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J. Schöpf · B. Rust

Follow-up and family study of postpartum psychoses**Part I: overview**

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Abstract A group of 119 patients suffering from a severe psychiatric postpartum disorder who were admitted for the first time in their life to a psychiatric hospital has been investigated. The onset of illness occurred within 3 months following delivery. The patients represented 92% of the total sample fulfilling the inclusion criteria. A follow-up investigation was performed after a mean of 21 years (range 2–35 years). Of the patients 66% had nonpuerperal psychotic episodes in later life. The diagnosis, taking into account the long-term course, was affective psychosis in 57%, schizoaffective psychosis in 18%, schizophreniform psychosis in 12%, brief reactive psychosis in 4% and schizophrenia in 9%. A bipolar psychosis was found in 31%. The relation of unipolar to bipolar psychoses corresponded to that in a control group of affectively ill women without puerperal onset. The frequency of a manic syndrome in bipolar psychoses at the index episode was the same as in nonpuerperal episodes, which does not suggest a mania-provoking pathoplastic effect of the puerperium. The comparison with female nonpuerperal controls matched for age and diagnosis revealed evidence of a better long-term course in the index patients. The risk of a puerperal relapse for further pregnancies was 35%. The global morbidity risk for functional psychoses in first-degree relatives was 11%, with affective psychoses representing the majority of secondary cases (6.8%). The index patients showed a nonsignificant lower morbidity risk in relatives than a control group of psychotically ill women without puerperal onset. The major aetiological factor found for postpartum psychoses is the relation of these disorders to functional psychoses. There is strong evidence that the postpartum period tends to provoke affective psychoses and other nonschizo-

phrenic psychoses, but not, or only to a lesser degree, narrowly defined schizophrenias. The liability to puerperal decompensations suggests some common pathophysiological mechanism, the nature of which remains unknown.

Key words Affective disorder · Schizoaffective disorder · Schizophrenia · Schizophreniform disorder · Brief reactive psychosis

Introduction

Up to and including the past century it was believed that postpartum psychoses were caused by some pathological condition specifically related to childbirth (e.g. Esquirol 1838). With the concept of endogenous psychoses – here called functional psychoses – most of these disorders were classified as manic depressive psychosis or schizophrenia (Kraepelin 1913). However, the symptomatology of postpartum psychoses is often quite complex, which makes diagnosis difficult.

Postpartum psychoses remain insufficiently characterised with respect to the knowledge required for clinical practice. Furthermore, their investigation may contribute to the nosology of functional psychoses. Compared to the frequency in women of childbearing age, the incidence of psychoses is highly increased in the postpartum period. In an epidemiological study (Kendell et al. 1987) the psychiatric hospitalisation frequency during the 3 months following delivery increased 12.7-fold, and in the first 4 weeks 21.7-fold. An important question is whether the distribution of diagnoses corresponds to that of a cross section of women in childbearing age or whether the incidence of certain psychoses is selectively increased.

This paper, which is an extension of a former investigation (Schöpf et al. 1984, 1985), gives an overview of a follow-up and family study of postpartum psychoses. Certain aspects are treated in separate publications (Schöpf and Rust 1994a–c). A comprehensive presentation of the entire study, using mainly another classifica-

J. Schöpf (✉)
Psychiatric University Hospital of Zurich, P.O. Box 68,
CH-8029 Zurich, Switzerland

B. Rust
Psychiatric Clinic, University Hospital of Zurich,
CH-8091 Zurich, Switzerland

tion ("study criteria"), however, is given elsewhere (Schöpf 1994).

Patients and methods

Two groups of patients, admitted to the Psychiatric University Hospitals of Lausanne and Zurich, were included. The index episode of the Lausanne sample had taken place in 1949–1980. The follow-up investigation of the first part of patients (hospitalisation 1958–1977) was performed in 1982, and that of the second part (hospitalisation 1949–1957; 1978–1980) in 1984. A second follow-up investigation was performed in 1990 for patients with a follow-up period of less than 10 years. In the Zurich sample the index episode had occurred between 1956 and 1964. The follow-up investigation was performed in 1990.

Patients were included in the investigation if the index episode had begun within 3 months postpartum, if this episode of illness was the first leading to psychiatric hospitalisation and if the patient had not died during the index episode. Patients with purely depressive reactions following a severe traumatic event not directly related to childbirth, like being abandoned by the partner, were not taken into account. Among the foreign patients hospitalised in Zurich who later returned to southern Europe, no attempt was made to contact them because this had been difficult in the Lausanne sample.

At the Psychiatric University Hospital of Lausanne a list of women suffering from postpartum psychosis had been kept for decades. Patients of the Zurich sample were identified by control of all case histories of female patients aged up to 45 years at the time of their first hospitalisation.

Classification

Most results are presented using the DSM-III-R. Overall, the investigation concentrated on disorders traditionally called functional psychoses, i.e. affective psychoses, schizophrenia and other nonorganic psychoses.

The DSM-III-R diagnosis of a schizoaffective psychosis was made applying the criterion "that the duration of all episodes of a mood syndrome has not been brief relative to the total duration of the psychotic disturbance" to the overall course. The very few cases with purely affective episodes of illness and with schizophrenic or schizophreniform episodes, but without episodes showing a period of mixed symptomatology (as required for the DSM-III-R diagnosis of schizoaffective psychosis), were also included among schizoaffectives. Concerning the diagnosis of brief reactive psychosis, the presence of a stressful event is required, and the birth of a child was considered as such. In patients with schizophrenic symptoms (including cases with schizoaffective psychosis) a classification into the pure paranoid subtype of schizophrenia (referred to as paranoid syndrome) vs all other subtypes was performed. Bipolarity was defined as occurrence in the long-term course of a manic, a schizoaffective manic or a hypomanic episode lasting at least 2 weeks. All DSM-III-R diagnoses were made by one investigator (J.S.).

A reliability investigation on the "study criteria" showed that the clinical syndromes could be recognised from case histories; the κ value for diagnoses of the index episode was 0.88, and that of diagnoses taking into account the long-term course was 0.79. The DSM-III-R criteria were not investigated for reliability.

For special questions, particularly in order to investigate patients for "atypical" psychopathology often described in the literature, the diagnostic concept of cycloid psychoses was used. According to Leonhard (1986) cycloid psychoses are a distinct entity characterised by episodes of illness with special symptomatology followed by full remission. For diagnosis the psychopathological criteria of Perris and Brockington (1981) were applied (see also Perris 1988). Because it was decided to base the diagnosis on psychopathological criteria only, and not on the course of illness, an

abrupt beginning and an outcome of full remission were not considered necessary criteria. The classification for the presence of a cycloid psychosis was made by one investigator (J.S.).

Index episode

The principal source of information was the case history of the patient. For patients hospitalised between 1949 and 1954 in Lausanne, the private notes of G. Schneider, who had personally examined these women, were used (Schneider 1957).

Besides the diagnostic classification patients were evaluated for the presence of confusional or delirious symptoms, referred to as confuso-oneiroid syndrome. French psychiatrists in particular (e.g. Rancunel and Marnie 1975) have considered this type of psychopathology highly characteristic of postpartum psychoses. A confuso-oneiroid syndrome was rated as present if at least three of the following symptoms were found: (1) disorientation; (2) incoherence; (3) delusions; (4) acoustic or optical hallucinations, or optical illusions. The individual delusions and the perceptual disturbances should not be phenomena coherently developed for longer periods; (5) if there was no disorientation, in addition to symptoms 2–4, psychomotor agitation must be present.

Psychological stress preceding the onset of the index episode was considered present if the patient had no partner, if there were obviously severe partnership conflicts, if the attitude of the patient concerning motherhood was persistently negative and if there was a case of death or severe malformations of the child.

The onset of illness was defined as the moment of first manifestation of psychopathological symptoms. Early-onset cases, beginning within 2 weeks following delivery, were distinguished from late-onset cases. Isolated cases which could not be classified with respect to this variable were included among early-onset cases (for an exception, see Schöpf and Rust 1994a).

The onset of illness was considered acute if the interval between the appearance of the first symptoms and invalidating or otherwise severe signs of illness was not more than 2 weeks. In addition, the age and parity at the index delivery were noted, also whether or not the patient had significant psychiatric symptoms during the index pregnancy; these must be differentiable from the index episode, i.e. they had to be essentially absent at the time of delivery, otherwise the case would have been considered prepartum onset and, therefore, excluded. Also investigated was whether before the index episode psychotic episodes not leading to psychiatric hospitalisation had occurred.

Follow-up study

The follow-up investigation was performed if possible by contacting the patient and by use of case histories on inpatient and outpatient treatments. If patients were in psychiatric treatment, the treating physician was asked for information. If necessary additional information was obtained from relatives, friends or the family doctor. In patients who had died or in cases of impossibility of personal contact for other reasons, someone who knew the patient well was questioned. The catamnestic interview took place in a semi-structured form using a check list.

The first contact was generally established by a telephone call. In the 1982 investigation a personal interview was arranged on this occasion. In patients still in psychiatric treatment the consent of the treating physician was obtained. Patients living far away as well as patients who only wanted this type of contact were interviewed by telephone. This latter reaction appeared to occur in women who recognised the utility of the investigation but who wanted to complete the interview rapidly because of disturbing memories. For practical reasons one author (J.S.) performed the investigations of 1984 and 1990 mainly by telephone. The two other investigators (C.B., see Schöpf et al. 1984; B.R.) performed personal interviews whenever possible.

It was evaluated whether the patient had nonpuerperal relapses, i.e. further psychotic episodes unrelated to childbirth, including

chronic psychotic evolutions starting with the index episode. In patients who had further episodes of depression only, at least one episode had to be of the DSM-III-R melancholic subtype and of invalidating consequences to be considered a relapse. Puerperal relapses were defined as psychotic episodes beginning within 3 months following further pregnancies.

The global psychopathological long-term outcome was classified by four degrees of severity: (1) favorable evolution: no nonpuerperal relapses and absence of or only minimal psychopathological symptoms; (2) relatively favorable evolution: nonpuerperal relapses not more frequent than once every 5 years on the average, and/or only slight other psychopathological symptoms; (3) relatively unfavourable evolution: more frequent nonpuerperal relapses and/or marked and predominantly chronic other psychopathological symptoms; (4) unfavourable evolution: invalidity most of the time or permanent hospitalisation.

It was noted whether the child grew up with the patient and whether the partner relation continued, i.e. did not end by divorce or separation.

Family study

First-degree relatives were evaluated for psychotic disorders as part of the catamnestic interview. In relatives who had been in psychiatric treatment, an attempt was made to obtain the case histories of outpatient and inpatient services. If uncertainties remained concerning the psychological health of a relative, further sources were contacted and sometimes even the relative.

All first-degree relatives with functional psychosis (melancholic subtype with incapacitating features in unipolar depressives) were considered secondary cases. In all psychotically ill female relatives who had given birth to a child, it was investigated if an episode of illness occurred within 3 months postpartum. The age-corrected morbidity risks were calculated according to Slater (1938) and Strömberg (1935).

Control groups

For a better interpretation of some characteristics of the index patients, control groups were established.

First control group: The index patients were compared with a matched group for the long-term course and morbidity risk in first-degree relatives. The controls were women hospitalised in Zurich for a nonpuerperal illness. Because the Lausanne and Zurich samples of index patients differed in outcome (nonsignificantly) and in the family history of functional psychoses (significantly), the comparison was limited to the Zurich patients.

The controls with affective or schizoaffective psychosis were hospitalised between 1959 and 1963 at the Psychiatric University Hospital of Zurich and followed up (Angst 1966, 1988). The sources of information were the same as in the investigation: the patient, relatives and doctors. The controls with schizophrenia were recruited from another study of patients hospitalised in Zurich between 1970 and 1976 (Scharfetter and Nüsperli 1980) and also followed up; the relatives were generally personally interviewed. Female patients with the same age (18–41 years) at first hospitalisation (which must have taken place at the Psychiatric University Hospital Zurich) and with absence of temporal relation (6 months) from the beginning of this episode of illness to childbirth were considered. They were matched for diagnosis and presence or absence of psychotic episodes (not leading to hospitalisation) before the index episode. The diagnostic criteria used for matching were the "study criteria" (Schöpf 1994).

A particular aspect of the inclusion criteria of the study on the controls with schizoaffective psychoses (Angst 1966, 1988) had to be considered. No cases were included whereby the episode leading to the first hospitalisation was schizophreniform, therefore index cases with this symptomatology were also excluded from the comparison.

Second control group: The frequency of unipolar vs bipolar (affective or schizoaffective) psychoses in the index patients was com-

pared to that of female patients with the same diagnosis, hospitalised for the first time in their life at the Psychiatric University Hospital of Zurich between 1959 and 1963 and followed up (Table 2) (Angst 1966, 1988). Their index episode also had to be unrelated to childbirth. Unlike the first control group, these controls were not matched.

Statistics

The mean and standard deviation were computed for interval data and also as orientation for ordinal data. As the level of significance $\alpha = 0.05$ was fixed. If justified by pre-existing data or hypotheses, one-tailed tests were used.

In two-group comparisons the χ^2 and the Fischer-Yates test (expected frequency < 5), the u-test and the *t*-test were used according to the scale niveau. For parallel group comparisons the χ^2 test of McNemar, the Wilcoxon test and the paired *t*-test were used, respectively. Multigroup comparisons of nominal data were performed using the χ^2 -test. For individual comparisons in the presence of a significant global test the χ^2 - and the Fischer-Yates test with the Bonferroni correction were used. The Spearman rank correlation coefficient was determined to measure a correlation of two variables with ordinal and interval scale niveau, respectively. The distribution of a binary variable (one-sample case) was examined using the binomial test.

In addition to the significance of differences, measures of correlation were systematically calculated. In two-group comparisons the phi-coefficient was used for nominal data, and the point-biserial correlation coefficient was used for interval data. These measures of correlation correspond to the effect sizes (Cohen 1977). Effect sizes exist for nominal and interval data, but not for ordinal data. For ordinal values the corresponding parametric test was used as an approximation of the correlation and the effect size. The *t*-test is robust against the violation of the premisses (Havlicek and Peterson 1974).

Results

Characteristics of patients and controls

The inclusion criteria were fulfilled by 130 patients (86 in Lausanne; 44 in Zurich). Of the 130 patients 119 were included (i.e. 92%) (79 in Lausanne; 40 in Zurich), the main reason for noninclusion being the impossibility of finding the present address (9 cases). In addition to patients who were hospitalised for the first time, about half as many were rehospitalised with postpartum psychoses. The estimated proportion of female patients hospitalised for postpartum psychoses was 0.8% in Lausanne and 1.2% in Zurich.

In all, 84% of patients ($n = 100$) were interviewed, 44.5% ($n = 53$) personally and 39.5% ($n = 47$) by telephone. In most cases ($n = 92$, i.e. 77%) information could be obtained from more than one source, including case records from psychiatric hospitals in 70 cases (59%). After the purpose of the study had been explained, the collaboration of most patients was excellent. In a few manifestly paranoid patients who were reluctant to answer all questions, further information could be obtained from other sources. The good collaboration also concerned the hereditary part of the study. Apparently, the occurrence of psychotic disorders had been discussed openly in these families. In addition, a detailed family history had already been taken at the index hospitalisation. Of the patients not

Table 1 Characteristics of patients and their first-degree relatives

| | |
|---|--|
| <i>General information</i> | |
| No. of patients eligible | 130 |
| No. of patients investigated | 119 (92%) |
| Duration of follow-up | 22.7 ± 8.0 years (range 3–35 years) |
| Duration of follow-up (duration of survival in patients who had died) | 21.2 ± 8.5 years (range 2–35 years) |
| <i>Index episode</i> | |
| DSM-III-R diagnoses: | |
| Major depression | 54% |
| Mania | 10% |
| Schizoaffective depression | 6% |
| Schizoaffective mania | 5% |
| Schizophrenia | 2% |
| Schizophreniform psychosis or brief reactive psychosis | 23% |
| Cycloid psychosis | 30% |
| Confusio-oid syndrome | 31% |
| Paranoid syndrome | 11% |
| Acute onset of illness | 46% |
| Onset within 2 weeks post partum | 74% |
| Major psychological stress | 22% |
| Age at index delivery | 26.9 ± 4.8 years |
| Primiparae | 60% |
| <i>Personal history before index episode</i> | |
| Psychic disturbances in pregnancy (remitted at time of delivery) | 20% |
| Former psychotic episodes not leading to psychiatric hospitalisation | 13% |
| Age at first episode of illness | 26.2 ± 4.9 years |
| <i>Follow-up study</i> | |
| Nonpuerperal relapses | 66% |
| Further episodes of illness (nonpuerperal or puerperal) | 69% |
| Further psychopathology of any type | 80% |
| DSM-III-R diagnoses (long-term course): | |
| Affective psychosis | 57% |
| Schizoaffective psychosis | 18% |
| Schizophrenia | 9% |
| Schizophreniform psychosis or brief reactive psychosis | 16% |
| Unipolar psychoses | 43% |
| Bipolar psychoses | 31% |
| Child grew up with patient | 83% |
| Partner relation continued | 73% |
| <i>Family study</i> | |
| Global morbidity risk for functional psychoses | 11.0% |
| Morbidity risk: | |
| Affective psychoses | 6.8% |
| Schizoaffective psychoses | 1.3% |
| Schizophrenia | 1.5% |
| Schizophreniform psychosis or brief reactive psychosis | 1.4% |
| Bipolar psychoses | 2.6% |
| Unipolar psychoses | 5.7% |

contacted personally, 15 had died and 4 others were unavailable (total 16% not contacted). Two of the 15 second interviews in Lausanne patients could not be performed because of impossibility of tracing the patient.

The duration of the follow-up varied between patients (Table 1). For two variables which might have been influenced by the length of the observation period, i.e. occurrence of nonpuerperal relapses and global outcome, no correlation with the duration of follow-up was found ($\phi = 0.00$; $\rho = 0.11$).

The 11 patients not followed up (out of the original 130) did not differ in any of the variables of the index episode or any background characteristic. However, the time elapsed since the index episode was longer than in the group of 119 patients described here (26.4 ± 4.6 years compared to 22.7 ± 8.0 years; $t' = -2.358$; $p < 0.03$), indicating the difficulty of tracing patients after a long time.

Patients of the Lausanne and Zurich sample showed few differences concerning the characteristics evaluated. The Zurich patients had, except for a longer follow-up duration (29.7 ± 2.9 vs 19.1 ± 7.4 years; $t' = -11.182$; $p < 0.001$), a significantly higher rate of psychological stress at the index episode (35% vs 15%; $\chi^2 = 6.103$; $p < 0.02$; $\phi = 0.23$), of not taking care of the child (30% vs 10%; $\chi^2 = 7.501$; $p < 0.007$; $\phi = 0.25$), of separation from the partner (44% vs 18%; $\chi^2 = 9.020$; $p < 0.004$; $\phi = 0.28$) and of a positive family history of functional psychoses (47.5% vs 28%; $\chi^2 = 4.541$; $p < 0.04$; $\phi = 0.20$). No obvious explanations are available for the differences, except that two characteristics (separation from the partner, family history) are possibly related to the follow-up duration.

When the 37 patients of the Zurich sample were compared for background characteristics with the matched cases of the first control group, the groups did not differ regarding age at the index episode and at first manifestation of illness (Table 3). The duration of the catamnesis was shorter in the controls. The index patients with affective or schizoaffective psychosis did not differ in any of the three characteristics from the second control group (Table 2).

Index episode

The distribution of diagnoses and other characteristics of the index episode are shown in Table 4. Evidence for an organic psychosis, though not of conclusive type, was found in 2 of the 119 cases (2%). One patient suffered from puerperal sepsis and the other from eclampsia. In the former, psychotic symptoms were definitely present before septicaemia, and in the latter psychosis persisted for months after normalisation of the somatic state.

Almost one-third of patients had a cycloid psychosis and nearly the same proportion showed a confusio-oid syndrome (Table 1). There was an almost complete overlap between the two characteristics: 33 of the 37 patients with confusio-oid syndrome had a cycloid psychosis, and 33 of the 36 patients with cycloid psy-

Table 2 Index patients with affective or schizoaffective psychosis compared to controls with the same diagnosis (second control group). *Statistical tests:* (1) *t*-test; (2) χ^2 ; (3) eta; (4) phi coefficient. † = Because of variance heterogeneity the effect size could not be determined

| | Index patients (<i>n</i> = 89) | Controls (<i>n</i> = 41) | <i>p</i> -value | Correlation |
|---------------------------------|------------------------------------|------------------------------|-----------------|-------------|
| Age at index delivery | 26.8 ± 4.7 | 27.5 ± 6.7 | n.s. (1) | † |
| Age at first episode of illness | 25.9 ± 4.8 | 25.9 ± 6.3 | n.s. (1) | 0.00 (3) |
| Duration of follow-up | 21.2 ± 8.3 | 21.7 ± 5.0 | n.s. (1) | † |
| Proportion of bipolars | 42% | 46% | n.s. (2) | 0.05 (4) |

Table 3 Comparison of Zurich patients (*n* = 37) with matched controls (first control group)

| | Index patients | Controls | <i>p</i> -value | Correlation |
|--|----------------|------------|----------------------|-----------------------|
| Age at index delivery | 27.2 ± 5.1 | 27.6 ± 6.3 | n.s. (1) | 0.03 (2) |
| Age at first episode of illness | 26.3 ± 5.2 | 26.2 ± 5.8 | n.s. (1) | 0.00 (2) |
| Duration of follow-up | 27.9 ± 6.0 | 20.8 ± 5.1 | <i>p</i> < 0.001 (1) | 0.54 (2) |
| Further episodes of illness (nonpuerperal or puerperal) | 76% | 86% | n.s. (3) | 0.13 (4) |
| Global outcome | 1.3 ± 1.0 | 1.7 ± 0.8 | n.s. (5) (0.04)* | 0.22 (2) ^a |
| Global morbidity risk for functional psychoses | 12.1 | 14.0 | n.s. (6) | 0.03 (4) |

^a Approximate measure (ordinal scale niveau)

* *p*-value using or one-tailed test. *Statistical tests:* (1) paired-*t*-test; (2) point-biserial correlation coefficient; (3) χ^2 test of McNemar; (4) phi coefficient; (5) Wilcoxon; (6) χ^2

Table 4 Diagnoses of the index episode in patients with postpartum psychosis (%). (*D* depression; *M* mania; *DSCH* schizoaffective depression; *MSCH* schizoaffective mania; *SCHF* schizophrenia, including other psychotic episodes without affective syndrome)

| Investigator | <i>n</i> | Postpartum period | D | M | DSCH | MSCH | SCHF | Other diagnoses | Diagnostic criteria |
|-------------------------------|-----------------|-------------------|----|-----|------|------|-------------------------------------|-----------------|---------------------|
| Martin (1958) | 75 | 6 months | 36 | 1 | 32 | 7 | 20 | 4 | Syndrome diagnosis |
| Brockington et al. (1981) | 56 | 2 weeks | 39 | 31 | 7 | 14 | 9 | – | RDC |
| Da Silva and Johnstone (1981) | 48 | 1 year | 46 | 6 | 13 | 2 | 27 | – | PSE |
| Makanjuola (1982) | 57 | 1 year | 14 | 3.5 | 3.5 | | 75.5 ^a (65) (10.5) | 3.5 | RDC |
| Lammel (1984) | 41 ^b | 3 months | 34 | 10 | 12 | – | 44 | – | Syndrome diagnosis |
| Meltzer and Kumar (1985) | 142 | 1 year | 44 | 24 | 2 | 4 | 8 ^a (6) (2) | 18 | RDC |
| Kendell et al. (1987) | 120 | 3 months | 55 | 18 | 4 | 3 | 14 ^a (3) (11) | 6 | RDC |
| Agrawal et al. (1990) | 144 | 3 months | 22 | 3 | 3 | 3 | 69 ^a (22) (47) | – | RDC |

^a Includes RDC diagnoses of schizophrenia (upper number in parentheses) and of unspecified functional psychosis (lower number in parentheses); ^b One patient with psychosis of pregnancy is included in this group, the diagnoses of whom is unknown

chosis had a confuso-oneiroid syndrome (ϕ = 0.86; *p* < 0.001). In all but 5% of patients with chronic psychotic evolution starting at the index episode (*n* = 6), eventually full or partial remission occurred.

Follow-up study

Table 1 shows the proportion of patients with further nonpuerperal episodes of illness. The distribution of DSM-III-R diagnoses, considering the long-term course, is also indicated.

Among the 45 women who had a total of 57 additional children, 17 had puerperal relapses. One patient was excluded because no conclusion concerning her psychic health following a further delivery could be made. Two patients with an episode of illness in months 4–6 following an additional delivery were not considered. Two other patients with chronic psychotic evolution since the index episode, but without exacerbation of symptoms in the postpartum period, were considered as having no relapse. This means that among the 42 remaining patients, 17 (40%) had puerperal relapses. The proportion of relapses was 19 per 54 childbirths (35%).

Using the definitions given in this study, 23% of the patients ($n = 27$) had a favourable, 38% ($n = 45$) a relatively favourable, 30% ($n = 36$) a relatively unfavourable and 9% ($n = 11$) an unfavourable global psychopathological outcome. Of the 119 patients, 13 (11%) committed suicide. In at least 12 cases this happened during an episode of illness. Two other patients died of natural causes.

A slightly higher proportion of patients of the Zurich sample had more than one episode of illness in life, compared to the first control group, the difference not being statistically significant (Table 3). Applying a one-tailed test, the global severity of psychopathology in the long-term course was significantly less in the index patients.

The bipolar patients were investigated for special characteristics. The proportion of a manic syndrome at the index episode in the bipolars was 47%. This proportion in the subgroup of 27 patients with nonpuerperal relapses and in whom the symptomatology of most episodes of illness could be determined was 44%, whereas the mean frequency of a manic syndrome for all nonpuerperal episodes was 45%, the difference not being statistically significant. The relation of unipolar vs bipolar psychoses in the index patients with affective or schizoaffective psychosis was not different from that in second control group (42% vs 46%, Table 2).

Family study

The 119 patients had 552 first-degree relatives who reached the age risk for functional psychoses (Strömberg 1935; Slater 1938). The index patient was the main source in 72% ($n = 86$), a relative in 12% ($n = 14$) and a doctor in 8% ($n = 10$). In 8% ($n = 10$) an additional source was contacted because the information was not sufficiently precise.

Among the 552 relatives no information could be obtained on 2 mothers, 6 fathers and 2 siblings. Moreover, 15 living first-degree relatives could only be traced up to variable periods before the follow-up investigation. There were 52 relatives suffering from functional psychoses. In 39 cases it was possible to use their case history. Of the 119 index patients, 34% ($n = 40$) had a positive family history of functional psychoses (at the index episode 26%, $n = 31$). The global morbidity risk among relatives for functional psychoses was 11%. Siblings were affected somewhat more frequently than parents (11.9% vs 10%), and female secondary cases prevailed over males (13.4% vs 8.5%), but the differences were not statistically significant. The diagnostic distribution of the secondary cases is shown in Table 1.

Bipolar secondary cases were mainly found among relatives of bipolar index patients (8 among 12 relatives). The morbidity risk for bipolar psychoses was higher in relatives of bipolar patients (5.1%) than in relatives of unipolar patients (1.6%) ($\chi^2 = 3.252$; $p < 0.03$; one-tailed test). Among the 25 psychotically ill female first-degree relatives who had children, 11 (44%) had puerperal episodes of illness. The global morbidity risk for functional psychoses in relatives of the 37 patients of the Zurich

sample was nonsignificantly lower than that in control group (Table 3).

Discussion

The retrospective approach and the method applied in the present study are associated with a number of limitations, which are discussed in the following. On the other hand, it is difficult to perform prospective long-term studies meeting optimal methodological standards. The investigators had the occasion to study a sample which was well documented and a part of which had already been the subject of other investigations (Schneider 1957; Jonquière-Wichmann 1981). They took advantage of the low mobility of the population in Switzerland and the fact that in Switzerland the address of all inhabitants is registered, which permitted tracing most of the patients.

According to the knowledge of the authors, no other comprehensive study on the phenomenon of postpartum psychoses, including long-term follow-up and a family investigation, has been performed on a comparable number of patients. Several questions related to the nosology of postpartum psychoses need a sufficiently large sample in order to be investigated.

The sample consists of hospitalised patients only. Conclusions drawn from this study are not necessarily applicable to less-ill women treated as outpatients. It is possible that the outcome in hospitalised patients is less favourable. The sample may be considered representative, except that an increased proportion of women from upper social classes were hospitalised in private hospitals.

Because of the retrospective approach with the use of case records, a loss of information has to be assumed. Therefore, the characteristics studied had to be relatively global.

The evaluation had to be adapted in a flexible way according to the individual needs of the patients. It was attempted to investigate as many patients as possible fulfilling the inclusion criteria. The adherence to a standardised protocol would have led to the loss of a considerable number of patients. Although a certain inhomogeneity of information resulted in this way, it seems unlikely that a misclassification of the relatively global items occurred in a notable proportion of cases.

There were fewer sources of information in women without nonpuerperal relapses. This is mainly due to the fact that few of these patients were rehospitalised, and that most of them were not in psychiatric treatment anymore, so that no further case histories existed and no psychiatrist could be questioned. Although information might have been selectively overlooked in these patients, no concrete evidence points to this possibility. One result suggests that differences obtained between patients with and patients without nonpuerperal relapses are genuine findings. The difference in the family history for functional psychoses was found not only at the follow-up investigation, but also considering the data gathered at the index hospitalisation (Schöpf and Rust 1994b).

An obvious weakness of this investigation represents the lack of a reliability study of the DSM-III-R criteria and other characteristics.

The relatives were not systematically interviewed, which certainly caused a loss of information. However, the evaluation was limited to severe psychiatric disorders. These were likely to be known to the patient or the other principal source. As mentioned, the willingness to give information appeared generally favourable.

The diagnosis of further episodes of illness was not made blindly with respect to that of the index episode, and psychotic disturbances in relatives were diagnosed knowing the status of the index patient. Although the investigators tried to avoid a diagnostic bias, this possibility cannot be excluded.

The outcome of illness observed reflects only partially the spontaneous course of the illness, because the patients received therapy of various types. The treatments applied in different diagnostic groups were not standardised, but generally were performed according to modern standards. The proportion of cases with relapses was not influenced, however, because no patient was permanently on prophylactic therapy.

Because the evaluation of the controls differed slightly from that of the index patients, the results of the comparisons have to be interpreted cautiously.

Index episode

There is agreement in the literature concerning the distribution of diagnoses of the index episode, when studies performed in developing countries (Makanjuola 1982; Agrawal et al. 1990) are not considered. A depressive syndrome was the most frequent psychopathology in all these studies (Table 4). A manic syndrome was reported quite often in some investigations. The high proportion (47%) in the study by Brockington et al. (1981) can be explained partially by the 2-week limit for the postpartum period, because most manic episodes occur in the early puerperium (Brockington and Cox-Roper 1988; Meltzer and Kumar 1985; Schöpf and Rust 1994a). Important differences concerning the frequency of a schizophrenic episode were noted not only in the literature but also in this study, depending on the diagnostic criteria. When the narrowly defined criteria of schizophrenia of DSM-III-R were applied, the diagnosis was generally rare. The finding in the studies of Makanjuola (1982) and Agrawal et al. (1990) that schizophrenias and unspecified functional psychoses according to the Research Diagnostic Criteria (RDC) (Spitzer et al. 1978) comprised more than two-thirds of cases raises the question of geographical differences of the relative frequency of illnesses. Organic psychoses in the postpartum period are definitely rare today (Protheroe 1969; Rehman et al. 1990). Despite this a considerable minority of patients showed signs of confusion. As found by other investigators (Grosse 1968; Lanczik et al. 1990), a sizeable proportion of patients fulfilled the criteria of cycloid psychoses.

Follow-up study

In the present investigation, as in the previous one (Schöpf et al. 1984), approximately two-thirds of patients suffering from a psychotic postpartum episode as their first major psychiatric decompensation had episodes of illness unrelated to childbirth in later life. Few comparisons are available in the literature. Davidson and Robertson (1985) followed up patients from 6–30 years after and found a 50% relapse rate. In an earlier investigation performed by Thuwe (1974) the proportion was 43% after a duration of 35 or more years, as can be deduced from the data of the publication. Among patients for whom the postpartum episode was not necessarily the first one in life, Protheroe (1969) in his well-known investigation found nonpuerperal relapses in 39% after 1–35 years. The author concluded that after a sufficiently long observation period, more than 50% of patients with postpartum psychoses have nonpuerperal relapses.

A high frequency of puerperal relapses was noted in this study, which is consistent with the results of other investigations (see Schöpf 1994). The occurrence of an episode of illness following 35% of further deliveries clearly exceeds the frequency of psychotic episodes expected. As noted elsewhere (Schöpf 1994), the mean cycle length, i.e. the average interval from one episode of illness to the next, was 3.9 years in unipolar depression, 2.1 years in bipolar affective psychosis, 2.7 years in unipolar schizoaffective psychosis and 2.6 years in bipolar schizoaffective psychosis. No cycle length for schizophrenia was determined. If one estimates conservatively a mean interval of 2.5 years between two episodes of illness for all patients, the probability of an episode of illness within a 3-month period is 10%. The frequency of 35% is much higher (binomial test; $p < 0.001$; $\phi = 0.31$).

Most studies on postpartum psychoses that consider the index episode suggest that mainly affective psychoses, some other nonschizophrenic psychoses and relatively few schizophrenias are provoked by childbirth (Table 4). This has been confirmed in the present investigation, in which the long-term course and therefore the possibility of a shift in psychopathology was considered. It is very likely that these relative frequencies do not represent merely a cross-section of functional psychoses in women of childbearing age, but result from a specific tendency of certain functional psychoses to appear during the puerperium. In studies investigating the probability of a puerperal relapse in women with pre-existing functional psychosis, a high liability has been found for affective psychoses (Bratfos and Haug 1966; Reich and Winokur 1970; Kendell et al. 1987) and a low liability for schizophrenia (Yarden et al. 1966; Kendell et al. 1987). Another factor to be considered for the low frequency of schizophrenias starting in the postpartum period is that women with schizophrenia have a moderately decreased fertility (Saugstad 1989). As discussed elsewhere (Schöpf and Rust 1994c) schizophreniform psychoses and brief reactive psychoses may be assumed to have an increased tendency to puerperal onset compared to schizophrenia.

The long-term course of postpartum psychoses has been considered generally better than that of functional psychoses. This has been confirmed in the present study insofar as affective psychoses and other nonschizophrenic psychoses, which predominate among postpartum psychoses, have a better course of illness than schizophrenia. Concerning the question of whether postpartum psychoses have a more favourable course of illness than the corresponding subgroup of functional psychoses, only few data are available. Kadrmas et al. (1979) found that patients with puerperal mania had fewer relapses than manic controls without puerperal onset. Platz and Kendell (1988) followed up patients with postpartum psychosis and nonpuerperal controls matched for diagnosis and confirmed the more favourable prognosis of postpartum-onset cases. Rohde and Marneros (1992) compared patients with schizoaffective psychosis and puerperal onset vs cases without puerperal onset and found a better course of illness in the former.

In this investigation a more favourable evolution was also found in the index patients than in the controls. It is unlikely that the shorter follow-up duration in the controls influenced this finding. After a longer observation period their outcome would most likely have been the same or even less favourable. In affective and schizoaffective psychoses, the longest interval of remission is between the first and second episodes of illness, and in the long-term course there is no tendency for a decreased frequency of episodes (Angst 1980, 1988). In the control cases with schizophrenia the outcome was generally quite unfavourable, and only a major improvement, which occurs rarely, would have influenced the global rating.

The high suicide rate (11%) is surprising. Almost all of these women lived in stable social conditions. Davidson and Robertson (1985) found a rate of 5%. On the other hand, the suicide rate in functional psychoses is generally 10–15% (Guze and Robins 1970; Angst et al. 1990; Caldwell and Gottesman 1990).

In this investigation 31% of patients were bipolars in the long-term course. Davidson and Robertson (1985) found 26% bipolars. The relation of bipolar to unipolar psychoses corresponded to that expected in women of childbearing age in this study, which suggests that also unipolar psychoses are prone to puerperal decompensations. In the investigation by Brockington et al. (1981), 45% of patients were bipolars, considering only the index episode. If one assumes that approximately half of bipolar patients were manic at the index episode, as in this study, the total proportion of bipolars should be close to 90%. Other studies suggest that bipolar psychoses are not the only diagnostic group found among postpartum psychoses, but are somewhat overrepresented compared to unipolar psychoses. In the study by Kendell et al. (1987) the risk of a puerperal episode of illness was higher in bipolar women (21%) than in unipolar women (13%). In an investigation by Rohde and Marneros (1992) on schizoaffective psychoses, the proportion of bipolars compared to unipolars was slightly and nonsignificantly higher in puerperal-onset cases (57%) than in cases with nonpuerperal onset (45%).

The frequency of a manic syndrome in bipolar patients at the index episode was the same as in nonpuerperal episodes of illness in this study. In bipolar psychoses generally, the probability of a manic syndrome is constant in the long-term course (Angst 1978). Thus, it appears that the postpartum period does not have a special mania-provoking effect in bipolar patients. Rohde and Marneros (1992) suggested a pathoplastic effect of the puerperium. They found that schizoaffective psychoses with puerperal onset more often had a manic syndrome than schizoaffective psychoses without puerperal onset. However, they did not compare the frequency of a manic syndrome at the postpartum episode with the frequency in the long-term course in the individual patients. The higher frequency of a manic syndrome in patients with puerperal onset might also result from an overrepresentation of bipolar psychoses with predominantly manic episodes.

Family study

It is well known that there is an increased number of psychiatrically ill relatives in the families of patients with postpartum psychosis (see Schöpf 1994). Due to variations in methodology, including diagnostic criteria, it is difficult to compare the 11% risk found in this investigation with that of other studies. Protheroe (1969) found morbidity risks of 6.7–11.7%, depending on the diagnostic subgroup and degree of certainty of the diagnosis. Only secondary cases showing marked impairment were included. Whalley et al. (1982), using the broad definition of major depressive disorder, found a morbidity risk of 25.6%, and Platz and Kendell (1988) found a risk of 10.1%. Dean et al. (1989) found a 20% risk using psychiatric inpatient or outpatient treatment as the criterion, and a 50% risk when considering contacts with general practitioners because of psychiatric disorders.

The global morbidity risk was relatively low in this investigation. This is particularly true because early-onset cases were studied. Early onset is associated with increased morbidity risk in relatives (Gershon et al. 1976; Baron et al. 1981). Because the first-degree relatives were not systematically interviewed, it is possible that some secondary cases were missed. However, the evaluation was limited to severe disorders, which are very likely to be detected. The morbidity risk was nonsignificantly lower than in the control group. Furthermore, Kadrmas et al. (1979) found a nonsignificant lower rate of family history of functional psychoses in patients with puerperal mania than in women with mania unrelated to childbirth. In a comparison between puerperal and nonpuerperal affectively ill patients, no difference in morbidity risks was found by Whalley et al. (1982). However, the age of the controls was significantly higher, a characteristic which itself is associated with a decreased morbidity risk. Platz and Kendell (1988) found a nonsignificantly lower global morbidity risk in relatives of patients with puerperal psychosis than in those of the nonpuerperal controls. However, Dean et al. (1989) reported that the morbidity

risk was higher in the puerperal group than in the controls.

Another finding of this investigation suggests that the global morbidity risk in the total group of patients with postpartum psychosis was somewhat decreased: In the subgroup of patients with puerperal episodes only, the relatives had a significantly lower morbidity risk than those in the group with puerperal and nonpuerperal episodes, and no evidence pointed to an increased morbidity risk in the latter (Schöpf and Rust 1994b).

In this investigation mainly affective psychoses were found among secondary cases, which confirms the results of another study reporting the morbidity risks for subgroups of functional psychoses (Platz and Kendell 1988).

A minority of 44% of psychotically ill female first-degree relatives who gave birth to children had postpartum episodes of illness. This frequency is close to the risk of puerperal episodes in female patients with affective psychosis (Bratfos and Haug 1966; Reich and Winokur 1970), which does not suggest a selective transmission of psychoses with postpartum episodes of illness. It also appears to agree with investigations showing the same risk of postpartum episodes in relatives of patients with postpartum psychoses and relatives of psychotically ill female patients without puerperal onset of illness (Whalley et al. 1982; Platz and Kendell 1988; Dean et al. 1989).

A morbidity risk of only 2.7% for bipolar psychoses was found in this investigation. Bipolar secondary cases were concentrated in the families of bipolar index patients. Thus, there is little evidence that nonbipolar postpartum psychoses are nosologically related to bipolar psychoses from the genetical point of view.

Questions of nosology

The finding of a marked increase in the incidence of psychosis in the postpartum period raises questions concerning aetiological factors related to childbirth. There is no evidence suggesting an organic aetiology (including endocrine pathology) in a significant proportion of these disorders (see Schöpf 1994). Moreover, unusual psychological stress is not a necessary precursor of postpartum psychoses (Brockington et al. 1990; Dowlatsahi and Paykel 1990; Marks et al. 1992). Many patients suffering from postpartum psychosis have psychotic episodes unrelated to childbirth, and the family history is often positive for functional psychoses. At least the majority of postpartum psychoses may therefore be considered as ordinary functional psychoses provoked by events of the postpartum period. It appears likely that biological factors, presumably the hormonal changes of the postpartum period, represent the primary precipitating element. Life event research has shown that the psychological factors, including severe stressors, increased the incidence of psychiatric disorders 1.6–7.6 fold (Paykel 1978; Surtess et al. 1986; Kendell et al. 1987), whereas in the postpartum period a much higher increase is found.

Particularities often mentioned in connection with postpartum psychoses can be explained by the high frequency of certain psychoses, e.g. signs of confusion by the presence of cycloid psychoses. The favourable long-term course of postpartum psychoses is related to the overrepresentation of psychoses with good prognosis. It is likely that the course is favourable also for the individual diagnostic subgroups. This might be caused by the possibly lower hereditary predisposition in postpartum psychoses. Corresponding to the diathesis-stress model of functional psychoses, it appears reasonable to assume that the postpartum period is able to provoke episodes of illness in patients with little genetical predisposition, whereas events of lesser impact (or the spontaneous evolution) are not able to do so.

Since affective psychoses, schizoaffective psychoses, schizophreniform psychoses and brief reactive psychoses are preferentially provoked in the postpartum period, one may assume that a common pathophysiological mechanism is involved in the appearance of these illnesses. However, it is not possible presently to state anything about the nature of such a mechanism or about how intimately it might be linked to the disease process.

Among the hormonal changes of the puerperium possibly related to the biology of functional psychoses, the fall of oestrogen plasma concentration has received particular attention. Oestrogen withdrawal leads to increased dopamine receptor sensitivity (van Hardesfeldt and Joyce 1986; Cookson 1982; Vinogradov and Csernansky 1990), which could explain the appearance of manias and schizophreniform psychoses, but hardly that of depressions, because these have not been associated with hyperfunction of the dopaminergic system. Furthermore, the relative absence of puerperal schizophrenias cannot be explained in this way.

The finding of a preferential appearance of affective psychoses and other nonschizophrenic psychoses in the postpartum period is in apparent contradiction with a hypothesis recently formulated by Häfner et al. (1991a, b), according to which the increased schizophrenia incidence in women in higher age groups is related to lack of oestrogen, this hormone acting as a protective factor by increasing the vulnerability threshold for psychosis through the downward regulation of dopamine neurotransmission. However, the rapid decrease of a very high oestrogen concentration in the puerperal period and the slow and progressive decline of oestrogen production in the years preceding menopause are such different phenomena that they might not have the same effects on brain functions, and therefore might dispose to different disorders.

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