effective in 12 out of 15 animals when given for three months,¹² and extends previous preliminary results in women with endometriosis.^{13 14}

The one patient who did not respond to the treatment had a particularly severe form of the disease and was treated with agonist only once daily. During the course of this and other studies it became apparent that more frequent administration of the agonist might be more effective in maintaining suppression of follicular oestradiol (J Brancroft, R W Shaw, H M Fraser, unpublished findings).

As reported in other studies on the effects of long term treatment with a luteinising hormone releasing hormone agonist for contraception^{6 8} the return of ovulatory cycles after the end of treatment was not delayed. Indeed, one of the patients who had presented with infertility became pregnant two months after stopping treatment with the agonist.

Although no important side effects of the agonist were reported during the six month treatment regimen, longer term treatment may lead to a degree of oestrogen suppression that results in hot flushes developing in some women, as has been observed in patients receiving agonist treatment for the premenstrual tension syndrome (J Brancroft, R W Shaw, H M Fraser, unpublished findings). It may well be necessary, however, to endeavour to achieve almost total suppression of ovarian function to allow endometriotic lesions to resolve and avoid the problem of prolonged unopposed oestrogen acting on the endometrium.

We thank Dr P Magill of Hoechst for supplying the luteinising hormone releasing hormone analogue and Mr L MacKenzie for assessing the endometrial biopsy specimens.

References

- Karnaky KJ. The use of stilbestrol for endometriosis—preliminary record. *South Med J* 1948;**41**:1109-11.
- Kistner RW. The use of progestins in the treatment of endometriosis. *Am J Obstet Gynecol* 1958;**750**:264-78.
- Friedlander RL. The treatment of endometriosis with danazol. *J Reprod Med* 1973;**10**:197-9.
- Laversen NH, Wilson KH, Birnbaum S. Danazol: an antigonadotropin agent in the treatment of pelvic endometriosis. *Am J Obstet Gynecol* 1975;**123**:742-7.
- Schmidt-Gollwitzer M, Hardt W, Schmidt-Gollwitzer K, et al. Influence of the LHRH analogue buserelin on cyclic ovarian function and on endometrium. A new approach to fertility control. *Contraception* 1981;**23**:187-95.
- Bergquist C, Nillius SJ, Wide L. Intranasal LHRH agonist treatment for inhibition of ovulation in women: clinical aspects. *Clin Endocrinol* 1982;**17**:91-8.
- Vickery BH. Female contraceptive potential of "super" agonists of LHRH as assessed in intra-human primates. In: Zatuchni G, ed. *LHRH peptides as male and female contraceptives*. Philadelphia: Lippincott, 1982: 109-25.
- Fraser HM. Effect of treatment for one year with a luteinizing hormone-releasing hormone agonist on ovarian, thyroidal and adrenal function and menstruation in the stump-tailed monkey (*Macaca arctoides*). *Endocrinology* 1983;**112**:245-53.
- Howie PW, McNeilly AS, Houston MJ, et al. Fertility after childbirth: infant feeding patterns, basal PRL levels and post partum ovulation. *Clin Endocrinol* 1982;**17**:315-22.
- Fraser HM, Sandow J, Krauss B. Antibody production against an agonist analogue of luteinizing hormone-releasing hormone: evaluation of immunochemical and physiological consequences. *Acta Endocrinol* 1983;**103**:151-7.
- Kistner RW, Siegler AM, Behrman SJ. Suggested classification of endometriosis relationship to infertility. *Fertil Steril* 1977;**28**:1008-10.
- Werlin LB, Hodgen GD. Gonadotropin-releasing hormone agonist suppresses ovulation, menses, and endometriosis in monkeys: an individualized intermittent regimen. *J Clin Endocrinol Metab* 1983;**56**:844-8.
- Meldrum DR, Chang RJ, Lu J, et al. "Medical oophorectomy" using a long-acting GnRH agonist—a possible new approach to the treatment of endometriosis. *Clin Endocrinol Metab* 1982;**54**:1081-3.
- Lemay A, Quesnel G. Potential new treatment of endometriosis: reversible inhibition of pituitary ovarian function by chronic intranasal administration of a luteinizing hormone-releasing hormone (LHRH) agonist. *Fertil Steril* 1982;**38**:376-9.

(Accepted 14 September 1983)

Acne and anticonvulsants

R GREENWOOD, P B C FENWICK, W J CUNLIFFE

Abstract

The severity of acne and rate of excretion of sebum were assessed in 243 patients with epilepsy taking various anticonvulsants who were in hospital long term and in matched controls derived from a normal population of 2176 people. Neither the prevalence of acne nor the sebum excretion rate significantly increased in the patients compared with the controls or in patients taking phenytoin compared with those not.

It is concluded that anticonvulsant treatment does not cause acne.

Department of Dermatology, General Infirmary, Leeds LS1 3EX
R GREENWOOD, BM, MRCP, senior registrar
W J CUNLIFFE, MD, FRCP, consultant dermatologist

Maudsley Hospital, London SE5 8AZ

P B C FENWICK, MRCPsych, DPM, consultant neuropsychiatrist

Correspondence to: Dr R Greenwood.

Introduction

Phenytoin was first made available for the treatment of epilepsy in 1938. Since then, despite a lack of clinical and scientific evidence, it has been widely believed and taught that anticonvulsants, and in particular phenytoin, cause or aggravate acne.¹ We report the results of a study of patients with epilepsy who were taking anticonvulsants and were in hospital long term. We set out to ascertain whether acne was more prevalent in patients with epilepsy than in the general population. Seborrhoea is cited as being one of the causative factors in acne,² and we therefore measured the rate of excretion of sebum in a selected number of the patients. We also studied particularly those patients taking phenytoin as this is the drug most commonly linked with acne.

Subjects and methods

We studied 131 men (aged 16-70) and 111 women (aged 17-70). We graded the severity of their acne with a standardised technique with a high degree of interobserver correlation.³ The grades were compared with those assessed in 1077 men (aged 18-69) and 1099 women (aged 18-69) taken from a normal factory population and not receiving any drug.⁴ Statistical analysis for this comparison was by the χ^2 method.

The sebum excretion rate was measured in 37 men with epilepsy (mean age 32 (SD 1.67) years) by the gravimetric technique of Strauss and Pochi⁵ as modified by Cunliffe and Shuster.² Results were compared with the sebum excretion rate in a population of men not taking anticonvulsants but with acne of comparable severity.⁶

All the patients with epilepsy were taking at least one anticonvulsant. Exact data on drugs being taken by the women were not available. Of the men, 57 were taking phenytoin with or without other drugs. Other drugs included phenobarbitone, carbamazepine, sodium valproate, primidone, ethosuximide, and clonazepam.

Results

Severity and prevalence of acne—Table I shows the numbers of patients and controls studied, their ages, and the severity of acne. The prevalence and severity of acne in both male and female patients were similar to those in the normal population.

Rate of excretion of sebum—The figure compares sebum excretion rate and severity of acne in the men. There was no significant difference between the group with epilepsy and the normal group at any grade of acne.

Phenytoin—Table II shows the mean severity of acne and the rate

TABLE I—Grades of acne in patients with epilepsy compared with a normal population

	Men		Women	
	Epileptics	Non-epileptics	Epileptics	Non-epileptics
Aged 16-29				
Total No of subjects	40	612	30	746
No (%) with:				
No acne	15 (37.5)	86 (14)	10 (33)	103 (14)
Physiological acne	20 (50)	404 (66)	15 (50)	506 (68)
Clinical acne	5 (12.5)	122 (20)	5 (17)	137 (18)
Aged 30-70				
Total No of subjects	89	465	81	353
No (%) with:				
No acne	71 (78)	326 (70)	72 (89)	219 (62)
Physiological acne	17 (19)	130 (28)	9 (11)	113 (32)
Clinical acne	1 (1)	9 (2)		21 (6)

TABLE II—Mean (SD) acne grade and sebum excretion rate in men taking and not taking phenytoin

	Acne grade	Sebum excretion rate (ug/cm ² /min)
Men taking phenytoin	0.3 (0.07)	1.36 (0.21)
Men not taking phenytoin	0.4 (0.11)	1.32 (0.25)

Comparison of sebum excretion rates in patients with epilepsy and non-epileptic controls according to grade of acne. Figures are numbers of patients and controls.

of excretion of sebum in men with epilepsy according to whether they were taking phenytoin. There was no significant difference in either variable between the two groups.

Discussion

Phenytoin may cause hirsutism^{7,8} and has been widely assumed to cause acne.^{1,8} One case has been reported of a patient whose acne improved dramatically on withdrawal of phenytoin having previously failed to respond to conventional acne treatment.⁹

High doses of testosterone increase the sebum excretion rate by 10% in men and by more in women. Drugs that have an androgenic effect can thus theoretically produce acne. Because of the apparent androgenic effect of phenytoin any increased prevalence in acne has been presumed to be caused by stimulation of the pilosebaceous unit.⁹ Evidence of hormonal changes caused by phenytoin is conflicting,⁸ and testosterone concentrations in men receiving phenytoin treatment have only recently been measured in conjunction with the present study (P Fenwick *et al*, unpublished findings). The concentrations were all within the normal range. The acne grades and sebum excretion rates grouped according to testosterone concentrations (low, medium, and high portions of the normal range) failed to show any variation, presumably because even at the lowest testosterone concentration there was already maximal stimulation of the sebaceous glands.

Our results indicate that there was no difference in severity of acne between people taking anticonvulsants and those in the normal population. When acne does develop in patients with epilepsy it develops at the same age as in the normal population and is as prevalent. There was no difference between the patients receiving phenytoin and those not.

The results of the study of sebum excretion rates uphold the clinical results, the sebum excretion rate measured being that expected for the severity of the acne. The sebum excretion rate was not increased in the patients taking phenytoin or phenobarbitone. This conflicts with the only other work on sebum excretion rates in such patients, which found a raised sebum excretion rate in patients taking phenobarbitone compared with those receiving promethazine and phenothiazine, the rates in these two groups being those found in a normal population.¹⁰

We suggest that it is a myth that anticonvulsants cause acne.

References

- Shuster S. *Dermatology in internal medicine*. Oxford: Oxford University Press, 1978:45.
- Cunliffe WJ, Shuster S. Pathogenesis of acne. *Lancet* 1969;i:685-7.
- Cunliffe WJ. *Acne*. London: Update Publications, 1981:10-1. (Post-graduate centre series.)
- Cunliffe WJ, Gould DJ. Prevalence of facial acne vulgaris in late adolescence and in adults. *Br Med J* 1979;ii:1109-10.
- Strauss JS, Pochi PE. The quantitative gravimetric determination of sebum production. *Journal of Investigative Dermatology* 1961;36:293-8.
- Cunliffe WJ, Cotterill JA. *The acnes*. Eastbourne: W B Saunders, 1975:141.
- Bray PF. Diphenylhydantoin (Dilantin) after 20 years. A review with re-emphasis by treatment of 84 patients. *Pediatrics* 1959;23:151-61.
- Sparberg M. Diagnostically confusing complications of diphenylhydantoin therapy. *Am J Med* 1963;59:914-30.
- Jenkins RB, Ratner AC. Diphenylhydantoin and acne. *N Engl J Med* 1972;287:142.
- Stuttgen G. Zentralnervensystem und Talgsekretion. *Archiv für Klinische und Experimentelle Dermatologie* 1964;219:795-9.

(Accepted 16 September 1983)

THE GUMS, AND THEIR INFIRMITIES—For a Scurvy in the gums—Take Cloves, and boil them in Rose-water, then dry them, and beat them to powder, and rub the gums with the powder, and drink the decoction in the morning fasting an hour after it. Use red Rosewater, for that is the best. For rotting and consuming of the gums—Take Sage-water, and wash your mouth with it every morning, and afterwards rub your mouth with a Sage-leaf. (Nicholas Culpeper (1616-54) *The Complete Herbal*, 1850.)