INTRODUCTION

The biopsychosocial model is a useful conceptual model allowing GPs to think about patients in a holistic manner during consultations (1). It also produces better outcomes for patients. The mechanism that underpins this is based on the interaction between hormones and neurotransmitters that mediate psycho-social processes and their effects on the immune system. This is the field of psycho-neuro-immunology (PNI).

Take a moment to reflect on the importance of this finding in explaining how we are affected by our environment and how evolution and natural selection may work.

NEED TO KNOW

Work in PNI shows a 2-way relationship between the neuro-endocrine system (producing neurotransmitters and hormones), and our immune system (2). Work in this field shows that white cells have specific receptors for neurotransmitters and hormones. These receptors mediate immune cell responses such as the production of antibodies and cytokines (3). Conversely, white cells produce neurotransmitters and hormones that in turn affect our psychological functioning (2). It is therefore a fallacy to suggest that the mind and body are somehow separate; as the chemicals that mediate our mind are partly produced by our immune system, which resides in many parts of our bodies.

What are the implications of this statement?

We shall now examine in more detail the mechanisms and health outcomes that underpin these statements.
INFLUENCE OF NEGATIVE PSYCHOSOCIAL VARIABLES ON DISEASE OUTCOMES

It is well-known that stress responses to adverse social and psychological events produce increased levels of adrenaline and cortisol. It has become apparent that these chemicals have inhibiting effects on immune function. These effects include reductions in antibody, interleukin, interferon and tumour necrosis factor levels. The effects also result in reduced killer T cell function and suppression of growth hormone, which has broadly beneficial effects on immune function (4). The immune system is not only responsible for our responses to 'external' infection but also 'internal' processes such as inflammation, neoplasia, obesity, ageing and autoimmunity. ¹

Therefore, we find that adverse psychosocial events result in immune dysfunction and produce an array of negative health outcomes. Some of the evidence is outlined below:

- Short term stress in medical students due to exams produces reductions in Interleukin 1, reduced response to vaccinations and a 40% reduction in wound healing (5, 6).
- Long term stress caused by environmental (job stress, relationship problems, unemployment) and climatological changes are all associated with immune dysregulation, including reduced T-cell activity (4).
- Social isolation produces a 2-3-fold increase in all-cause mortality (7, 8).
- Perceived stress reduces T-cell function in response to the HPV-16 virus in women with cervical dysplasia (9).
- The probability of contracting a viral illness is directly related to psychological stress (10).
- Caring for a spouse of parent with dementia produces immune dysfunction resulting in endocrine and wound healing dysfunction (4).
- The average age at death in the poorest part of the UK is 58, the age of death in the richest is 85.

In short, we can see that negative psychosocial events produce negative health outcomes across a range of immune-regulated activity including; cancer, viral infection, endocrine dysfunction and wound healing. It is therefore not always helpful to distinguish certain diseases as 'psychosomatic' as almost all health outcomes are related to social and psychological variables.

¹ This is a relatively recent (1989) finding based on vaccine research and the role of adjuvants. Vaccines and arguably the field of immunology were discovered by the GP Edward Jenner. For a fascinating and highly readable account of immunology and PNI read The Beautiful Cure by Daniel M Davies. Alternatively read Janeway.C (2002). A trip through my life with an immunological theme (Ann Rev Immunology 20 (1-28)
INFLUENCE OF POSITIVE PSYCHOSOCIAL VARIABLES ON DISEASE OUTCOMES

Conversely, positive social and psychological events enhance immune function and produce better health outcomes. This is through reducing the levels of stressor hormones such as cortisol and adrenaline and increasing levels of substances like growth hormone.

- Relationship continuity with a family doctor produces a statistically significant reduction in all-cause mortality (11).
- Close social ties result in increased levels of natural killer cell function in those caring for spouses with cancer (12).
- Learning mindfulness techniques can lower cortisol and inflammatory markers and increase T cells (13).
- Survival times in cancer (malignant melanoma) are significantly increased amongst those who have undergone a 6-week intervention to increase their feelings of self-control and ability to problem solve (14).

MEDICALLY UNEXPLAINED SYMPTOMS

The interplay between physical and psychological can result in some of the most interesting but difficult areas of medicine - where the combination of physical and psychological can result in symptoms that medicine at present is not fully capable of accounting for. Functional disorders, conversion disorder, medically unexplained symptoms are all words that try to express this dynamic. We will use medically unexplained symptoms (MUS).

PREVALENCE

Many research studies over the past twenty years have indicated that unexplained symptoms are very common in both primary and secondary care settings. The prevalence estimates for primary care range from 30 to 50% (15). The problem is by no means confined to primary care, a retrospective case notes review of patients seen at two London hospitals (16) revealed an average of 52% of participants across a range of medical out-patient clinics as having MUS. The highest rate of unexplained symptoms was 66% in gynaecology clinics, but neurology (62%), gastroenterology (58%), cardiology (53%) and rheumatology (45%) also had a very high prevalence of no clear organic diagnosis, three months after the initial appointment and all appropriate investigations.

COSTS

These high rates of unexplained symptoms suggest that a significant number of patients are likely to have undergone potentially avoidable referrals and investigations. This is associated with major costs - both in terms of difficulties and frustration in the relationship between patients and their clinicians, as well as the potential for harm done with invasive tests, the associated anxiety when this fail to give a clear diagnosis and the significant accompanying financial costs.
Research indicates that the costs to the UK economy of MUS are £3 billion in the year 2008-9, with wider costs to the economy in terms of absence from work and impaired quality of life of £14 billion (17).

**MANAGEMENT**

There is evidence that good communication skills and an empathy can help to reduce investigations and health-care costs in MUS (18). Giving effective explanations for 'unexplained' symptoms, in a way which make sense to both the patient and the practitioner and help the patient to function better have been shown to be very important (19). There is some evidence that patients with unexplained physical symptoms may seek emotional support more than other patients (20). Psycho-social factors should be explored as part of any initial history, but particularly whenever cases are atypical and there is a possibility of MUS. A significant proportion of such patients (around 30 to 40%) will have significant underlying psychological or social difficulties and physical symptoms may be their way of presenting these difficulties (21).

**CONCLUSION**

A mechanism linking our outside world with our internal world has been elucidated and has profound implications for health.

From an endocrine and immunologic perspective, some of generalist medicine can therefore be an attempt to reduce negative psychosocial factors and to increase positive psychosocial factors because both actions have profound positive effects on the immune system and consequently health. The practical implications are that to reduce negative psychosocial factors, GPs may need to become agents of social change. However, this can be very time intensive. To increase positive psychosocial factors, we need to focus relentlessly on the nature of our relationships with patients - bearing in mind what a strong effect on immunity and health this can have. It is to this topic therefore that we turn to next.
A NOTE ON PSYCHONEUROIMMUNOLOGY RESEARCH

The PNI field is in its infancy and has several challenges:

- Large-scale studies are needed to show effects as there are many confounding factors and effects may be small or variable. Psychosocial interventions such as increasing social ties do not carry patents unlike medications. There is far less money available to do the research. There is a paradox therefore in that despite having potentially profound effects on human health, research in PNI receives negligible funding.
- Reducing negative psychosocial variables such as improving housing, improving working conditions and engaging meaningfully in environmental improvement is difficult, costly and ideologically unpalatable to some.
- Concepts such as ‘stress’, ‘poor housing’, ‘psychosocial intervention’ - whilst relatively easy to visualise in a common-sense way, are far more difficult to define with sufficient clarity for trials.

ACTIVE LEARNING

✓ Talk with your placement provider about the contents of this theme. Do these findings resonate with their experience?

✓ How might you construct a study in general practice to investigate the relationship between events in patient’s lives and immune function?

✓ Try to find a patient where there are medically unexplained symptoms, or the frequency of appointments is high. Look back in the notes. Are there adverse childhood experiences (ACEs)? Find out more about these and their effects on physical and psychological conditions.

✓ Have you seen any examples of effective explanations being given to patients for their unexplained symptoms - what were important factors in how this was done?

✓ Try and speak to a patient with unexplained symptoms about their thoughts and what they have found helpful or otherwise in their contacts with health professionals.
FURTHER LEARNING

RESOURCES

- Try reading ‘The Beautiful Cure’ by Daniel Davis (2018). It’s a very readable account of the field of immunology and a fascinating insight into the world of research.
- Try watching ‘Safe’ (Julianne Moore) - this film explores (amongst other issues) the relationship between emotional states and immune function.
- A very readable introduction to medically unexplained symptoms (MUS) is written by the neurologist Suzanne O’Sullivan; ‘It’s All in Your Head; stories from the frontline of psychosomatic illness’. - it was winner of the Wellcome book prize in 2016.

REFERENCES


The following resources have been developed in conjunction with SAPC Heads of GP Teaching. If you have any queries or questions regarding the resources on offer, please contact Prof. Joe Rosenthal or Prof. Alex Harding, Co-Chairs of SAPC’s Heads of GP Teaching Group.