1951). Brodie in 1818 described five cases with Reiter's disease, of which two suffered from recurrent attacks of iritis. Stanworth and Sharp (1956), after a careful study of the whole problem, concluded that iritis was especially associated with Reiter's disease and all forms of spondylitis, but that its association with rheumatoid arthritis was probably coincidental. Csonka (1958) found iritis developed in 21 of a series of 185 patients with Reiter's disease and that 9 of the patients with iritis also had evidence of sacro-iliitis. Ford (1953) and others have described cases of Reiter's disease in which the patients have suffered multiple attacks of iritis after apparent recovery from the arthritis.

Of the 12 patients with iritis in the group showing sacro-iliac disease studied here, no fewer than nine had recurrent attacks. In the majority, most of the episodes of iritis were not associated with arthritis or obvious genito-urinary disorder. Careful examination showed evidence of prostatitis in all. The attacks of iritis persisted over a period of years in many of the patients, and four had to have an iridectomy performed. As iritis is often the sole manifestation of the disease such patients usually seek advice in ophthalmic departments, and the correct diagnosis of Reiter's disease is easily overlooked. A further fact which renders diagnosis difficult is that patients do not like to vouchsafe information relating to past episodes of urethritis, especially if these have been gonococcal.

Much diagnostic difficulty is met with when considering patients with ankylosing spondylitis who present with iritis (Birkbeck *et al.*, 1951). In such patients backache is not often a prominent feature, though restriction of spinal movements is usually present and indeed may be severe. The only differences between these patients and those described here with recurrent iritis is that the latter group all gave a past history of arthritis associated with urethritis and in addition there was little evidence of restriction of spinal movement. Patients with true ankylosing spondylitis sometimes give such a history, and it must be admitted that in a number of cases it is impossible to decide upon an exact diagnosis.

The development of radiographic evidence of sacro-iliitis in a patient suffering from Reiter's disease is of more than academic interest. Such a patient may suffer from recurrent attacks of iritis over a long period of time. He also seems to be more likely to develop recurrent or chronic arthritis, and on occasion the full syndrome of ankylosing spondylitis may be a sequel, though actual spinal involvement does not seem to be common.

Summary and Conclusions

Sacro-iliac disease demonstrable radiographically is common in Reiter's disease. Clinically appreciable involvement of these joints is probably common only during the acute stages of the disease, but the diagnosis may be easily missed. In cases of Reiter's disease special attention should be paid to the presence, site, and distribution of backache.

Sacro-iliac disease in this condition often appears to be associated with recurring attacks of iritis. This iritis is usually the only symptom. The occurrence of frequent attacks of iritis in the male should always lead to inquiry into the presence of a past history of Reiter's disease or its components. Evidence of sacro-iliac disease and genital infection should be carefully sought in such patients.

The difficulty of distinguishing cases of Reiter's disease with sacro-iliitis and associated iritis from some cases of ankylosing spondylitis is discussed.

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LETHAL HAZARDS OF THE LUTEAL PHASE OF THE MENSTRUAL CYCLE

BY

I. L. MacKINNON, M.B., Ch.B.

Department of Anatomy, King's College, London

P. C. B. MacKINNON, M.B., B.S., Ph.D.

Department of Anatomy, Royal Free Hospital School of Medicine, London

AND

A. D. THOMSON, M.A., M.D., M.R.C.P.

Bland-Sutton Institute, Middlesex Hospital, London

MacKinnon and MacKinnon (1956) reported that, in a series of 47 post-mortem examinations on women of reproductive age, death was found to have occurred in 45 cases during the luteal phase of the menstrual cycle. In the last two years 55 post-mortem examinations have been added to the series, and in these also the great majority of deaths occurred during the luteum. The present report is an analysis of the total of 102 post-mortem examinations.

Methods

Uteri were collected from a consecutive series of 131 necropsies on women aged 18-46 years carried out at one London mortuary. The uteri were opened, were fixed in 10% formol-saline, and a portion of the posterior wall was removed for histological examination. Sections (7 μ) were cut at right angles to the uterine cavity, stained with haematoxylin and eosin, and their endometria examined; 29 were discarded as menopausal or diseased. The remaining 102 were

Arrangement of a Consecutive Series of Deaths of 102 Women Aged 18-46 Years Into the Phases of the Menstrual Cycle in Which They Occurred

Phase of Menstrual Cycle and Duration in Days	Suicide	Accident	Disease
Bleeding (4) ..	Aspirin		Aortic incompetence mitral sten.
Follicular (10)	3 carb. monox.	Fract. skull Strangulation	Coron. occl. Congest. h. fail. Resp. failure Fibrous phthisis Aortic stenosis Rupt. aort. aneur. Septal defect Mitral stenosis Subarach. haem.
Early luteal (2)	4 carb. monox.	2 fract. skull Electrocution Drowning	6 subarach. haem. 5 coron. occl. 3 cereb. haem. 2 peritonitis 2 mitral sten. 2 rupt. aort. aneur. Cerebral emb. Coarct. aort. Status epilep.
Mid-luteal (7)	14 carb. monox. 8 barbiturate 2 aspirin Cyanide Hanging	4 carb. monox. 3 fract. skull Incised wounds	Hypost. pn. 2 coron. occl. Subarach. haem. Cerebral haem. Chr. anaemia Chr. bronchitis Status epilept.
Late luteal (5)	3 carb. monox. Barbiturate	Carb. monox. 5 fract. skull	

classified into five phases of the menstrual cycle: bleeding, follicular, early luteal, middle luteal, and late luteal, with average durations of 4, 10, 2, 7, and 5 days respectively (see Table). The endometrial appearances on which the classification was based were described by Lloyd (1951). They were that: (1) Follicular endometrium (Fig. 1) is relatively thin and contains small straight mucous glands lined by cuboidal epithelium containing deeply pigmented central nuclei. The stroma shows signs of proliferation with not infrequent mitotic figures. (2) Early luteal endometrium (Fig. 2) is slightly thicker and contains somewhat larger glands lined by columnar cells, the nuclei of which are slightly displaced towards the lumen by subnuclear globules of secretion. (3) Mid-luteal endometrium (Fig. 3) is thicker than early luteal endometrium and its glands are correspondingly larger. The cells lining the glands are increased in number, their nuclei being displaced towards the base of the cells and their globular material shifted towards the lumen. (4) Late luteal endometrium (Fig. 4) is much thicker than mid-luteal endometrium, its glands being longer and coiled, and the luminal margins of the cells frayed owing to extrusion of secretions. At this stage the stroma has a decidual appearance and contains large, plump, poorly staining cells.

FIG. 1.—Follicular endometrium.

FIG. 3.—Mid-luteal endometrium.

FIG. 2.—Early luteal endometrium.

FIG. 4.—Late luteal endometrium.

Results

The Table lists the causes of death which were established at the 102 necropsies in which the uterine endometrium was found to be both normal and cyclic.

During the first 14 days of the menstrual cycle—that is, during the bleeding and follicular phases—13 deaths occurred, while the remaining 89 deaths occurred during the luteal days of the cycle (see Table). On the basis of binomial distribution (Chambers, 1952) the expected number of deaths during the first 14 days—that is, before ovulation—was $102 \div 2 = 51$, while the actual number was 13, a difference of 38; and the standard deviation of the 102 chances was $\sqrt{102 \times \frac{1}{2} \times \frac{1}{2}} = 5$, which is less than one-seventh of the actual difference. Therefore $P < 0.001$.

During the mid-luteum, of seven days' duration—that is, half the total number of luteal days—60 deaths occurred, while 29 deaths occurred during the remaining seven days of the luteum (see Table). The significance of this result as tested by the use of binomial distribution is $P < 0.001$.

Statistically, therefore, the deaths in this series were significantly more frequent after than before ovulation, and significantly more frequent in the mid-luteum than in the remainder of the luteum.

Discussion

The main interest in these results is whether they apply to the total population of women in the age bracket 18–46 years.

The necropsies at which the suprarenal glands were obtained were performed in a coroner's mortuary and consequently the causes of death were specifically selected. This is borne out by comparison with the Registrar-General's report on the deaths, during the year 1957 in England and Wales, of women aged 15–44 years. The report records 18,998 deaths, of which 458 were suicides and 567 accidents. The combined suicides and accidents therefore amounted to 5% of the total, whereas in our series suicides and accidents formed more than 50%. The reason for this difference is clearly that a coroner's mortuary automatically receives the suicides and accidental deaths in the district but deals with deaths from disease only in exceptional circumstances.

Out of the 458 suicides reported by the Registrar-General, domestic gases were used in 50%, analgesic and soporific substances in 15%, the percentages in each of the other many causes being very small. In our series much the most common cause of death was domestic gases followed by analgesic and soporific substances, the two groups accounting for most of the suicides.

Of the 567 accidental deaths reported by the Registrar-General, half were road accidents, drowning accounted for 9%, barbiturates and other drugs 8%, fire and gases 6% each. In our series 50% of the accidental deaths were due to fractured skulls, no doubt largely due to road accidents, and 20% to gases, the two groups accounting for 16 out of the 20 cases.

Out of the 17,973 deaths from disease reported by the Registrar-General infections and parasitic disease claimed 10,177, neoplasms 2,650, diseases of the circulatory system 1,550, diseases of the respiratory system 1,047, and diseases of the C.N.S. and sense

organs 942. This pattern of causes is totally different from that of the present series, in which there are only three infections and one neoplasm out of a total of 44 deaths. However, deaths from these causes are usually anticipated and a diagnosis reached beforehand, with the result that few of them are directed to a coroner's mortuary. Deaths from diseases of the circulatory system accounted for 32 out of a total of 44 deaths. This high proportion could be expected because sudden deaths are so commonly of circulatory origin.

Frank (1931), Morton (1950), Bickers and Woods (1951), and many others have pointed out that emotional balance in women is less stable during the luteal phase of the menstrual cycle, and it is therefore not surprising that certain tragic consequences of their behaviour—suicide and death from misadventure—are more frequent during that phase. However, the reason for the high frequency of death from disease, or at least from diseases of circulatory origin, during the luteal phase of the cycle is not clear.

The premenstrual syndrome, a group of signs and symptoms in which emotional instability is prominent, has been said to reach its peak during one of the last 10 days of the cycle (Stieglitz and Kimble, 1949), but Greene and Dalton (1953) found that in 70 patients the syndrome was limited to the last five and the first four days of the cycle, with a peak on the penultimate day of the cycle. The peak of the premenstrual syndrome would therefore appear to be rather later in the luteum than the peak of luteal deaths.

Summary

One hundred and two consecutive deaths of women aged 18–46 years and having normal cyclic endometrium were placed, on the basis of their endometrial histology, in one of five phases of the menstrual cycle—namely, bleeding (four days), follicular (10 days), early luteal (two days), mid-luteal (seven days), and late luteal (five days).

The frequency of death was found to have been significantly higher during the luteum than during the bleeding and follicular phases, and to have reached its peak during the mid-luteal phase.

The possibility that these results apply to a wide population of women of reproductive age is discussed.

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Scientific and Learned Societies of Great Britain gives information on more than 800 societies, including details of objects, membership, publications, and library facilities. A list of the main research establishments other than university departments, technical colleges, and those attached to commercial undertakings is also given. The 59th edition of this handbook (215 pp.; 1958) is published by George Allen and Unwin Ltd., London, price 35s.