**Comorbidity of Mental and Physical Disorders** 

## **Key Issues in Mental Health**

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# Comorbidity of Mental and Physical Disorders

Volume Editors

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#### **Key Issues in Mental Health**

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### Foreword

The editors are to be congratulated in having obtained contributions from experts on a wide range of physical disorders in order to throw light on those physical disorders which have a higher rate of psychological disorders associated with them. Recognition and treatment of these disorders have been shown to improve the patient's quality of life, and also collaboration with the treatment regimes for their physical illness.

Of course, the shoe can be fitted to the other foot, and one can ask to what extent do particular psychological disorders have higher rates of expected physical disorders. Both of these are valid questions, but while the second is of great scientific interest, the first is more important from the viewpoint of patient care.

In probing the reasons for these higher than expected comorbidities, it is often found that there is no single way in which one form of morbidity influences the other: each one exacerbates the other, and good clinical care must not be blind to the psychological disorders with which a particular physical disease is associated. This book provides examples of the various ways in which such vicious circles establish themselves.

In addition to the possible factors mentioned by the editors in their preface that may account for the high comorbidity between psychological disorders and physical illnesses, there are a number of other possible relationships. First, the number of different pains caused by the physical illnesses increases the probability of depression: in one primary care study, patients with a single pain were no more likely to be depressed than those without pain, but with two different pains the probability of depression was double, and with three or more pains the probability of depression was five times higher [1]. Secondly, chronic physical illness carries with it the risk of disability, which can be very depressing for an adult who has previously been healthy. For example, Prince et al. [2] showed that the attributable fraction of disability or handicap for the prediction of onset of depression among the elderly was no less than 0.69, and Ormel et al. [3] showed similar findings in Holland. Thirdly, there are physical changes in some diseases which may underlie the development of depression, such as changes in the allostatic load. Allostasis refers to the ability of the body to adapt to stressful conditions. It is a dynamic, adaptive process. Tissue damage, degenerative disease (like arthritis) and life stress all increase allostatic load and can induce inflammatory changes which produce substances such as bradykinin, prostaglandins, cytokines and chemokines. These substances mediate tissue repair and healing, but also act as irritants that result in peripheral sensitisation of sensory neurons, which in turn activate central pain pathways [4]. These are all ways in which a physical disorder can produce higher than expected rates of psychological disorders.

There are also psychological disorders that antedate episodes of physical disorder, such as a depressive illness. Systematic reviews of 11 prospective cohort studies in healthy populations show that depression predicts later development of coronary heart disease in all of them [5, 6]. The occurrence of a depressive episode before an episode of myocardial infarction has been reported by Nielsen et al. [7]. Three prospective studies have also shown that depression is an independent risk factor in stroke [8-10]. In prospective population-based cohort studies, depression has been shown to predict the later development of colorectal cancer [11], back pain [12], irritable bowel syndrome [13] and multiple sclerosis [14], and there is some evidence that depression may precede the onset of type 2 diabetes. Prince et al. [15] argue that there is consistent evidence for depression leading to physical ill-health in coronary heart disease and stroke, as well as depression in pregnancy potentially leading to infant stunting and infant mortality.

It has been hypothesised [16] that increases in pro-inflammatory cytokines in depression and increased adrenocortical reactivity may also lead to atherosclerosis, and with it increased risk for both stroke and coronary artery disease. In the latter, autonomic changes in depression may also cause ECG changes which favour development of coronary disease. Changes in natural killer cells and T-lymphocytes in depression may lead to lowered resistance to AIDS in HIV infections. Menkes and McDonald [17] have argued that exogenous interferons may cause both depression and increased pain sensitivity in susceptible individuals by suppressing tryptophan availability and therefore serotonin synthesis. More prosaic explanations include reduced physical activity in people suffering from depression [18].

It is clear that relationships between the two forms of morbidity are complex and that causal relationships that may be true for one physical disorder may not apply to another disorder. The chapters of this book bring together in one place a comprehensive account of these comorbidities, and an important step has therefore been taken in a field in which there is still much to learn in the future.

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#### References

- Dworkin S, Vonkorff M, Le Resche L: Multiple pains, psychiatric and social disturbance: an epidemiologic investigation. Arch Gen Psychiatry 1990;47:239– 245.
- 2 Prince MJ, Harwood RH, Blizard RA, et al: Impairment, disability and handicap as risk factors for late life depression. Psychol Med 1998;27:311–321.
- 3 Ormel J, Kempen GI, Penninx BW, et al: Chronic medical conditions and mental health in old people. Psychol Med 1997; 27:1065–1067.
- 4 Rittner HL, Brack A, Stein C: Pro-algesic and analgesic actions of immune cells. Curr Opin Anaesthesiol 2003;16:527– 533.
- 5 Hemingway H, Marmot M: Evidence based cardiology: psychosocial factors in the aetiology and prognosis of coronary heart disease: systematic review of prospective cohort studies. BMJ 1999;318: 1460–1467.
- 6 Nicholson A, Kuper H, Hemingway H: Depression as an aetiologic and prognostic factor in coronary heart disease: a meta-analysis of 6,362 events among 146,538 participants in 54 observational studies. Eur Heart J 2006;318:1460– 1467.
- 7 Nielsen E, Brown GW, Marmot M: Myocardial infarction; in Brown GW, Harris T (eds): Life Events and Illness. London, Unwin Hyman, 1989, pp 313–342.

- 8 Everson SA, Roberts RE, Goldberg DE, et al: Depressive symptoms and increased risk of stroke mortality in a 29year period. Arch Intern Med 1998;158: 1133–1138.
- 9 Ohira T, Iso H, Satoh H, et al: Prospective study of stroke among Japanese. Stroke 2001;32:903–908.
- 10 Larson SL, Owens PL, Ford D, et al: Depressive disorder, dysthymic disorder and risk of stroke: thirteen-year follow up from Baltimore Epidemiologic Catchment Area study. Stroke 2001;32: 1979–1983.
- 11 Kroenke CH, Bennett GG, Fuchs C, et al: Depressive symptoms and prospective incidence of colorectal cancer in women. Am J Epidemiol 2005;162:839–848.

- 12 Larson SL, Clark MR, Eaton WW: Depressive disorder as a long-term antecedent risk factor for incident back pain: a 13-year follow-up study from the Baltimore Epidemiological Catchment Area sample. Psychol Med 2004;34:211–219.
- 13 Ruigómez A, García Rodríguez LA, Panés J: Risk of irritable bowel syndrome after an episode of bacterial gastroenteritis in general practice: influence of comorbidities. Clin Gastroenterol Hepatol 2007;5:465–469.
- 14 Grant I, Brown GW, Harris T, et al: Severely threatening events and marked life difficulties preceding onset or exacerbation of multiple sclerosis. J Neurol Neurosurg Psychiatry 1989;52:8–13.
- 15 Prince M, Patel V, Saxena S, et al: No health without mental health. Lancet 2007;370:859–877.
- 16 Wichers M, Maes M: The psychoneuroimmuno-pathophysiology of cytokineinduced depression in humans. Int J Neuropsychopharmacol 2002;5:375– 388.
- 17 Menkes DB, McDonald JA: Interferons, serotonin and neurotoxicity. Psychol Med 2000;30:259–268.
- 18 Whooley MA, de Jonge P, Vittinghoff E, et al: Depressive symptoms, health behaviors, and risk of cardiovascular events in patients with coronary heart disease. JAMA 2008;300:2379–2388.

## Preface

There is little doubt about the fact that comorbidity – the simultaneous presence of two or more diseases – is a major challenge for health services. The prevalence of comorbidity has increased rapidly and continues to grow for several reasons, mainly the increase in life expectancy following successes in medicine and socioeconomic development. However, also playing a role are environmental factors (such as air pollution), changes in lifestyle, rapid urbanization and medical factors including iatrogenic disease and the fragmentation of medical services which often result in the late recognition of comorbid diseases and the consequent failure to treat them.

An area of particular neglect is the comorbidity between mental and physical disorders. One of the main reasons for this development is the long-standing separation of psychiatry from other branches of medicine. The geographic separation of mental health institutions from the hospitals and departments dealing with other physical diseases is a material expression of the perception that psychiatric disorders are not diseases like others, and a consequence of this perception is the growing distance and separation between psychiatry and the rest of medicine. In practice, this has led to many psychiatrists failing to recognize the presence of physical illness in their patients and being reluctant to provide treatment for the physical disorder when a diagnosis is made. The same is true for specialists in other branches of medicine who pay insufficient

attention to the presence and treatment of mental disorders in their patients.

The neglect of comorbidity of mental and physical illness is also linked to the fact that its prevalence has been, for a long time, severely underestimated. This was due in part to the lack of recognition described above; however, it also reflects the fact that the stigma of mental illness makes patients reluctant to speak about their mental health problems to nonpsychiatric physicians. Comorbidity of mental and physical illnesses often leads to a tacit collusion with patients and healthcare professionals agreeing to deal with the physical illness as if the mental disorder did not exist. The fact that people with mental illness are often poor and less well educated may have also contributed to lesser utilization of health services that might have recorded the number and frequency of comorbidity of mental and physical illness.

The scant attention given to the comorbidity of mental and physical disorders is of major public health concern. The simultaneous presence of mental and physical diseases worsens the prognosis of both types of disorders and increases the personal and social cost of dealing with them. Complications of the comorbid diseases become more probable and their treatment is more complex. What is particularly worrisome is that comorbidity of mental and physical disorders is becoming more frequent at a time when medicine is becoming increasingly fragmented into super-specialties and when the numbers of general practitioners who can follow the rapid development of knowledge in the many disciplines of medicine is diminishing.

The reasons for the high prevalence of mental and physical illness are only partially clear. To an extent this may occur because some people with mental illness do not pay sufficient attention to their bodies and do not follow elementary rules of healthy lifestyle, hygiene and disease prevention. That many people with mental illness live in conditions of poverty and deprivation where they may be exposed to the considerable dangers of violence and abuse might also be a part of the explanation. People with mental illness often abuse alcohol and other drugs which expose them to the health consequences of substance misuse such as hepatitis and HIV infections. Although these reasons are important, they do not explain all of the excess comorbidity. A number of biological changes seen in mental illness may also predispose to physical ill health, including enhanced inflammation or endocrine dysfunction, but genetic factors are also important. We are still lacking longitudinal studies of comorbidity that could offer insights into the mechanisms. The recent findings on the effects of early childhood abuse on the prevalence of cardiovascular diseases and on the prevalence of depression are good examples of the gains that might result from long-term and life-perspective studies.

Our main goal for this book was to assemble and present material that will help in efforts to raise awareness of the magnitude and nefarious consequences of comorbidity of mental and physical illnesses while stimulating relevant research as well as the application of knowledge that is already available. We invited leading experts in the field of comorbidity to participate in the production of this volume. We have tried to exemplify issues that arise in three main areas of concern. The first of these are the public health aspects of comorbidity focusing on the ways in which comorbidity can be conceptualized, on the cost that comorbidity presents to society and on the interaction of comorbidity with factors stemming from the context of socioeconomic development. In the second group of chapters we assembled reviews of evidence that illustrate the two main approaches to the understanding of evidence about comorbidity. For the first approach, the chapters look at specific issues that arise in relation to comorbidity of mental disorders with disease groups of major public health importance, such as cardiovascular illness, cancer and infectious diseases. For the second approach we examined physical comorbidity in relation to a range of mental and behavioral disorders, including substance abuse, eating disorders and anxiety. The message imbedded in this way of presenting evidence - using one of the two approaches - is that both are necessary: taking a position of looking at comorbidity from only one side may hide important issues and clues. The last group of chapters includes contributions that deal with the elements of the response to the problems arising from comorbidity - the organization of health services (especially the role of the general practitioners), the training of different categories of health personnel and the multisectoral engagement necessary to prevent comorbidity.

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