; Freyberg and others, 1958; Dubois, 1958). The healing of the ulcer in this patient and of two gastric ulcers due to previous prednisone therapy in another who was treated simultaneously with triamcinolone and an anti-ulcer regimen, corroborate the impression of a decreased ulcerogenic stimulus. Caution in interpretation is warranted, however, since ulcers have also been observed to heal during the administration of other steroids.

Gastric analyses suggested increased gastric-juice production in the post-histalog specimens in a few instances. When these results were compared with the figures given for normal controls (Kirsner and Ford, 1955), they were found to fall into the normal range for the age and sex of the patients involved,

and their significance was, therefore, questioned. The effect of triamcinolone on gastric-juice formation was not consistent; and, in fact, any response would be difficult to prove by the analyses obtained from our patients.

Since the gastric biopsy utilizing the Wood's technique was a blind procedure, the specimens obtained during triamcinolone therapy in the nine patients studied were not necessarily from the same area of the stomach as those from the controls. Nevertheless, no alteration in histological structure was apparent.

Interesting side-reactions which might be peculiar to triamcinolone were erythema of the face and neck, flushes, headache, and dizziness. Explanations for these manifestations are wanting.

The absence of diabetes in this series would bear further observation, but a diabetogenic effect has been noted by other investigators (Freyberg and others, 1958).

The diminished mineralocorticoid action obviated the problem of sodium retention. Electrolyte determinations revealed no abnormalities for the dosage range used.

These studies indicate that triamcinolone may be satisfactorily employed in the treatment of rheumatoid arthritis. Since this addition to the armamentarium of anti-inflammatory steroids may offer certain advantages, its use should prove of benefit to many patients. However, undesirable physiological reactions should also be considered; this applies to the other anti-rheumatic steroids as well. The physician to-day, having several of these preparations to choose from, should carefully weigh the advantages and disadvantages of each before prescribing for his patient.

Summary

Triamcinolone was administered to fifty patients with rheumatoid arthritis and gave a satisfactory anti-rheumatic response. The maintenance dose averaged 7.5 mg. daily. This compound was more potent than prednisone or prednisolone in a dosage ratio of 4 to 5. Comparison of the acetate and free alcohol forms of triamcinolone revealed no significant difference. Most of the cushingoid-type reactions complicating other steroid therapy occurred with triamcinolone with equal or greater frequency. The ulcerogenic effect of this preparation may be minimal, as only one patient out of 24 x-rayed revealed gastric ulceration. Studies of gastric-juice production in fourteen patients showed no consistent change which could be considered due to hormone administration. Gastric biopsies in nine patients were also non-revealing. Other

physiological effects, such as anorexia, weight loss, erythema of the chest and face, flushes, headache, and dizziness, may be peculiar to triamcinolone. Diabetes did not occur. This last observation merits further evaluation.

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Traitement à la triamcinolone de l'arthrite rhumatoïdale

RÉSUMÉ

On administra de la triamcinolone à 50 malades atteints d'arthrite rhumatoïdale et la réaction antirhumatoïdale fut satisfaisante. La dose moyenne de soutien fut de 7,5 mg. par jour. Ce composé fut 4 à 5 fois plus puissant, dose pour dose, que la prednisone ou la prednisolone. On ne trouva pas de différence appréciable entre l'acétate et l'alcool libre de la triamcinolone. La plupart des réactions du type "Cushing", qui compliquent la thérapie par d'autres stéroïdes, se produisit aussi avec la triamcinolone avec une fréquence similaire ou plus grande. L'effet ulcérogène de ce produit peut être minime, car un seul malade sur 24 radiographiés révéla une ulcération gastrique. L'examen de la sécrétion du suc gastrique chez 14 malades ne révéla pas d'altérations définies attribuables à l'administration de l'hormone. Des biopsies gastriques chez 9 malades donnèrent également un résultat négatif. D'autres effets physiologiques, tels que anorexie, amaigrissement, érythème de la poitrine et du visage, bouffées de chaleur, céphalée et vertige pourraient être particuliers à la triamcinolone. Il n'y eut pas de diabète. Cette dernière observation demande une vérification ultérieure.

Tratamiento con la triamcinolona de la artritis reumatoide

SUMARIO

Triamcinolona fué administrada a 50 enfermos con artritis reumatoide, obteniéndose una reacción antirreumática satisfactoria. La dosis media de sostén fué de 7,5 mg. diarios. Este compuesto se reveló 4 o 5 veces más fuerte, en dosis iguales, que la prednisona o la prednisolona. No se encontró diferencia apreciable

entre el acetato y el alcohol libre de la triamcinolona. La mayoría de las reacciones del tipo "Cushing", que suelen complicar la terapia con otros esteroides, ocurrieron también con la triamcinolona con una frecuencia igual o superior. El efecto ulcerígeno de este producto parece mínimo, ya que un solo enfermo de 24 radiografiados reveló una ulceración gástrica. La investigación de la secreción del jugo gástrico en 14 enfermos

no reveló alteraciones que se pudieran atribuir a la administración de la hormona. Biopsias gástricas en 9 enfermos dieron también un resultado poco revelador. Otros efectos fisiológicos, como anorexia, pérdida de peso, eritema del pecho y de la cara, rubores, jaqueca y vertigo podrían ser particulares a la triamcinolona. No hubo diabetes. Esta última observación necesita una verificación ulterior.