PROGESTERONE AND THE NASAL MUCOSA

BY

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The association between the condition of the nasal mucosa and the menstrual cycle has been noted from time to time. So far as we are aware no reference has as yet been made to the therapeutic effect of corpus luteum hormone on the nasal mucosa. A chance observation by one of us (J. K. W.-P.) while treating a case of menorrhagia with progesterone has led us to investigate more fully the effect in that patient of this substance on her nasal mucosa.

The patient had suffered from menorrhagia for two years, and from spasmodic rhinorrhoea of considerable severity for eighteen months. The nasal passages had been examined by an ear, nose, and throat surgeon, and the nasal sinuses radiographed, but no evidence of infection had been found. The nasal septum was removed, as it was partially blocking the airway, but this operation failed to bring relief. After the first injection of progesterone the nasal discharge and congestion immediately subsided. The relief was as unexpected as it was complete. At the outset this effect was regarded as coincidental, as the patient was receiving progesterone intramuscularly in order to relieve the menorrhagia. Her inquiry as to whether the injection could possibly have had this surprising effect on her nose was met with a flat denial. The failure of the rhinorrhoea to reappear for several weeks has led us to inquire further. The details of the case and of the investigation are as follows.

Case Report

The patient was a widow aged 36, a children's nurse in an orphanage, with one child aged 11.

History.—For two years she had had menstrual bleeding every fourteen days, lasting five to seven days, but sometimes continuous on and off throughout the month. This was associated with backache and tiredness. For eighteen months she had also suffered from a watery nasal discharge, which sometimes streamed profusely. There was no mucus. The onset had been gradual, and had occurred while on holiday at Filey. The start of menorrhagia had also occurred in the same locality six months previously, probably a coincidence. There was nasal congestion associated, before operation, with pain across the bridge of the nose and forehead. These attacks came on two or three times a week, lasting several hours, ever since the onset. There was no seasonal variation, no apparent relation to pollen, dust, feathers, or food, and it was not apparently influenced by emotional stress. It was, however, definitely of the vasomotor type, being brought on by changes of temperature. Her general condition, along with certain difficulties in connexion with her work, combined to produce great mental depression. Her past history showed a catamenia for three days in twenty-eight, pneumonia at the age of 5, but no other illnesses. There was no history of hay-fever, asthma, or skin trouble. There was nothing relevant in her family history, which furnished no record of any allergic diseases.

Physical State.—She was of small stature and very underweight, looking tired and run down. Her nasal passages were small and poorly developed; the nasal septum was deflected, making a very bad airway. No evidence of thyroid abnormality was found, and both heart and lungs were normal. There was no clinical evidence of uterine or ovarian abnormality.

Progress.—Internal nasal applications of various kinds having been tried over a prolonged period and having failed, she was advised to see an ear, nose, and throat surgeon, who reported there was no evidence of inflammatory disease in the nasal cavities, and advised submucous resection of the septum. He expressed some doubt as to whether this operation would relieve her rhinorrhoea, though he thought it might help with the congestion and headache. A radiograph of the nasal sinuses showed no sign of inflammatory disease. The septum was resected in June, 1938. Apart from relieving the pain, this procedure produced no beneficial effect, and in fact the patient stated that the rhinorrhoea was becoming more profuse. Further intranasal applications were tried, but without success. It was then decided to investigate the nasal condition from the point of view of allergic sensitivity.

Investigation for Allergy.—As there was no lead in the history the cutaneous reactions of a number of substances were tested by the intradermal method. Slight positive reactions to milk, wheat, egg, dog, cat, feathers, wool, and dust were obtained, and from this it was concluded that she was an allergic individual who had not become strongly sensitized to any particular foreign protein or proteins. We thought it reasonable, therefore, to try non-specific desensitization in the hope of improving her present condition, or at least of preventing any further sensitization from taking place. In mid-October, 1938, the patient took to her bed with severe menorrhagia and rhinorrhoea. She was advised to go into hospital for exploratory dilatation and curettage of the uterus, and examination under an anaesthetic, but refused. It was then decided to try empirically a course of extract of corpus luteum in order to check the menorrhagia. Meanwhile it had been arranged to give her a desensitizing vaccine for the nasal condition as soon as this could be prepared. This vaccine was never used, as will be seen below.

HORMONE THERAPY

From October 19 gestone (Paines and Byrne), 5 international units, was given intramuscularly daily for the three days preceding the menstrual period. Gestone is a synthetic form of progesterone dissolved in arachis oil. As such, it is of course entirely free from any other ovarian extract. The result of this treatment was a greatly diminished period. After the first of these injections, but before the period was due to begin, the patient asked whether the sudden improvement in her nasal condition could possibly be due to this injection. She was assured that this was not possible, as the injections were intended to relieve her excessive menstrual bleeding, and that they would have no effect on her nose.

One week after the cessation of menstruation the patient began a course of gestone (progesterone), 2 international units intramuscularly, on alternate days, five injections over a period of ten days being given. This resulted in menstruation being postponed until the full twenty-eight days had elapsed. No nasal congestion or discharge occurred for five weeks dating from the first injection. Eleven days after the last injection, and during menstruation, there was a very slight recurrence of rhinorrhoea for half an hour. During the period of freedom from symptoms the cutaneous reactions were repeated, and the results differed in no material respect from those obtained on the previous occasion. Owing to stress of work the patient was unable always to present herself at the appropriate time for injection, but as near as possible twice-weekly injections of progesterone (gestone), 2 international units, were given for the latter fortnight of a normal menstrual cycle. This was continued for two months.

RESULTS

During this time the patient had an average of two attacks of rhinorrhoea per month, of greatly diminished intensity. The menstrual cycle lengthened out to twenty-four and twenty-six days respectively, with normal loss over a five-day period. Thereafter, following the great diminution in the intensity and frequency of the attacks, treatment has been withheld, and since withholding treatment she has had one slight attack of spasmodic rhinorrhoea in a month. The patient regards herself as cured of both conditions and is highly delighted with the

result. The attacks themselves have been reduced from twice or three times a week to once a month, with a great diminution in severity.

It should be emphasized that the relief of nasal symptoms occurred before the patient could possibly have known how beneficial the treatment was going to prove in the relief of her menorrhagia. While under treatment with progesterone it was noted that the two attacks of rhinorrhoea coinciding with menstruation developed thirty-six and forty-eight hours respectively after the last injection. The remaining attacks, not coinciding with menstruation, were separated by an interval of not less than seven days after the last injection. Throughout treatment there has been no alteration in her environment, daily life, in the nature of her work, or in the length of her working hours. She is at present continuing in the same post that she has held for the last four years.

Discussion

That some relationship may exist between the nasal mucosa and sexual activity has been observed for centuries. In recent times Mackenzie (1884) noted that some women, with otherwise healthy noses, suffered from nasal congestion at the time of menstruation, and also that this congestion was sometimes present in members of both sexes as a result of sexual activity; more recently still, work has been done on monkeys and on the human subject which appears to prove beyond reasonable doubt that oestrin, whether applied locally or given by injection, can cause nasal turbescence (Mortimer *et al.*, 1936a, 1936b), and that this effect can also be produced by the male sex hormone (Hamilton, 1937-8). Hoseason (1938) describes cases of vasomotor rhinorrhoea and nasogenic asthma associated with the menses, and recommends treatment by intranasal zinc ionization. The effect of progesterone, however, does not appear to have received attention, and we feel that its success in controlling severe rhinorrhoea in our one case merits further investigation. A promising line for clinical research is indicated, which can be simply carried out. The effect of progesterone can be observed in a series of cases of spasmodic rhinorrhoea, and we hope to observe its effect on hay-fever during the coming summer.

Spasmodic rhinorrhoea is, of course, often due to allergic sensitivity, but, as Oriel (1936) points out, there is an important group of cases in which the patients are not specifically sensitive, as judged by skin tests, and which cannot be attributed to occupational or environmental factors. These cases may, like that under review, be suffering from a change in the secretion of the sex hormones, and may respond to suitable therapy. We think it possible that in our case, for instance, the patient was producing excessive amounts of oestrin, which caused her apparently unrelated symptoms. The physical factor—changes in temperature—may be taken as the exciting cause of her rhinorrhoea—"the last straw."

On the evidence available we are unable at present to say whether progesterone acts in direct antagonism to oestrin, whether it is inhibitory to the production of oestrin by the ovary, whether it has a specific action on the nasal mucosa, or whether some other factor may be responsible.

Summary

A case of spasmodic rhinorrhoea associated with menorrhagia has been treated with progesterone, and the results have been discussed.

We make no pretence of drawing conclusions from one isolated case such as this.

We wish to emphasize that the sole purpose of this paper is to draw attention to a possible line of research

which, if carried out on a sufficient number of suitable cases, we believe might yield valuable results.

We wish to express our thanks to Mr. R. Thomas, surgeon in charge of the ear, nose, and throat department, the York County Hospital, for his advice and help, and to Messrs. Paines and Byrne, Ltd., manufacturers of gestone, for the information they have very kindly supplied.

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PSYCHIATRIC SYNDROMES IN MYASTHENIA GRAVIS

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Recently two patients with different psychiatric syndromes were admitted to the Royal Edinburgh Mental Hospital, and in both the symptoms of myasthenia gravis were prominent. One of these patients was referred with the diagnosis of a severe psychoneurosis, and the other was admitted because he had become very disturbed in a general hospital ward. The case record of the former patient will be presented briefly to emphasize the necessity for differentiating between a psychogenic disorder and a myasthenia gravis, and also to convey a warning of the possibility that a frank organic process may develop insidiously in a patient with a psychiatric syndrome. The case record of the second patient will be presented briefly to illustrate a complicating factor of myasthenia gravis which proved to be difficult to handle therapeutically and which contributed to the fatal outcome.

Case I

A single woman aged 40 was admitted to the Jordanburn Nerve Hospital with the following complaints: sadness and crying spells, difficulty in swallowing and chewing, double vision, and weakness of the neck. Her past history was essentially negative. Inquiry into the family history showed that her father, who died from cerebral haemorrhage at 60, was a very domineering person, and was feared by his children. Her mother, at the age of 75, suffers from trigeminal neuralgia, and has been very domineering since her husband died, being feared by the children. The patient has three younger brothers—all well, and with a cheery open disposition. There is no neuropathic or psychopathic trend in the rest of the family.

PRESENT ILLNESS

The patient stated that as long as she could remember she has had various pains, aches, sensations of fatigue, anxiety, headaches, spells of sadness and blueness, and, in fact, cannot recall a day when she was well. She was reared in an atmosphere of extreme discipline, which engendered fear, anxiety, and trembling, and much personal suffering. In 1918 she experienced her first severe depression, at the age of 20. The occasion was a disappointed love affair, the mother refusing to consent to the patient marrying at this age. The