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In Review

# Melancholia: Past and Present

**David Healy, MD, FRCPsych**[1]

[1] Professor of Psychiatry, North Wales Department of Psychological Medicine, Bangor University, Hergest Unit, Wales;
Correspondence: North Wales Department of Psychological Medicine, Bangor University, Hergest Unit, Wales LL57 2PW; david.healy54@googlemail.com.

**Key Words:** melancholia, remission, mortality, depressive psychoses

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**Objective:** To investigate commonalities in the clinical presentation of melancholia over time.

**Method:** I conducted a comparative study to 2 epidemiologically complete databases from 1875–1924 and 1995–2005.

**Results:** Patients in the historical period (1875–1924, compared with 1995–2005) with a diagnosis of melancholia show a classic profile of endogenous onset, with remission after 6 months, neurovegetative features, and, commonly, psychosis. The incidence of psychotic presentations appears to have fallen in recent decades. Patients in the contemporary period (1995–2010, compared with 1875–1924) at first admission for severe depressive disorders are more likely at an older age, more likely to go on to die by suicide, and will have much more frequent admissions.

**Conclusions:** The data from this study support classical perceptions of melancholia. The poor outcomes in contemporary cases of severe depressive disorders support arguments for distinguishing between melancholia and other depressive disorders.

## La mélancolie : passée et présente

**Objectif :** Rechercher les éléments communs de la présentation clinique de la mélancolie au fil du temps.

**Méthode :** J'ai mené une étude de comparaison de 2 bases de données épidémiologiques complètes de 1875–1924 et de 1995–2005.

**Résultats :** Les patients de la période historique (1875–1924, comparée avec 1995–2005) ayant reçu un diagnostic de mélancolie présentent un profil classique d'apparition de la maladie endogène, avec rémission après 6 mois, des traits neurovégétatifs, et communément, une psychose. L'incidence des présentations psychotiques semble avoir diminué dans les récentes décennies. Les patients de la période contemporaine (1995–2010, comparée avec 1875–1924) à leur première hospitalisation pour de graves troubles dépressifs sont plus susceptibles d'être âgés, de mourir par suicide, et seront hospitalisés beaucoup plus fréquemment.

**Conclusions :** Les données de cette étude appuient les perceptions classiques de la mélancolie. Les piètres résultats des cas contemporains de troubles dépressifs graves soutiennent les arguments en faveur de la distinction entre la mélancolie et les autres troubles dépressifs.

Melancholia has been in continuous use as a diagnosis for millennia. For much of this time, it did not refer to a depressive disorder. The restriction to a distinctive and generally severe depressive disorder took place in the middle years of the 19th century, coinciding with the birth of the notion of a disease entity in medicine.

Prior to that, patients with illnesses had complaints that their doctors managed according to the wisdom or the fashions of the time. History shows that complaints can be readily tailored to fashionable remedies, whereas a disease entity has a relative invariance. The disease may wax and wane in virulence, treatments and associated conditions may modify its course, but the disease has a continuity that underpins a commonality of clinical presentations across time.

From the mid-19th century, when the asylums opened, through to 1900, a melancholia diagnosis implied the patient was psychotic. In 1880, Carl Lange, in Denmark, delineated a disorder with the neurovegetative features of melancholia but without psychosis, which became endogenous or vital depression.[1]

In 1899, Emil Kraepelin[2] amalgamated melancholic and bipolar depression into manic-depressive illness, and brought nonpsychotic depression more clearly into view. Episodes of this new disorder were characterized by their acute onset and remission within a period of months.[2]

Kurt Schneider[3] then focused attention on the major psychopathological features of melancholic states, such as diurnal variation of mood, psychomotor retardation, and lack of mood reactivity. These were the hallmarks of vital depression in contrast to neurotic depression or depressive personality disorders. Schneider's emphasis on the clinical features of schizophrenia and affective disorders laid the basis for the operational criteria that emerged in the 1980s.

Through to the 1980s, vital (endogenous) depression was thought to have a sudden onset, an apparent lack of precipitants, and a propensity to remit. It responded to ECT and TCAs when these were introduced.

In 1980, although included as a specifier for MDD in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, melancholia (vital depression) vanished as a distinct diagnosis as its operational criteria overlapped heavily with those for MDD. There are proposals to reinstate it, given its distinct phenotype, its linkage to biological markers, such as raised cortisol levels and a more specific response to treatments, such as ECT and TCAs, than is found for MDD.[4,5]

Many of the claims that are now made for the natural history of MDD, including rates of recurrence and periodicity, as well as comorbidities with physical disorders, such as cancer or cardiovascular disease, and risks, such as suicide, stem from studies on melancholia or endogenous depression antedating 1980. Therefore, a key question for clinicians today is, How do formerly melancholic patients compare with a contemporary sample of depressive patients?

## Investigating Melancholia

In North Wales, we (that is, my research group, principally Dr M Harris, Dr J LeNoury, and myself) have a complete set of admissions to the Denbigh asylum between 1875 and 1924 and to the District General Hospital serving the same area from 1994 to 2010. Adopting the disease entity assumption that disorders are not simply an expression of distress or dislocation, we have reported on a rise in the incidence of schizophrenia in the 19th century (see Healy et al[6]), the benign course of acute and transient psychoses (see Linden et al[7]), a recent marked drop in the incidence of postpartum psychoses (see Tschinkel et al[8]), and increased mortality in patients with schizophrenia today, compared with the historical period (see Healy et al[9]).

To shed light on melancholia, we have reviewed 597 consecutive first admissions between 1875 and 1924 along with 203 first admissions with severe MDD, with or without psychotic features, between 1995 and 2005. For full details of the methods I adopted, see Harris et al.[10,11]

**Clinical Implications**

- Depressive psychoses are declining in frequency.
- Severe depressive disorders have poor clinical outcomes today.

**Limitations**

- There was no control on medications in the contemporary sample; the medication status of the patients in the study is unknown.
- The duration of follow-up data are limited.

### *Incidence and Prevalence*

The 597 historical patients had 767 admissions between them over their lifetime. Among the sample, 342 (57%) were female. In total, 69% of patients were admitted for depressive psychoses and the remainder for severe depressive disorders. There were no admissions for mild or moderate depressive disorders.

Among this cohort, 121 (20%) had recurrent admissions and 51 had prior episodes managed outside hospital, giving 172 (29%) patients with evidence for recurrences. There was nowhere else for patients to go, thus we can confidently state that over 50%, and perhaps up to 70%, of patients only had one significant episode.

The contemporary sample had 203 patients who, as of 2010, had over 800 admissions between them. Among these, 57% were female, and 38% were admitted with depressive psychoses.

Historically, the average age at first admission (46.5 years) was significantly lower than today (56.8 years). Among the contemporary sample, 20% were 75 years or older at first admission.

Standardizing by age for incidence rates gives the admission rates laid out in Table 1. The incidence rate for all contemporary admissions for depression, including mild, moderate, and severe, was 29.0 per 100 000 per year. The incidence rate was 21.6 per 100 000 per year for admissions for mild to moderate depressions.

These contemporary incidence rates map onto rates of first admissions for affective disorders to London hospitals in 1957,[12] which were of the order of 20 per 100 000. Comparable rates had been reported for the interwar years in America.[13]

Against this background, the data in Table 1 show an apparent fall in the incidence of hospitalization for depressive psychoses. Indeed, if all subjects over the age of 75 were excluded, the differences in incidence between the 2 cohorts would be even more striking. These data are more consistent with a slow disappearance of a cohort of patients prone to psychotic depression than with a fall in incidence because of earlier detection and treatment as there is a large increase in rates of admission, and little reason to think psychotic depressions would escape admission.

**Abbreviations**

| | |
|---|---|
| AD | antidepressant |
| ECT | electroconvulsive therapy |
| MDD | major depressive disorder |
| SMR | standardized mortality rate |
| SSRI | selective serotonin reuptake inhibitor |
| TCA | tricyclic AD |

**Table 1 Incidence rates for psychotic and nonpsychotic depression in historical (1875–1924) and contemporary (1995–2005) samples**

| | Sample *n*/100 000/year | |
|---|---|---|
| Patient type | Historical | Contemporary |
| Complete sample | 6.5 | 7.7 |
| Depressive psychoses | 4.6 | 2.9 |
| Nonpsychotic | 1.9 | 4.8 |

There are very few other datasets on the incidence of depressive psychosis. Perälä et al[14] reported a prevalence of depressive psychosis of 3 per 1000 in a community sample. There is a 100% difference between these prevalence figures and our incidence rates. This divide can be bridged by multiplying our incidence figures by years at risk, but still points to a higher incidence rate for the condition that may stem from a detection of never-admitted patients.

### *Precipitants*

In these records, over 50% of historical patients with melancholia were designated by the admitting clinician as arising endogenously. In 29% of patients, no precipitating factor was listed. In 12% of patients, the current episode was put down to heredity, in 10% to ill health, and in 2% to previous attacks or old age. In contrast, 17% of patients were attributed to worries, 9% to bereavement, 3% to an accident, 3% to family trouble, 3% to war, and 2% to disappointment.

### *Recovery and Length of Stay*

In the historical sample, we have data on length of stay to point of recovery for 420 patients. For 576 of the 597 patients at first admission, we also have figures for the duration of episode prior to admission. The median length of illness prior to admission was 60 days and the modal duration was 14 days. Adding these figures to the length of time in hospital to point of recovery gives a sample of 407 patients, for whom the mean length of episode was 420 days, with a median length of 217 days. The median stay for depressive psychoses was 251 days.

There were several clusters of episode duration. The largest (66%) had a mean length of episode of less than 1 year. Among these, 180 had an episode lasting less than 6 months. A further 26% had an episode lasting between 1 and 3 years. A small group (8%) had a disorder lasting up to 6 years.

It is impossible to generate figures for mean length of episode for the contemporary sample as many patients were discharged as on the road to recovery. A failure of the index admission to resolve after discharge may have contributed to an increased rate of readmissions seen in the contemporary sample.

Tracking the historical sample during the 10 years following their first admission, 87% had their index admission only, 12% had 2 admissions, and 1% had 3 or more admissions. In the contemporary sample, 102 patients had 10-year outcome data; 42% had their index admission only; 12% had 2 admissions only; 17% had 3 admissions only; and 29% had 4 or more admissions. Patients with 10-year follow-up data had a mean of 3.85 admissions, with a mean total length of stay of 114 days. These admissions and readmissions give the numbers for bed days at 3 and 5 years outlined in Table 2.

Reporting on a cohort of first admissions to London hospitals in 1957, Norris[12] noted that 40% had at least 1 readmission within 4 years of discharge and 20% had 2 readmissions. In the contemporary sample, 47% had at least 1 readmission within 3 years of discharge and 26% had 2 or more. In contrast, in the historical sample, only 7% had been readmitted within 3 years of discharge. It is possible that some of the agents used today make recurrence more likely. Alternately, so-called recoveries today may involve symptomatic improvements rather than a resolution of the underlying disorder, leaving the patient vulnerable to relapse until the underlying episode clears.

### *Mortality*

Mortality in both contemporary and historical samples was substantial (Table 3). Historically, there were high rates of death from tuberculosis in patients not discharged within the first year after admission, especially among women. When standardized by age, tubercular deaths were 9-fold to those of the general population. Another common cause of death was from exhaustion, linked to catatonic presentations.

The SMR for both historical and contemporary samples (Table 4) are in excess of those reported in recent studies.[15] While this study has recruited a more severely ill patient group than other studies, the data remind us that melancholia had a substantial mortality. In lieu of death from tuberculosis, a one-quarter of the deaths in the contemporary sample come from suicide.

In line with the data used by my colleagues and myself, older studies reporting SMRs reported a relative death rate for affective psychosis 6 times that of the general population[16]; Odegaard[17] reported a relative death rate in manic-depressive psychosis for women 6 times and for men 4 times greater than for the general population rate. Dalgard[18] and Bratfos and Haug[19] reported mortality rates in affective psychosis of the order of 2.5 times greater than for the general population. Among admissions for depression in London just before the introduction of the ADs, Norris[12] reported a crude death rate at the end of year from first admission for men of 121 per 1000 and for women of 77 per 1000, noting this was 9 and 6 times greater than the rate for the general population.

We found that between 20% and 25% of deaths in the contemporary sample were deaths from suicide[10]; this maps almost precisely on to the 26% figure reported by Avery and Winokur[20] for severe affective disorders. Avery and Winokur note that a series of studies from the 1960s suggested that the advent of effective ADs led to increased rates of suicide in patients.

This is an emblematic issue. Current sales of psychotropic drugs are fuelled heavily by claims that untreated MDD is linked to high suicide rates.[21] In fact, these claims

**Table 2 Number of bed days and admissions for melancholia at 3 and 5 years in historical and contemporary samples**

| | Historical | | Contemporary | |
|---|---|---|---|---|
| Variable | 3 years | 5 years | 3 years | 5 years |
| *n* | 597 | 597 | 203 | 203 |
| Total admissions | 641 | 657 | 443 | 587 |
| Average number of admissions | 1.07 | 1.10 | 2.18 | 2.89 |
| Length of stay, mean (SD), days | 431 (369) | 546 (576) | 78 (99) | 91 (119) |
| Length of stay, median, days | 274 | 290 | 46 | 51 |

**Table 3 Mortality at 3, 5, and 10 years in historical and contemporary samples**

| Variable | 3 years *n* (%) | 5 years *n* (%) | 10 years *n* (%) |
|---|---|---|---|
| Historical, *n* = 597 | | | |
| Discharged or in care | 472 (79) | 455 (76) | 420 (70) |
| Confirmed dead | 125 (21) | 142 (24) | 177 (30) |
| Contemporary, *n* = 203 | | | *n* = 102 |
| Alive | 177 (87) | 158 (78) | 69 (68) |
| Confirmed dead | 26 (13) | 45 (22) | 33 (32) |

**Table 4 SMRs for melancholia in historical and contemporary samples**

| Study cohort | 1-year SMR (95% CI) | 5-year SMR (95% CI) |
|---|---|---|
| Contemporary: male and female | 3.20 (1.75 to 5.01) | 1.92 (1.40 to 2.56) |
| Historical | | |
| Male | 4.96 (3.32 to 7.13) | 2.17 (1.63 to 2.83) |
| Female | 6.52 (4.86 to 8.58) | 2.64 (2.12 to 3.26) |

draw on studies of melancholia before the emergence of MDD.[12,13,19,20,22] There is almost no research on rates of suicide in MDD,[23] and no research that attempts to construct relatively comparable modern and historical cohorts.

This links to the issue of treatment. For more than 20 years since the 1960s, one of the underpinnings of a melancholia diagnosis was treatment responsiveness. Melancholia predicted a response to ECT.[24,25] It was the clinical syndrome that led to the discovery of the TCAs.[26]

In the 1980s, some dismissed the specificity of AD treatment to melancholia,[27] as TCAs were shown to benefit a range of anxiety states, from panic disorder to obsessive–compulsive disorder, and growing awareness that SSRIs were ineffective for melancholia.[28,29]

The inefficacy of SSRIs in melancholia or depressions with raised cortisol, along with poor outcomes in this sample of patients with severe depressions, many of whom are likely to have been treated with SSRIs, argues for the validity of distinctions between melancholic and nonmelancholic disorders. There is little room for complacency as stripping out deaths from tuberculosis and exhaustion from the historical sample would give worse outcomes today than a century ago.

## Conclusions

These data are consistent with classical perceptions that melancholia was liable to abrupt onset, that in many patients it had an ominous outcome, but that more commonly it remitted after about 6 months.

For research, the implications are that any theories about the pathology underpinning the disorder need to incorporate proposals regarding mechanisms that may lead to recovery.

For clinical practice, the implications are that many statements made about depression, such as the increased mortality rates and endocrine changes linked to the condition, are drawn from research on melancholia. However, in the absence of specific criteria for melancholia, there is almost no modern research on the epidemiology of this condition or of depressive psychosis.

In practical terms, a failure to draw this distinction may be contributing significantly to an apparent deterioration in outcomes for severe depressive disorders.

The data from this study support arguments for distinguishing melancholia (vital depression) from other depressive disorders. Lumping them together is liable to obscure associations that any of these conditions may have with cancer, cardiovascular, and other physical disorders,

and cloud any research on outcomes, and this will not be to the benefit of patients.

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