SPECIAL ARTICLE

Menstrual psychosis

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This paper reviews the literature on menstrual psychosis and proposes a new classification, adapting that of v. Krafft-Ebing (1902) and Jolly (1914). The world literature consists mainly of case reports; they include a few with data good enough for a statistical demonstration of the link between onset and menses. These well-documented cases include examples of pre-menstrual, catamenial, paramenstrual and mid-cycle onsets, and continuous illnesses with phasic shifts rhythmic with the menstrual cycle. In sufferers, episodes seem to be concentrated around the menarche and after childbirth. The clinical picture resembles that of puerperal psychosis, and there are at least 20 women who have suffered both psychoses at different epochs in their lives. Both seem to fall within the manic depressive rubric, so that menstruation can be another trigger of a bipolar episode. Some work suggests an association with anovulatory cycles. Cases starting before the menarche suggest a diencephalic origin.

Key words: Menstrual psychosis, menstruation, puerperal psychosis, manic depressive (bipolar) psychosis, menarche

The first observations of a possible connection between menstruation and psychological disorder appeared in the 18th century (1). At an early stage, menstrual mood disorder aroused forensic interest (2,3), and in 1827 was used as a defence in a case of filicide (4). Premenstrual psychosis was briefly described by Amard in 1807 (5), and by Brière de Boismont in 1842 (6), who also described catamenial psychosis in 1851 (7), and conducted the first survey of menstrual mood disorder. In 1858, Schlager (8) thoroughly reviewed the influence of menstruation on established mental illness, epilepsy, admission to mental hospital, suicide and crime. Berthier (9) and Icard (10) each amassed over 200 cases, which were, however, related to *all* menstrual disorders, including dysmenorrhoea, menorrhagia, amenorrhoea and the menopause. Their basis of classification was the presenting symptoms (e.g., kleptomania, pyromania, dipsomania, nymphomania, homicidal mania), not the timing of onset. In 1878, v. Krafft-Ebing (11) made the first of his two major contributions, describing 19 cases. In 1902 he wrote his monograph "Psychosis Menstrualis" (12), which introduced a temporal classification, under the headings of menstrual developmental psychosis, ovulation psychosis (single, relapsing and periodic) and epochal menstrual psychosis. In 1914, Jolly (13) revised this classification, emphasising the stage of reproductive life: psychoses starting before the menarche, at the menarche, at the menopause, recurrent menstrual psychosis, and epochal cases.

In spite of the excellence of these clinical observations and the eminence of v. Krafft-Ebing, the concept was not universally accepted. Indeed, it is probable that many psychiatrists have no knowledge of this disorder. The present review covers about 400 references, of which only the most important are cited here. A modified classification is proposed, adapting the ideas of v. Krafft-Ebing and Jolly: cases will be classified first by their timing within the menstrual cycle, and then by the reproductive epoch in which they occur.

DEFINITION

Menstrual psychosis has the following characteristics: a) acute onset, against a background of normality; b) brief duration, with full recovery; c) psychotic features: confusion, stupor and mutism, delusions, hallucinations, or a manic syndrome; d) a circa-mensual (approximately monthly) periodicity, in rhythm with the menstrual cycle.

Premenstrual tension and depression, or the menstrual exacerbation of chronic mental illness, are excluded.

Many of the cases described in the literature are based on retrospective accounts, reports from relatives and prospective studies without adequate duration or dating. These are considered *possible cases*. For a *confirmed case*, there must be enough detail on the onset of menses and psychosis to perform statistical tests, indicating a probability of <0.01. I have used a non-parametric and a parametric test. In both, the mean intermenstrual interval is calculated. In the non-parametric test, two episodes are used to define an interval within which the psychosis starts (the spread of onsets), and the number of episodes with exact timing is counted: $p = (a/b)^{n-2}$, where a = spread of onsets in days, b = mean inter-menstrual interval in days, n = number of timed episodes. In the parametric test, $t = \frac{\bar{x} - \mu}{s/\sqrt{n}}$, where x = mean onset of psychosis, μ = half the intermenstrual interval, s = standard deviation of the onsets of psychosis, n = number of timed episodes. This is referred to the t-distribution with n-1 degrees of freedom.

CLASSIFICATION BY TIMING WITHIN MENSTRUAL CYCLE

Premenstrual psychosis

These psychoses start during the second half of the cycle, and sometimes end with abrupt recovery at the onset of menstrual bleeding. This is an example:

A 16 year old girl had four mentally ill relatives on her mother's side (her grandmother and three aunts). Her menses began at 13. She presented with the history of three episodes of manic illness starting 12 days before and ending suddenly with the onset of the menses. She had a further six observed episodes for

which precise timing was available. The 4th episode began April 4th 1894 and ended suddenly with the menses on April 13th. The 5th started April 26th and ended with the menses on May 10th. The 6th started May 29th and ended with the menses on June 14th. In June, July and August there was no episode. The 7th episode began August 26th and ended with the menses (date not stated). She then had regular but increasingly mild premenstrual episodes until they ceased in March the following year. The menstrual cycle averaged 31 days and episodes began 9-16 days before menstrual flow. Using the non-parametric test, p = 0.027, and with the parametric test, t = 4.2 with 5 degrees of freedom (p<0.001). The abrupt cessation of symptoms with the onset of menstrual bleeding on four occasions adds further support [12, case 7].

This is one of seven confirmed cases (12,14-17). The first five satisfied at least one statistical test in relation to the timing of onset of the psychosis. In addition, the cases of v. Krafft-Ebing (12, case 7) and Knaus (18) fulfilled criteria in respect of the resolution of symptoms with the menses. There are 64 possible cases (5-7,9,11,16,19-62). Some authors published multiple cases. In view of the exaggerated claims made for the frequency of premenstrual tension, and the association of the premenstruum with poor examination results, shop-lifting, pyromania and suicide, these cases must be approached with scepticism, but there are a large number of them.

Catamenial psychosis

These are psychoses which begin with the onset of menstrual flow. There are three confirmed (11,63,64) and thirty possible cases (7,9,11,12,14,48,50,65-80). This is an example:

A 29 year old woman, who had earlier suffered prolonged attacks of mania, developed a recurrent episodic illness which returned every month for two years. The onset of the menses was recorded in 17 successive cycles, and averaged 25 days. The onset of 16 episodes was recorded. Their mean duration was 10 days. One started two days before menstrual bleeding. The others began up to six days (mean one day) afterwards. Using the non-parametric test, the probability that this sequence occurred by chance was $8/25^{12} = 0.0000007$. With the parametric test, t = 18.8 with 15 degrees of freedom (p<0.001) [11, case 12].

Paramenstrual psychosis

These are psychoses with variable timing, always in harmony with the menstrual cycle. Because of the broad spread of onsets, they require many episodes to reach the statistical threshold. Nevertheless, there are six confirmed (12,14,47,81-84) and 34 possible cases (11-13,26,30,35,43,48,50,85-99). This is Ewald's case (81,82):

A 36 year old multiparous woman suffered a series of 'stupors' and psychotic episodes, starting after her 7th child was born. No less than 35 were dated. The inter-menstrual interval was long, with only 10 menstrual periods per year. Attempts were made to arrest the process by irradiation. The spread of onsets was about 10 days before to one day after the end of menstrual bleeding, a span of 16 days. Using only the 20 episodes which occurred before castration, the probability that this sequence of onsets occurred by chance was $16/36.5^{18} = 0.00000026$.

Mid-cycle psychosis

This is comparatively uncommon. There are three confirmed (30,99,100) and eight possible cases (30,47,78,101-104). This is Wollenberg's case (99):

This patient had 14 manic episodes related to 15 menstrual cycles. The average onset was almost mid-way between the beginning of menstrual bleeding (18 days after the last and 16 days before the next), but the spread was wide, between 6 and 25 days before menstrual flow. The first half of the cycle was spared. With a mean cycle length of 34 days, the probability that this sequence of onsets occurred by chance was $20/34^{12} = 0.0018$. Using the parametric test, with the mid-cycle as the reference, t = 9.04 with 13 degrees of freedom (p<0.001).

Epochal menstrual psychosis

This is a term introduced by v. Krafft-Ebing to denote bipolar psychoses lasting for the complete cycle, with switches linked to menstruation. There are three confirmed (105-107) and six possible cases (9,12,92,108-110). This is an example:

A 22 year old patient suffered from depression after a life event, followed by a brief manic episode. She then embarked on a cyclical illness, with 8 manic and 7 depressive episodes, related to 8 menstrual cycles. Manic episodes lasted a mean of 15 days, starting 4-6 days after the onset of menstrual bleeding. Depression lasted a mean of 8 days, starting 1-5 days before the onset of the menses. With a mean menstrual interval of 24 days, the probability that this sequence of onsets occurred by chance was 0.00003 for mania, and 0.00004 for depression. The parametric tests were also highly significant [105].

CLASSIFICATION BY STAGE OF REPRODUCTIVE LIFE

Under this heading, I shall consider prepubertal cases, single episodes at the menarche, post-partum onset, sequences during periods of amenorrhoea, and onset after the menopause.

Single episodes at the menarche

Single episodes are a poor form of evidence. If there is an association of psychiatric illness with the menarche, it will

have to be established by case control or cohort studies. Nevertheless, it is interesting that such single episodes have often been described (10,13,34,40,67,69,78,92,108,111-115). Indeed, there is a possible reference in the Hippocratic apocrypha [111]: "At the first eruption of the menses… the blood appears in the womb. If it cannot escape, it hurls itself against the heart and the diaphragm, leading to torpor, drowsiness and insanity. This is followed by fever, fears, homicidal impulses, terrible utterances, command hallucinations and suicidal desires. I recommend these young ladies to get married as soon as possible. Pregnancy cures them."

This is a more modern example:

A 17 year old girl became ill on February 6th and was admitted to hospital the following day. Her condition worsened, and she became delirious on 8th and mute on 11th. On 13th, she suddenly recovered with the onset of her first menstrual period [12].

Prepubertal cases

These cases, of the greatest interest as aetiological clues, were first described in 1891 by Werner (116). Three years later, Friedmann (113) coined the term *primordiale menstruelle Psychose (menstruale Entwicklingspsychose)*, which was adopted by v. Krafft-Ebing (11). But some of the claimed cases have started after puberty, and it is important to use the term only for girls who develop circamensual episodes *before the menarche*. This concept also differs from the modern term "periodic psychosis of puberty" or "periodic psychosis of adolescence", not all of which would meet this strict definition. Without the anchor of menstrual bleeding, it is harder to confirm these cases statistically. But there are 14 cases with circumstantial evidence, some more convincing than others, the most convincing being that of Friedmann (113). There is no correspondence between these cases and the timing of post-pubertal episodes. Some appeared to be premenstrual, some catamenial, some epochal, one mid-cycle and others uncertain.

As a variant, Belhomme (117) described a 45 year old woman who had never menstruated, but who suffered a circamensual psychosis lasting several days, and remained perfectly calm in the interim. Two other reports describe monthly psychoses in girls who had never menstruated (58,118). Yamashita (17) published this unique case:

This patient developed an ectopic pinealoma at 7. This was treated by irradiation of the pituitary, which in turn caused diabetes insipidus and a prolonged prepubertal state. At 16, she was treated with oestrogen and progesterone to bring on menstrual bleeding, but stopped taking them three years later. A month after stopping the hormones, she developed a series of depressive illnesses with persecutory ideas. The intervals between onsets were 39, 22, 31, 30 and 25 days.

Observations on two medical diseases associated with menstruation are relevant here. In diabetes, cyclical changes in diabetic control have been observed in pre-pubertal girls (119), even as early as 9 years of age. In three cases, the disturbance continued after the menarche, with an almost identical cycle length. This phenomenon seems to indicate "a menstrual cycle before menstruation", and makes the reports of prepubertal menstrual psychosis seem less improbable.

The other medical disorder, menstrual hypersomnalism, has striking parallels with menstrual psychosis. Indeed, the first patient described by Pomme in 1765 (120) seemed to have a bipolar disorder, with premenstrual somnolence and menstrual excitement. The 19 cases in the world literature (120-134) include three with prepubertal onset (124,126,132). The importance of this parallel disorder is that there can be little doubt about its diencephalic origin, so perhaps this is also true of menstrual psychosis, and other psychoses linked to the female reproductive process.

Circa-mensual psychosis during amenorrhoea

There are a number of examples of a menstrual psychosis continuing when the menses failed to appear. This is the case of Guiraud et al (135):

An 18 year old girl was always a little excited during the days before her menses. On September 22nd, the day of onset of scanty menses lasting only one day, she suffered an attack of excitement and motor agitation. She recovered 20 days later, but relapsed on October 22nd. This was the day her menses were expected, but they did not return until May of the following year. During this 7 month spell of amenorrhoea, she had six further episodes, lasting 6-13 days, starting on November 21st, December 19th, January 23rd, February 18th, March 18th and April 14th.

In this example, a frank psychosis occurred only during a period of amenorrhoea, and there are others like it (11,71,78,136). In some instances, the amenorrhoeic episodes occurred shortly after the menarche (12,113,137-140) and these cases are perhaps related to the prepubertal group described above. A fair number of other cases have been described (12,18,43,47,49,91-94,108,141). In menstrual hypersomnalism, symptoms appeared or continued during amenorrhoea in two patients (121,134).

Onset after childbirth

This was first described in 1822 by Pritchard (142). There are three confirmed cases (143-145). This is an example:

A patient suffered a puerperal psychosis, from which she recovered. She then had twelve relapses, which were precisely

timed. The first four occurred 3, 9, 3 and 5 days before menstrual onset, and the next seven 10-21 days before. The full range, from 3-21 days (18 days) was 60% of the cycle. With a mean menstrual cycle of 30 days, the probability that this sequence of onsets occurred by chance was 0.006. It is interesting that the relapses, which began premenstrually, shifted to the mid-cycle [144].

Fifteen patients with three or more menstrual or premenstrual relapses have been described (43,48,78,106, 143-152). Many others had only one or two relapses (11,12,14,44,81,87,88,92,93,103,153-166). The total number of reported cases is about 50. A menstrual psychosis can begin in the puerperium, without a preceding puerperal psychosis (48,88,93). The onset of menstrual psychosis has also been described after a miscarriage (167), and a weaning psychosis (154).

In addition to the puerperal onset of menstrual psychosis, at least 20 women have suffered menstrual and puerperal psychoses at different epochs of their lives (4,12,27,33,78,84,87,108,122,134,168-177). This is the association of a rare psychosis with an illness that afflicts only 1/1000 parturient mothers.

The menopause

If menstrual psychosis is associated with the beginning of menstruation, or its return after the furlough of childbirth, one might expect it to appear as the pituitary-ovarian axis begins to splutter in the 5th decade. In the published material, there does not appear to be an increased frequency during this epoch. There are, however, descriptions of cases which *began* after the menopause (9,10,178), and one which began after partial ovariectomy (179).

FEATURES OF THE ILLNESS

Frequency

Menstrual psychosis is rare but, because of widespread ignorance, many cases go unrecognised and one can only guess at its incidence. I have encountered at least eight possible cases in my clinical practice during the last 10 years. The only survey among hospital admissions found one case among 1,000 admissions to the Charité Hospital in Berlin (88). In sufferers, only a small proportion of the approximately 400 menstrual periods a woman experiences are affected by psychosis. The Japanese cases, and those from Iraq (56), India (46), Vietnam (174) and the Yemen (60), suggest a worldwide disorder.

There have been a few surveys. In Germany, Schröter (86), in a study of 184 female inpatients of childbearing age, briefly mentioned four depressed women who had "a change in symptoms exactly in rhythm with the absent menstruation"; three developed manic states, and one had a menstrual psychosis. This was a comprehensive survey, but individual cases were described only briefly. Algeri (180) surveyed 314 women of reproductive age at the Frenocomio di Reggio-Emilia between 1880 and 1882: he identified 28 patients with *pazzia periodica*, and described two illustrative cases. Näcke (181) surveyed 99 female inpatients with chronic psychosis between 25 and 52 years of age, and found two cases of periodic mania related to menstruation. Burckhart (94) studied 48 manic depressive patients and 55 with 'atypical' (i.e. cycloid or acute polymorphic) psychoses: only 9/70 of those who were currently ill had menstrual onsets; a higher proportion (15/34) of those currently well had menstrual onsets, of whom 11 had atypical psychoses. This is the kind of investigation that is required, but his criteria were too loose. Another German study by Mall (182) reported a considerable number of periodic relapsing psychoses with a definite relationship to the menstrual cycle. In Japan, Wakao (183) studied acute benign psychosis in women, with episodic course and stupor, confusion or oneiroid states. This report was followed by a series of papers from Mie university (100,106,184). The total number of patients reached 219. A surprisingly large number had their first onset in the second half of the menstrual cycle (98/110, if one excludes postpartum cases). Diamond et al (185) questioned 63 women attending a lithium clinic about premenstrual symptoms: 7/31 still menstruating reported premenstrual hypomania, and 3/31 menstrual hypomania, but the same was true of the controls (healthy wives and social workers). Recently, Abe and Ohta (186) studied 11 cases of recurrent brief psychoses in adolescents: 2/6 with regular menses had episodes linked to the menses. In USA, Price and DiMarzio (187) compared premenstrual symptoms in 25 patients with rapid cycling affective disorder and 25 controls: severe premenstrual symptoms were found in 15 rapid cyclers and 5 controls.

Nosology

Menstrual psychosis is *not* a 'specific disease entity'. The arguments about its nosological status echo the perennial dispute about puerperal psychosis (188). The crucial evidence against its specificity is the observation that the most typical examples have manifested non-menstrual bipolar disorder at another stage of life – e.g., that of Mendel (105), in which the phasic psychosis metamorphosed into a chaotic, continuous illness. There are several indications that menstrual and puerperal psychoses are related. Their clinical range is similar: mania, stupor, catatonia, schizoaffective depression or cycloid episodes. A proportion of patients with puerperal psychosis relapse in the premenstrual phase. There are a substantial number of women who suffer from both psychoses at different times in their lives. Since there is much evidence that puerperal psychosis belongs with the manic depressive (bipolar) group (188), menstrual psychosis may also belong under this rubric. Menstrual psychosis, like puerperal psychosis, offers an opportunity to investigate the triggers which

unleash manic depressive and cycloid episodes in susceptible women. Associations have also been observed with weaning (131,189), post-abortion (12,47) and post-operative (29,159) psychoses.

Genetics

There have been no formal genetic studies, but there are case reports mentioning first degree relatives with menstrual psychosis (6,29,36,40,59,86,136,190) or with other psychoses related to female reproduction (12,14,141,152). These sporadic reports suggest that an international prospective molecular genetic study would be productive.

Hormonal studies

Menstrual psychosis may be related to the pituitary-ovarian axis, but there have been few hormonal studies.

Apart from the astonishingly detailed single case study of Cookson (47), only the Japanese have conducted systematic investigations. In the most detailed study, Kitayama et al (106) evaluated thyrotropin-releasing hormone, lutein-releasing hormone, dexamethasone suppression, insulin tolerance, circadian cortisol rhythms and growth hormone response to hypoglycaemia in up to 23 patients. The Japanese work (49,50,106,184,191,192) provides evidence for an association with anovulatory cycles, which were suspected in 44/60 cases studied by the Mie group. This would accord with the concentration of cases soon after the menarche, and after childbirth.

Treatment

This comes under three headings: hormones, agents suppressing the menstrual process, and a miscellaneous group.

There are many claims of successful treatment with progesterone (38,44,49,51,96,103,191,193-196). In several other patients it had no effect (143,148,190). Occasional cases have responded to oestrogens (49,78,174) or androgens (144). Others have responded to combinations of steroid hormones and oral contraceptives (16,48,194), or testosterone plus progesterone (40). Thyroid hormones have been curative (106,148). The patient studied by Horwitz and Harris (197) relapsed when thyroid was stopped. There have been no randomised, double blind controlled trials.

A hint that menstrual suppression might solve the problem comes from claims that pregnancy is beneficial (10,12,14,21,24,27,65,111,136,198-200). The menopause has also brought recurrent or chronic illness to a close in certain instances (19,86,197,201,202). Evans (72) described a patient who was cured by ovariectomy. In other cases there was no improvement with the menopause – e.g., cases 10 and 11 of v. Krafft-Ebing (11) – while that of Kirn (87) became worse after the climacteric. In the days before hormonal treatments, castration or induction of an artificial menopause were tried several times (10,12,30,135,203,204). Indeed, there was a vogue for this in USA in the late 19th century. In the cases studied by Krömer (89), Ewald (81,82) and Bondarew (190), determined attempts at castration failed to stop the sequence. Danazol, a drug which (among other effects) inhibits gonadotropic hormones, arrests the menstrual process; it has been used successfully (151). The discovery of the releasing hormones introduced a new range of menstrual suppressant drugs: the gonadorelins. They have been used in many medical disorders related to menstruation, and I have used them to induce a remission in menstrual psychosis.

Clomiphene, which promotes normal menstruation, is a rational treatment in women with anovulatory cycles. It has been used in Japan (49,106,184,192) and also by Cookson (47), whose patient conceived, and suffered a post-abortion psychosis. Successful treatment with phenytoin (97) and acetazolamide (53) has been claimed.

The most important point is that, for this disorder, the narrow range of psychotropic drugs is greatly extended by unconventional treatments which can be tried in turn. Since this is a recurrent illness, long-term prospective single case studies are appropriate.

CONCLUSIONS

Menstrual psychosis is a forgotten disorder: less is now known than used to be known. To some extent this is due to a laudable scepticism on the part of psychiatrists. It is important to be sceptical about an association with menstruation, because women spend 40% of their reproductive lives in the premenstrual or menstrual phase. But this scepticism contrasts with the credulity of physicians. Among the hundreds of cases of menstruation-related medical illness, only two – porphyria (205) and hypersomnalism (131) – had the precise timing necessary for statistical tests. This compares with the 27 cases collected here, meeting strict criteria. But physicians have the advantage of biochemical and physiological measures, such as porphyrins, peak respiratory flow and electro-encephalography, which are more sensitive than symptoms.

The world literature consists mainly of case reports. These have a distorted temporal and geographical distribution, with many reported before the first world war. This unevenness is due to cultural and linguistic barriers, and nosological fashions. Most of the literature is French, German or Japanese. Many gems of clinical observation have disappeared from the canon of current knowledge. Some of these early case reports had inadequacies: lack of scepticism and accurate dating. There was a general failure to conduct long-term follow-up studies, studying the natural history of the disorder, and assessing the effect of childbirth and the menopause. But we should acknowledge the meticulous contribution of the German language authors, who have supplied more than half the best-established cases. I hope this review of 27 confirmed and 200 possi-

ble cases will bring this disorder back into the discourse of modern psychiatry. The value of this ancient literature is not "to amuse the mind by the remembrance of old words" (206), but to sharpen the focus of neuroscientific studies.

"Evidence-based medicine" is the shibboleth of the day. But its main agenda is the efficacy of treatment. We also need criteria for establishing the validity of our nosological concepts. Menstrual psychosis illustrates the quest for this validation. The data are mainly from case lore, but the identification of diseases will always start with clinical observation. This leads to provisional definitions, measurements of severity, epidemiology, treatment trials and aetiological investigations. At this stage, we can conclude that menstrual psychosis is a morbid phenomenon related to the bipolar and perhaps cycloid (acute polymorphic) group. In the clinic, all consultants should be aware of it, because treatment can be radical. In the universities and institutes it is an heuristic hypothesis. There are aetiological leads to be followed, including the Japanese work on anovulatory cycles (perhaps suggesting a role for unopposed oestrogen), and the prepubertal cases (suggesting an origin above the level of the pituitary-ovarian axis).

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