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Death after bereavement

Give sorrow words: the grief that does not speak
Whispers the o'er fraught heart and bids it break.

WILLIAM SHAKESPEARE, *Macbeth*

The broken heart is well established in poetry and prose, but is there any scientific basis for such romantic imagery? In Britain almost 2% of men and 8% of women aged between 45 and 59 are widowed. These rates increase until among those 75 and over 30% of the men and 64% of the women have lost a spouse—a potential at risk population of over 4 million.[1]

Among the earliest observations on mortality and marital state were those made on monks, nuns, and *tontine annuitants* by Deparcieux in France over two centuries ago.[2] Since then there have been many studies, but comparisons are difficult owing to geographical and cultural variations, absent or poor controls, and differences in design (prospective versus retrospective), sample selection (random versus referred), and sample size (ranging from 44 to 360 000), composition (both sexes versus men or women only), and age groups (subjects under 65 versus all ages). Despite these methodological problems,[3-5] all the studies (with the exception of three small ones[6-8]) show an association between conjugal bereavement and an increased risk of death. This risk seems greatest in the first six months of bereavement for widowers[9-15] and in the second year for widows,[15-17] but some studies have shown a more sustained effect.[15 18 19] There is also evidence that men[12 15 17 18 20] and the younger bereaved[9 15 19 21] are at greatest risk.

Why should there be this excess mortality? Various mechanisms have been suggested.[11 13 17] The selection hypothesis suggests that the fit and the unfit tend to marry their counterparts and that the bereaved who are in good health select themselves out by remarrying quickly. The common infection hypothesis was proposed in the 1940s when infectious diseases were a much commoner cause of death than today. The joint unfavourable environment hypothesis suggests that the surviving spouse continues in the same unfavourable environment that may have contributed to the partner's death. The loss of care hypothesis points out that the survivor may neglect hygiene, nutrition, social contacts, and medical care simply because of being alone—"loneliness can damage, if not break, the human heart."[22] This could explain the higher mortality in widowers. The desolation effects hypothesis suggests that the grief and life changes of bereavement may impair resistance to disease or result in unhealthy behaviour such as increased consumption of alcohol or tobacco, or both.[23 24]

The common causes of death among the bereaved are circulatory disorders, cancer, accidents, suicide, cirrhosis, and, in the older studies, infectious diseases.[9 10 13 17-19 25-28] Biological and sociological factors have been implicated in all these conditions and in other diseases associated with bereavement—cardiovascular disease,[13 23 24] malignancy,[4 29] ulcerative colitis, thyrotoxicosis, acute closed angle glaucoma, rheumatoid arthritis, asthma, Cushing's syndrome, pernicious anaemia, and osteoarthritis.[3 4] Precisely how these factors produce the excess mortality and morbidity in the bereaved is not known, but there are intriguing possibilities for future research. For example, neuroendocrine and immunological changes such as altered corticosteroid concentrations[30 31] and suppressed lymphocyte function[32 33] have been described in the bereaved. Loss of a close relative has been related to an increased risk of cancer,[34] and growing evidence implicates the immune system as a link between the central nervous system and disease processes.[34 35] Relocation and death of a spouse or close relative are accurate predictors of death in the elderly,[36] which is confirmed by the highly significant association between mortality and change of residence after widowhood for both sexes.[37]

Where do we go from here? Bereavement counselling provided by professional services and professionally supported voluntary and self help groups can reduce the increased morbidity of the bereaved, especially in high risk groups.[38 39] Could such interventions have a similar effect on mortality? We do not know, but the answer lies in carefully conducted prospective controlled studies.

BRIAN R MCAVOY

Senior Lecturer,
General Practice Unit,
Department of Community Health,
University of Leicester,
Leicester Royal Infirmary,
Leicester LE2 7LX

1 Office of Population Censuses and Surveys. *Social trends No 16*. London: HMSO, 1968.
2 Farr W. Part IV—Deaths. In: Humphreys N, ed. *Vital statistics: a volume of selections from reports and writings of William Farr*. Republished, with an introduction by Mervyn Susser and Abraham Adelstein. New Jersey: The Scarecrow Press, 1975:439.
3 Epstein G, Weitz L, Roback H, McKee E. Research on bereavement: a selective and critical review. *Compr Psychiatry* 1975;**16**:537-46.
4 Klerman GL, Izen JE. The effects of bereavement and grief on physical health and general well being. *Adv Psychosom Med* 1977;**9**:63-8.

5 Jacobs S, Ostfeld A. An epidemiological review of the mortality of bereavement. *Psychosom Med* 1977;**39**:344-57.
6 Clayton P. Mortality and morbidity in the first year of widowhood. *Arch Gen Psychiatry* 1974;**30**:747-50.
7 Gerber I, Wiener A, Battin D, Arkin AM. Brief therapy to the aged bereaved. In: Schoenberg B, Gerber I, Wiener A, Kutscher AH, Peretz D, Carr AC, eds. *Bereavement: its psychosocial aspects*. New York: Columbia University Press, 1975:310-33.
8 Ward AWM. Mortality of bereavement. *Br Med J* 1976;i:700-2.
9 McNeill DN. *Mortality among the widowed in Connecticut*. Yale University: New Haven MPH essay, 1973.
10 Niemi T. The mortality of male old-age pensioners following spouse's death. *Scand J Soc Med* 1979;7:115-7.
11 Young M, Benjamin B, Wallis C. The mortality of widowers. *Lancet* 1963;ii:454-6.
12 Rees WD, Lutkins SG. Mortality of bereavement. *Br Med J* 1967;iv:13-6.
13 Parkes CM, Benjamin B, Fitzgerald RG. Broken heart: A statistical study of increased mortality among widowers. *Br Med J* 1969;i:740-3.
14 Bowling A, Benjamin B. Mortality after bereavement: a follow-up study of a sample of elderly widowed people. *Biology and Society* 1985;2:197-203.
15 Helsing KJ, Szklo M. Mortality after bereavement. *Am J Epidemiol* 1981;**114**:41-52.
16 Cox PR, Ford JR. The mortality of widows shortly after widowhood. *Lancet* 1964;i:163-4.
17 Kraus AS, Lilienfeld AM. Some epidemiological aspects of the high mortality rate in the young widowed group. *J Chronic Dis* 1959;**10**:207-17.
18 Mellström D, Nilsson A, Oden A, Ründgren A, Svanborg A. Mortality among the widowed in Sweden. *Scand J Soc Med* 1982;**10**:33-41.
19 McMahon B, Pugh TF. Suicide in the widowed. *Am J Epidemiol* 1965;**81**:23-31.
20 Frankel F, Smith D. Conjugal bereavement amongst the Huli people of Papua New Guinea. *Br J Psychiatry* 1982;**141**:302-5.
21 Jones DR, Goldblatt PO, Leon DA. Bereavement and cancer: some data on deaths of spouses from the longitudinal study of Office of Population Censuses and Surveys. *Br Med J* 1984;**289**:461-4.
22 Lynch JJ. *The broken heart*. New York: Basic Books, 1977.
23 Parkes CM, Brown RJ. Health after bereavement: A controlled study of young Boston widows and widowers. *Pyschosom Med* 1972;**34**:449-61.
24 Maddison DC, Viola A. The health of widows in the year following bereavement. *J Psychosom Res* 1968;**12**:297-306.
25 Ciccio A. On mortality in husbands and wives. *Hum Biol* 1940;**12**:508-31.
26 Helsing KJ, Comstock GW, Szklo M. Causes of death in a widowed population. *Am J Epidemiol* 1982;**116**:524-33.
27 Horwitz O, Weber J. Aegteskabelig stilling og dødelighed. *Ugeskr Laeger* 1973;**135**:1089-104.
28 Koskenvuo M, Kaprio J, Kesaniemi A, Sarna S. Differences in mortality from ischaemic heart disease by marital status and social class. *J Chronic Dis* 1980;**33**:95-106.
29 Schmale AH, Iker H. Hopelessness as a predictor of cervical carcinoma. *Soc Sci Med* 1971;5: 95-100.
30 Frederick JF. Physiological reactions induced by grief. *Omega* 1971;2:71-5.
31 Hofer M, Wolff C, Friedman S, Mason JW. A psychoendocrine study of bereavement. *Psychosom Med* 1977;**39**:481-504.
32 Bartrop RW, Lazarus L, Luckhurst E, Kiloh LG, Penny R. Depressed lymphocyte function after bereavement. *Lancet* 1977;i:834-6.
33 Schleifer SJ, Keller SE, Camerino M, Thornton JC, Stein M. Suppression of lymphocyte stimulation following bereavement. *JAMA* 1983;**250**:374-7.
34 Cox T, Mackay C. Psychosocial factors and psychophysiological mechanisms in the aetiology and development of cancers. *Soc Sci Med* 1982;**16**:381-96.
35 Stein M, Schiavi RC, Camerino M. Influence of brain and behaviour on the immune system. *Science* 1976;**191**:435-40.
36 Rowland KF. Environmental events predicting death for the elderly. *Psychol Bull* 1977;84: 349-72.
37 Helsing KJ, Szklo M, Comstock GW. Factors associated with mortality after widowhood. *Am J Public Health* 1981;**71**:802-9.
38 Parkes CM. Bereavement counselling: does it work? *Br Med J* 1980;**281**:3-6.
39 Parkes CM. Bereavement. *Studies of grief in adult life*. Harmondsworth: Penguin, 1986.

Hyperplastic anaemia and parvovirus infection

Acute episodes of erythroid hypoplasia causing anaemia of rapid onset and a low reticulocyte count have been recognised as a complication of chronic congenital haemolytic anaemia for many years. Patients with red cell enzyme or membrane defects or with haemoglobinopathies are equally susceptible. These episodes typically occur in children (but not infants) and may affect more than one family member, with a modal interval of nine days between the index and subsequent cases.[1] The illness usually ends after 10-12 days and does not recur. In areas with a high prevalence of sickle cell disease outbreaks occur at three to five year intervals.[2]

Such epidemiological evidence suggests that the cause of these crises is a single infective agent, probably a virus. This notion is supported by the prodromal symptoms reminiscent of a virus infection and the accumulating evidence of associated human parvovirus infection. Virus antigen has been detected during crises in a few patients with sickle cell disease[2 3] and hereditary spherocytosis.[4] The more common detection of specific class IgM antibodies to human parvovirus has provided evidence of a recent infection in patients presenting in crisis.[4 5]

The human parvovirus is a small (20-25 nm) DNA virus, and infection in an otherwise healthy individual results in a mild febrile illness.[6] The same infection in some children probably results in erythema infectiosum (fifth disease),[7] when there is an associated rash; adult patients frequently complain of arthralgia. The antigen was first detected in the serum of healthy blood donors,[8] and the high frequency (30%) of specific antibody to the virus in the serum of unselected young adults shows that the infection is readily transmitted and causes subclinical illness in most cases.

Normal human erythroid colony growth has been inhibited in vitro (without complement mediation) by adding sera containing virus antigen,[9] and this is neutralised by adding convalescent serum containing antibody to human parvovirus. The target cell is a late erythroid progenitor[10]; granulocyte-macrophage colony growth is largely unaffected. Erythroid suppression together with a shortened red cell lifespan will produce a serious effect, whereas in those without haemolysis it produces only a subclinical fall in the haemoglobin concentration. Measures that prolong the red cell lifespan, such as splenectomy in hereditary spherocytosis or recent blood transfusion in sickle cell disease,[11] may protect against the abrupt cessation of red cell production.

Human parvovirus infection is not known to be associated with the more familiar severe aplastic anaemia that causes pancytopenia and has a very poor prognosis. In half of British cases a cause is identified—usually an idiosyncratic reaction to a drug. The only known infective causes are, rarely, non-A non-B hepatitis[12] and, even more rarely, infectious mononucleosis.[13] In addition to the patients with haemolytic anaemia many of those infected with parvovirus (either as sporadic cases[6] or as contacts of patients with aplastic crises of haemolytic anaemia[4]) have a transient leucopenia and thrombocytopenia—but this seems to be entirely benign and not specific for this virus.[14]

Patients with severe aplastic anaemia do not have evidence of recent human parvovirus infection,[10] nor is the frequency of IgG antibody to human parvovirus higher than in a normal population. These observations do not entirely exclude the parvovirus as a cause. Inquiry about infections should be included in the investigation of patients with severe aplastic anaemia in addition to the usual search for previous exposure to drugs and toxins. Modern DNA technology may eventually help to identify the role of virus infection in idiopathic aplastic anaemia.

The course of clinically evident parvovirus infection is benign, and, although many patients require red cell transfusion, there are no recently reported deaths. Whether parvovirus contributes to the more serious, though rare, severe aplastic anaemia, remains speculative. Although aplastic crises are rare in temperate areas, in areas where sickle cell disease is common about 10% of patients with sickle cell disease will suffer a crisis before the age of 15 years. It should be possible to produce a vaccine to protect against this self limiting disease in high risk groups.

D P BENTLEY

Consultant Haematologist,
Llandough Hospital,
Penarth,
South Glamorgan CF6 1XX