history of non-diabetic renal disease and for all of them bacterial culture of the urine yielded negative results. None were taking drugs other than insulin or had any disease other than diabetes.

The patients were recruited from three groups according to their albuminuria. Group 1 comprised 28 patients with normal urinary albumin excretion (<30 mg/24 h); group 2 comprised 25 patients with increased excretion (30-300 mg/24 h)—that is, with incipient diabetic nephropathy; and group 3 comprised 22 patients with increased excretion (>300 mg/24 h—that is, with clinical diabetic nephropathy. Seventeen healthy non-diabetic people served as controls.

The table gives details of the findings. The plasma concentration of von Willebrand factor, measured by microenzyme linked immunosorbent assay (ELISA),² was similar in controls and patients in group 1 but was significantly increased in groups 2 and 3 ($p<0.05$). The difference in concentration between groups 1 and 2 was 0.29 mU/l (95% confidence interval 0.09 to 0.49) and between groups 1 and 3, 0.36 mU/l (0.14 to 0.58 mU/l). In multivariate analysis of the logarithmically transformed urinary albumin excretion (ELISA), haemoglobin A_{1c} (chromatographic technique), serum creatinine concentration (reaction rate kinetic principle), and mean blood pressure (diastolic blood pressure plus 1/3 (systolic minus diastolic)), only the logarithmically transformed urinary albumin excretion was independently associated with the plasma concentration of von Willebrand factor. There was no independent association with retinopathy.

Results and clinical data on patients and controls. Values are means (confidence intervals) unless stated otherwise

Variable	Controls (n=17)	Group 1. Normal urinary albumin (<30 mg/24 h) (n=28)	Group 2. Incipient nephropathy (urinary albumin 30-300 mg/24 h) (n=25)	Group 3. Clinical nephropathy (urinary albumin >30 mg/24 h) (n=22)
No of men:	7	11	13	10
Median (range) age (years)	33 (22-47)	31 (19-48)	33 (22-53)	33 (19-48)
Blood pressure (mm Hg)	86 (92 to 90)	87 (84 to 90)	97 (92 to 102)	102 (97 to 107)
Serum creatinine (μmol/l)	76 (71 to 81)	78 (75 to 81)	82 (74 to 90)	90 (82 to 98)
Blood glucose (mmol/l)	4.2 (3.4 to 5.0)	9.7 (8.0 to 11.4)	8.6 (6.6 to 10.6)	10.9 (8.8 to 13.0)
Haemoglobin A _{1c} (%)		7.6 (7.2 to 8.0)	8.9 (8.1 to 9.7)	9.6 (8.9 to 10.3)
Insulin dose (IU/kg)		0.64 (0.57 to 0.71)	0.63 (0.55 to 0.71)	0.70 (0.59 to 0.81)
No of patients with:				
<3 Microaneurisms		23	11	1
Simplex retinopathy		4	10	9
Proliferative retinopathy		1	4	12
Mean (range) urinary albumin (mg/24 h)		8 (3-16)	96 (39-299)	638 (310-6000)
Plasma von Willebrand factor (mU/l)*	0.96 (0.79 to 1.13)	0.94 (0.83 to 1.05)	1.23 (1.06 to 1.40)	1.30 (1.11 to 1.49)

*Plasma concentration of von Willebrand factor was significantly increased in groups 2 and 3 compared with group 1 and normal subjects (multiple range test followed by unpaired *t* tests) $p<0.05$.

Comment

We found an increased plasma concentration of von Willebrand factor in diabetics with persistently but only slightly increased urinary albumin excretion but a normal concentration in those with normal urinary albumin excretion.

The von Willebrand factor is a glycoprotein synthesised by endothelial cells, and an increased plasma concentration indicates endothelial damage.³ Our findings suggest that an increased influx of the factor to the plasma is possibly caused by generalised endothelial damage in patients with early diabetic nephropathy. An increased concentration has been associated with diabetic microangiopathy (defined as retinopathy),⁴ though no information on urinary albumin excretion was given. As proliferative retinopathy is seen predominantly in patients with proteinuria the results reported by Porta *et al* could be explained by a higher prevalence of proteinuria among patients with retinopathy. This assumption is supported by our finding of no independent association between retinopathy and the plasma concentration of von Willebrand factor.

The relation of the increased plasma concentration of von Willebrand factor to the development of cardiovascular disease is uncertain, but the presence of this factor is essential for platelet adhesion to subendothelium.⁵ This adhesion is an important step in the first phase of the formation of a haemostatic plug, and increased platelet adhesion has been found in diabetic microangiopathy.

We believe that the increased plasma concentration of von Willebrand factor is due to a generalised vasculopathy in diabetics with albuminuria. Our study suggests that young diabetics with persistently increased urinary albumin excretion suffer not only from early renal disease but also from widespread vascular disease, which is possibly important for the development of macroangiopathy.

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Hidradenitis suppurativa associated with use of oral contraceptives

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Hidradenitis suppurativa is a disorder affecting the axillary apocrine sweat glands, anogenital regions, and breasts, resulting in recurrent boils at these sites.¹ We report seven cases that occurred in patients taking the combined oestrogen-progestogen pill.

Seven women, who had attended one of three family planning clinics or a general practitioner's surgery from February 1987 to December 1987 were identified in whom hidradenitis suppurativa had developed while

they were taking the contraceptive pill. The table gives details of the use of the pill in these patients and its temporal relation with the development and exacerbation of hidradenitis suppurativa. We have described one case in detail to illustrate the salient features of this association.

Case report

A 23 year old woman was prescribed Conova-30 (ethinylloestradiol 30 μg-ethynodiol 2 mg) in 1981. One month later she developed hidradenitis suppurativa of the anogenital region and was treated with antibiotics. A further three episodes occurred up until October 1982, when Conova-30 was changed to Eugynon-30 (ethinylloestradiol 30 μg-levonorgestrel 250 μg) because of mid-cycle bleeding. Between October 1982 and June 1987 another eight episodes

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Patient	Age (years)	Pill used before without development of hidradenitis suppurativa	Pill used at onset and during exacerbations of hidradenitis suppurativa	Duration from use of pill to development of hidradenitis suppurativa (months)	Part of body affected	Treatment	Pill used after development but without recurrence of hidradenitis suppurativa
1	26		Microgynon-30	2	Axillae	Two operations	
2	27	Brevinor	Ovranette	8	Anogenital Right groin	Antibiotics One operation	
3	39	Ovulen-50	Microgynon-30,	2	Axillae	Antibiotics	
4	18		Micronor Microgynon-30	1	Anogenital Right breast Right groin	Antibiotics	Logynon
5	21		Ovranette	24	Axillae	Antibiotics	Logynon
6	17		Microgynon-30	2	Anogenital	Antibiotics	
7	23		Conova-30, Eugynon-30, Microgynon	1	Anogenital	Antibiotics	Marvelon Logynon

Microgynon and Ovranette—ethinylestradiol 30 µg-levonorgestrel 150 µg; Brevinor—ethinylestradiol 35 µg-norethisterone 500 µg; Ovulen-50—ethinylestradiol 50 µg-ethynodiol 1 mg; Micronor—norethisterone 350 µg; Logynon—ethinylestradiol 30/40/30 µg-levonorgestrel 50/75/125 µg; Marvelon—ethinylestradiol 30 µg-desogestrel 150 µg; Conova-30—ethinylestradiol 30 µg-ethynodiol 2 mg; Eugynon-30—ethinylestradiol 30 µg-levonorgestrel 250 µg.

of severe hidradenitis suppurativa occurred, which required antibiotics despite a change of pill to Microgynon-30 (ethinylestradiol 30 µg-levonorgestrel 150 µg) in June 1986. In June 1987 Microgynon-30 was changed to Logynon (ethinylestradiol 30/40/30 µg-levonorgestrel 50/75/125 µg) and her symptoms did not recur.

Comment

In most cases reported, a strong temporal relation was apparent between the initiation of treatment with certain combined oral contraceptives (see table) and the onset of hidradenitis suppurativa. Complete resolution occurred in two patients with recurrent disease in whom oral contraceptives were discontinued. A further three patients benefited from a change to a combined pill containing a higher oestrogen:progestogen ratio. One patient relapsed within one month of changing to Marvelon (ethinylestradiol 30 µg-desogestrel 150 µg), a pill previously recommended for these patients as desogestrel is thought to have few or no androgenic properties.² The relapse may, however, have been a continued metabolic consequence of her taking Microgynon-30 before. The other patient who remained on a progestogen only pill continued to have relapses of hidradenitis suppurativa.

Although acne has been reported in women taking oral contraceptives,³ no association has been reported with hidradenitis suppurativa.⁴ Furthermore, since 1955 the Committee on Safety of Medicines has received only one report of abscess formation and a further report of pustular rash associated with the use of oral contraceptives. As in acne vulgaris, androgens appear to be a prerequisite for the development of hidradenitis suppurativa, and raised testosterone concentrations have been found recently in these women.⁴ Oestrogens benefit patients with acne and possibly hidradenitis suppurativa by increasing the concentration of circulating sex hormone binding globulin. Androgens are bound more avidly than oestrogen to this protein and are therefore less freely available to the

tissues. Possibly the progestogens in these contraceptives, all 19-nortestosterone derivatives, cause hidradenitis suppurativa because of their androgenic properties, though it seems that this effect can be overcome by preparations containing a higher oestrogen:progestogen ratio such as found in the sequential pill (Logynon). The degree of androgenicity of the progestogens may also differ, levonorgestrel and ethynodiol being more androgenic than norethisterone, and newer preparations, such as desogestrel and gestodene, being alleged to have minimal or no androgenic properties.² This would explain the lack of correlation of hidradenitis suppurativa with many other combined contraceptives and the benefit shown in three of our patients when changed to a sequential combined pill with a higher oestrogen:progestogen ratio. We suggest that treatment in these cases should be an alternative form of contraception or, if an oral contraceptive is indicated, one that has more oestrogenic properties.

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Correction

Aluminium accumulation and immunosuppressive effect in recipients of kidney transplants

An authors' error occurred in this paper by Dr K P Nordal and others (17 December, p 1581). "Haplotype" was omitted from the first sentence of the Patients and methods section. The sentence should have read, "We studied 94 adult patients, who gave their informed consent to participate and received a kidney graft from a cadaver (n=66) or a living donor haplotype identical for histocompatibility antigens (n=28) during one year (1983-4)."