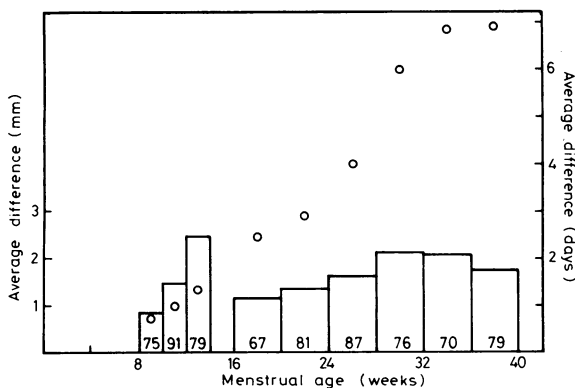


## Ultrasound evidence of sexual difference in fetal size in first trimester

Boys born at term weigh on average 50-150 g more than girls and are 0.5-1.0 cm longer.<sup>1 2</sup> At 1 year of age these differences have increased to 0.5 kg and 1-2 cm.<sup>1</sup> Conversely, among babies born prematurely a weight difference between the two sexes can be detected only in the last eight to 12 weeks before term.<sup>2</sup> These observations have led to the assumption that the sexual difference in weight and size is hormone dependent. In order to establish local normal tables of fetal growth a series of normal pregnancies were studied by ultrasonic scanning. Quite unexpectedly, male fetuses were already on average larger than female ones at the first measurement in the 8th to 12th week. Therefore a genetic rather than a hormonal mechanism is probably behind the sexual difference in fetal size.

### Subjects, methods, and results

The subjects studied were 101 healthy pregnant women with a reliable history of regular menstrual periods at 28-30 days' interval. Fetal age was calculated from the first day of the last period, knowing that fertilisation occurs two weeks later. In weeks 7 to 13 the fetal crown-rump length was measured two to four times at biweekly intervals.<sup>3</sup> From week 12 until term the transverse dimension of the fetal head, the biparietal diameter, was determined every four weeks.<sup>4</sup> The ultrasound scanner was a Nuclear Enterprises Disonograph NE 4102.



Difference between male and female fetus size during pregnancy (O = difference in days).

The columns in the figure show the average of the difference between measurements in male and female fetuses for each day during two-week periods (crown-rump length) and four-week periods (biparietal diameter). The number of observations in each period is given at the bottom of the columns. For each period the absolute difference was divided by the corresponding female growth velocity to express the difference in days. Analysis of the results showed that the fetuses tended to stay within tramlines. The growth curves of crown-rump length and biparietal diameter could be described by two square functions where the individual growth curves had a common curvature and almost identical slope but different level. The levels of crown-rump length and biparietal diameter were on average 2.0 mm ( $p < 0.01$ ) and 1.4 mm ( $p < 0.005$ ) higher in male fetuses than in female ones. Also, a simple sign test applied to the average values of crown-rump length and biparietal diameter for each day in the periods weeks 8 to 13 and 12 to 40, respectively, showed male fetuses significantly bigger than female ones ( $p < 0.05$  and  $p < 0.01$ ).

There were 52 girls and 49 boys in the series. The average birth weight of the boys was 40 g higher than that of the girls and they were 4 mm longer, which is less than the reported differences<sup>1 2</sup> but not significantly so. The picture might have been even clearer if the sample had had the usual birth-weight difference. There was no correlation between the mothers' height and fetal measurements of crown-rump length and biparietal diameter. This might be expected, since fetal weight is positively correlated to maternal height.

### Comment

In a series of 9846 measurements of biparietal diameter made from the 20th week till term Persson *et al*<sup>5</sup> found the diameter in male fetuses to be on average 1.7% larger than in female fetuses. Roughly

estimated, this must equal an average difference of 1.2 mm. Tables of fetal weight in weeks 28 to 40, based on birthweight data, show a small sexual difference at about the 28th week.<sup>2</sup> This increases towards term, and it has been generally assumed that the growth difference is hormone dependent.

The columns in the figure show the difference between male and female fetal size in two-week periods for crown-rump length and in four-week periods for biparietal diameter. To enable the differences in crown-rump length and biparietal diameter to be compared these are also expressed by the time necessary for female fetuses to reach male size. Expressed in this way the sex difference in fetal size apparently increases with fetal age, from approximately 1 day at 8 to 12 weeks of gestation to 6 to 7 days at term. Interpolation suggests an intercept with the time-axis to within a distance of a few weeks from the time of conception. Perhaps, therefore, the slightly lower growth rate of the female fetus is already encoded at conception—that is, it is determined by the sex chromosomes.

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## Outbreak of respiratory syncytial virus infection in the elderly

Respiratory syncytial virus mainly affects young children, with only about 2% of cases reported to the Communicable Diseases Surveillance Centre in the over-60 age group.<sup>1</sup> We describe an outbreak in a psychogeriatric hostel.

### Patients, methods, and results

Out of 40 residents aged 69-90 years, 17 suddenly developed fever, anorexia, and a non-productive cough. Findings in the chest ranged from a few basal crepitations to widespread rales and rhonchi. Most patients recovered rapidly in three to four days, but the first to become ill, an 81-year-old woman, developed a severe chest infection with left ventricular failure, deteriorated gradually, and died a month later. Six patients became ill about two weeks after the first case, eight a further five to eight days later, and two after a further five days. All were given antibiotics, usually amoxycillin or erythromycin.

Paired sera from two cases showed a rise in respiratory syncytial virus complement fixation titres (expressed as a reciprocal dilution) from less than 20 to 160. Convalescent sera from the other patients showed titres of 320 in three, 160 in eight, 80 in two, and 40 in two. Three residents who had not been ill were found to have titres of 20 in one case and 40 in the other two, and two members of staff who had been ill (one at the time of the index case) had titres of 80. Complement fixation titres to a wide range of other viruses, including influenza A and B and parainfluenza 3, were examined without any positive findings other than some mildly raised values to influenza A or B, or both, doubtless due to prophylactic immunisation three months before the outbreak described.

### Comment

Respiratory syncytial virus is a common cause of infection in children. Research in the United States has shown that in older

children and adults<sup>2</sup> infections are often mild, with only upper respiratory tract symptoms. Some are reinfections and also frequently mild illnesses. It is difficult to separate the effects of age and immunity in the expression of the disease.<sup>3</sup> Studies with adult volunteers show that the usual incubation period is three to seven days,<sup>4</sup> and the outbreak we describe had similar incubation periods. The symptomatic attack rate of about 40% seems high, but we were unable to study all the patients who were not ill, and possibly there were further asymptomatic infections, which may account for the apparent long incubation period between the first and subsequent cases. The asymptomatic residents who had titres of 20 and 40 may, in fact, have received a boost to their immune system.

Affected patients had illnesses which resembled mild attacks of influenza. Most had received influenza vaccine, and had virological studies not been undertaken the illness might have been ascribed to ineffective vaccines, particularly as the hostel had experienced an outbreak of influenza B infection the year before. In comparison the outbreak of infection with respiratory syncytial virus caused milder illness.

<sup>1</sup> The Communicable Diseases Surveillance Centre and the Communicable Diseases (Scotland) Unit. Respiratory syncytial virus activity in the United Kingdom 1979. *Journal of Infection* 1980;2:93-7.

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<sup>4</sup> Kravetz HM, Knight V, Chanock RM, et al. Respiratory syncytial virus. III. Production of illness and clinical observations in adult volunteers. *JAMA* 1961;176:657-63.

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## Systemic lupus erythematosus induced by aminoglutethimide

Aminoglutethimide has been used in the treatment of patients with advanced breast cancer, especially those with painful bone secondaries, as an alternative to adrenalectomy. It suppresses adrenocortical function and inhibits the conversion of androgens to oestrogens peripherally. The two main side effects are lethargy and skin rashes. We report a case of systemic lupus erythematosus induced by aminoglutethimide in a patient with stage IV carcinoma of the breast.

### Case report

A 57-year-old unmarried woman had a mastectomy for carcinoma of the breast (nodes positive) in December 1976. In July 1979 she had severe back pain. Radiographs showed metastatic disease of the dorsal spine. She was given palliative high-energy radiation to the spine, aminoglutethimide 250 mg four times a day, and cortisone acetate 25 mg twice daily. She was rather drowsy during the first week but had no rashes. On 9 January 1980 she presented with soft-tissue swelling of the fingers, inability to make a fist, and severe aching in the thigh muscles after ordinary exercise. There was no muscle tenderness and no evidence of vasculitis or skin changes. The erythrocyte sedimentation rate was 65 mm in the first hour, the sheep cell agglutination test for rheumatoid factor was negative, and the antinuclear factor test was positive on two occasions at a titre of 1:500 (homogeneous pattern). DNA binding was 68% (control 9%). Antinuclear antibodies had been monitored from the time of her mastectomy and none had previously been found. Radiographs of the chest and hands showed no abnormality. The most likely diagnosis was thought to be systemic lupus erythematosus despite the fact that the American Rheumatism Association criteria were not fulfilled. There was a polyclonal rise in serum immunoglobulin concentrations, as follows: G 210 IU/ml (normal range 128-199), A 340 IU/ml (normal range 60-129), M 330 IU/ml (normal range 97-181). Complement C3 and C4 and muscle enzyme concentrations were normal. The urine showed no abnormalities.

The patient's symptoms worsened, her erythrocyte sedimentation rate rose to 94 mm in the first hour, and on 6 February the aminoglutethimide was discontinued. Within three days her symptoms began to settle, but a week later her erythrocyte sedimentation rate was 103 mm in 1st hour. No treatment was given. During the next two weeks her erythrocyte sedimentation rate fell to 45 mm in 1st hour and she fully recovered. Three months later she was well, although the antinuclear factor remained positive (1:100) and DNA binding was 40%.

### Comment

Aminoglutethimide appears to be a promising drug in the management of breast carcinoma, but careful monitoring for side effects is essential. Aminoglutethimide is similar in structure to many anti-convulsant drugs (including methoin, phenytoin, primidone, troxidone, and ethosuximide) which are known to produce systemic lupus erythematosus.<sup>1</sup> It was originally given as an anticonvulsant but was withdrawn from use when pronounced hypothyroidism and adrenocortical insufficiency were noted as side effects. In our patient the test for antinuclear factor was negative before aminoglutethimide was started. Her symptoms responded rapidly to its withdrawal. Therefore the systemic lupus erythematosus may reasonably be ascribed to its administration.

"Spontaneous" systemic lupus erythematosus usually occurs in a younger age group. Wallach<sup>2</sup> described a lupus-like syndrome in two patients with breast cancer who had been treated with irradiation. In both cases the antinuclear factor showed a speckled pattern. Our patient had received high-energy radiation, but the rapid response to the withdrawal of aminoglutethimide suggests that irradiation was not the causative agent. There have been conflicting reports about the presence of autoantibodies in patients with cancer. Wasserman *et al*<sup>3</sup> confirmed that the incidence of antinuclear antibodies and smooth-muscle antibodies was greater in patients with carcinoma of the breast than in healthy age-matched controls, and Mittra *et al*<sup>4</sup> and Turnbull *et al*<sup>5</sup> found that this incidence was stage-related. Antinuclear antibodies were not present in our patient before she received aminoglutethimide, and therefore presumably were not related to her metastatic disease. We conclude that aminoglutethimide should be added to the list of agents capable of inducing systemic lupus erythematosus.

<sup>1</sup> Alarcon-Segovia D. Drug-induced systemic lupus erythematosus and related syndromes. *Clin Rheum Dis* 1975;1:573-82.

<sup>2</sup> Wallach HW. Lupus-like syndrome associated with carcinoma of the breast. *Arch Intern Med* 1977;137:532-5.

<sup>3</sup> Wasserman J, Glas U, Blomgren H. Autoantibodies in patients with carcinoma of the breast. *Clin Exp Immunol* 1975;19:417-22.

<sup>4</sup> Mittra I, Perrin J, Kumaoka S. Thyroid and other autoantibodies in British and Japanese women: an epidemiological study of breast cancer. *Br Med J* 1976;ii:257-9.

<sup>5</sup> Turnbull AR, Turner DTL, Fraser JD, Lloyd RS, Lang J, Wright R. Autoantibodies in early breast cancer: a stage-related phenomenon. *Br J Cancer* 1978;38:461-3.

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ONE HUNDRED YEARS AGO The metric system makes its way among English and American medical men with some difficulty. Some of the mistakes made in writing about these metric matters are truly comical. The editor of a Western medical journal informs his readers that the nickel five-cent piece is "just a metre in diameter"! This is as good in its way as the story of the New Jersey editor, who, during the Franco-German war, having read in the foreign telegrams that "Bazaine had moved twenty kilometers out of Metz," sat down and wrote the following editorial comment thereupon:—"All friends of humanity in warfare will be delighted to hear that all the kilometers have been removed, and that the innocent people of Metz are no longer endangered by the presence of these devilish engines of war—sleeping on a volcano, as it were." Then he went on to describe some experiments made with kilometers in the Crimea, in which one of them exploded and blew a frigate out of the water. (*British Medical Journal*, 1880.)