fall in diastolic pressure in patients on placebo treatment and the same patients on mio-pressin treatment; (2) there is a significant difference between the fall in diastolic pressure in patients on placebo treatment and a different group of patients on mio-pressin treatment; and (3) there is no significant difference between the fall in diastolic pressure in the two groups of patients on mio-pressin treatment.

Discussion

It is not surprising that a combination of hypotensive drugs produced a satisfactory initial fall in diastolic pressure or that treatment with active material was significantly better than treatment with inert material. It would have been more remarkable if the results had been otherwise.

The most interesting observations from this trial would appear to be those on the out-patients. Of the 52 patients treated, 44 maintained their blood pressure at the lowered level or even further reduced it. In no instance was it necessary to increase the dose of mio-pressin, and in 26 patients the daily dose has been greatly reduced from the original level.

Side-effects were negligible and there was no postural hypotension. One patient complained of dizziness, one of anorexia, and one of blurred vision, but these disappeared without alteration of the treatment.

Summary

Mio-pressin, a combination of rauwolfia, proto-veratrine, and dibenylamine, has been used in a controlled trial in hospital. Out-patient reviews have been made over periods from one to two and a half years.

In the controlled trial there was a satisfactory fall in diastolic pressure on active treatment and a significant difference between the results of active and inert treatment.

Of the 52 patients, 44 maintained or reduced the lowered blood pressure. None had the dose of mio-pressin increased, and 26 have had the maintenance dose reduced.

DOES SERUM GONADOTROPHIN CURE ACNE VULGARIS?

BY

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Acne vulgaris starts at puberty and ends in late adolescence or early adult life. This close connexion with the major period of hormonal imbalance has been recognized by the lay public as well as the medical profession for a very long time. Even to-day many doctors use the old cliché, "It's your age; you'll grow out of it," as an excuse for treating acne sufferers lightly, and this mentality has so affected the general public that large numbers of young people suffer agonies of embarrassment in the belief that nothing can be done, and a regrettably high proportion end up with severe scarring of the face, chest, and back.

What, then, can be done for these patients? As most of them have a very greasy skin, measures to counteract this should be of value, and dietary restrictions should be advised, associated with local degreasing by soap and water, application of detergents *N.F.*, or 1% cetrimide lotion. Exfoliation of the hyperkeratosis may

be obtained by local applications of sulphur or resorcinol or by weekly erythema doses of ultra-violet light. The control of the pustular element has been made much easier in the past few years by the prolonged administration of antibiotics at low dosage, the results of which were summarized by Cronk *et al.* (1956).

None of these treatments can expect to be curative, but with their prolonged administration the patient can be guaranteed that while the acne is present it will be less cosmetically unpleasant, and ultimately there will be much less scarring than might otherwise have occurred. This is useful for the patient but time-consuming for everybody, and better treatments must still be sought.

Theory

The closer investigation into the problem of hormonal imbalance was initiated by Pick (1921); a stream of articles followed this over many years until the work of Hamilton (1941) stimulated dermatologists to use oestrogens. Gradually the inadvisability of prescribing these for the male has been recognized, but there has remained a definite place for their use in women during the second half of the menstrual cycle. This is of most value in those whose acne is predominantly of the comedone type. This satisfactory advance led most people to assume that the androgen/oestrogen ratio was at fault, and that this was a fact of prime importance in the causation of acne. Few dermatologists were rash enough to claim that the administration of hormones could effect a permanent cure, as puberty is a dynamic disequilibrium of all hormones, whose ratio alters far too often to be affected by the physician's ministrations.

In 1950 Aron-Brunetiere and Fitoussi widened the scope of the theories about hormones by postulating that the imbalance was a result of the interrelation between androgen, oestrogen, and progesterone in the following ratio: $\frac{\text{androgen} + \text{progesterone}}{\text{oestrogen}}$. Following the work of

Vignes (1937) and Jausion *et al.* (1941) they produced evidence to show that the administration of 20–30 mg. of progesterone in two or three doses between the 21st and 25th days of the menstrual cycle aggravated acne. They also claimed that chorionic gonadotrophin did the same thing. From this they postulated that the

disequilibrium of the $\frac{A+P}{OE}$ ratio was due to a parallel

disequilibrium in the hypothalamopituitary mechanism responsible for the secretion of sex hormones. A series of experiments based on this concept led them to use serum gonadotrophin as a treatment, first by injection (Aron-Brunetiere, 1954) and later by oral administration and transmucosal absorption (Aron-Brunetiere, 1956). This treatment is claimed to give a 61% cure rate in women and 35% in men, with another 25% in women and 43% in men much improved. Only two brief annotations have appeared in British journals: MacKenna (1957) and Cohen (1957) each claim that about 60% of their cases showed considerable improvement.

Such claims warrant further investigation, most particularly when the word "cure" has slipped into the journals, and, unfortunately, into the literature of a pharmaceutical company.

Method

It is always difficult to decide how to investigate the effects of a new drug, especially when there is some

doubt in the investigator's mind about its possible efficacy. Published claims of "60% considerable improvement in three months," particularly with no reference to a controlled investigation, do not impress a dermatologist with an acne clinic and a pride in the results he already obtains. It was therefore thought unjustifiable to substitute for treatment which had shown some success a form of therapy whose results were problematical. It would also be unethical to prescribe an unproved drug for new patients on their first attendance at the department. For this reason a random group of patients was selected from those who had already been regular attendants at the department for at least three months. These people were able to act as their own controls. In all cases the treatment they had received with more or less satisfaction was continued unaltered, and the trial tablets were given in addition.

The treatment these people had been receiving was all part of the usual routine. The mildest cases were given 1% cetrimide as a degreasing application and a mild exfoliative lotion, usually calamine lotion *B.P.* with 3% sulphur. The more severe cases were also treated once a week with an exfoliative dose of ultra-violet light, while the most severe were in addition given the routine antibiotic treatment (usually tetracycline 250 mg. daily for three weeks out of every four), which both the patients and the department have found to be so useful in diminishing or preventing the severe pustulation.

All these people were then provided with tablets labelled A or B and asked to co-operate in an investigation to test the efficacy of a new drug. The course of treatment was for 12 weeks, and at the end of every four weeks each patient was seen and requested to assess whether the additional treatment had increased the effect of the treatment previously given. The actual course of treatment varied from month to month as recommended by the manufacturers, and the patients took two tablets a day for the first four weeks, one daily for the next four weeks, and then one every alternate day for the rest of the trial. They were also instructed not to swallow the tablets but to allow them to dissolve in the mouth.

The severity of each case was assessed at the start of the course: 1 (mild), 2 (medium), and 3 (severe); and the presence of pustulation, comedones, seborrhoea, and scarring was also noted individually for the face, neck, chest, and back. At intervals of four weeks the patient and the investigator between them decided whether or not there had been an increase in the rate of improvement, and this was noted by + for improvement, 0 for no change, and - for a definite deterioration. At the end of the course an overall assessment was made. With this method it has been possible to assess by a controlled technique the effect of serum gonadotrophin on acne. Throughout the investigation neither the patients nor the doctor knew which tablets contained the drug and which were dummies.

Results

The trial was started on a total of 49 patients (29 male and 20 female), of whom six men and three women failed to complete the course; and in none of the defaulters was this failure due to adverse effects of the drugs. The Table shows that 42.9% of those on tablet A and 42.1% on tablet B thought that the addition of the tablet had enhanced the speed of improvement, while 42.9% on A and 47.4% on B noticed no change in either way. 3 out

Table of Results

Grade of Severity	Tablet A			Tablet B		
	Improved	No Change	Worse	Improved	No Change	Worse
1	8	5	3	3	6	1
2	1	4	—	5	2	1
3	—	—	—	—	1	—
Total Percentage	9 42.9	9 42.9	3 14.2	8 42.1	9 47.4	2 10.5

of 21 (A) and 2 out of 19 (B) suffered a definite deterioration during the three months.

There is therefore no evidence at all in this trial that the use of oral serum gonadotrophin has any effect on the course of an acne which is already under treatment, and thus there is no justification for an attempt to treat patients in this way to the exclusion of other methods. This conclusion can be stated dogmatically without even the knowledge of which tablets contained the active ingredient.

It is interesting to note that only two patients complained of side-effects when asked. An 18-year-old youth who left the tablet in his mouth to dissolve overnight was sick nearly every morning for the first three weeks, but the symptoms did not reappear after a few days' rest from the tablets; a 20-year-old woman complained that for the first time in her life periods had become irregular. These complaints did not, however, provide a hint to the dispassionate observer of which tablet contained the serum gonadotrophin, as the patients were on different tablets. It was not until after this article was completed that it was disclosed by the manufacturers that B tablets contained the serum gonadotrophin.

Summary

A controlled investigation was performed to estimate whether the addition of serum gonadotrophin to the treatment of acne vulgaris altered the course of the disease. The course was of 100 units daily for four weeks, 50 units daily for the next four weeks, and 50 units on alternate days for the final four weeks. So far as can be ascertained all patients allowed the tablets to dissolve in the mouth, and so absorbed the drug transmucosally. There is no evidence whatsoever from this trial that the patients derived any benefit from the treatment. The uncontrolled trials reported in France and England have not been confirmed, and acne vulgaris remains a condition for the cure of which there is no known remedy.

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