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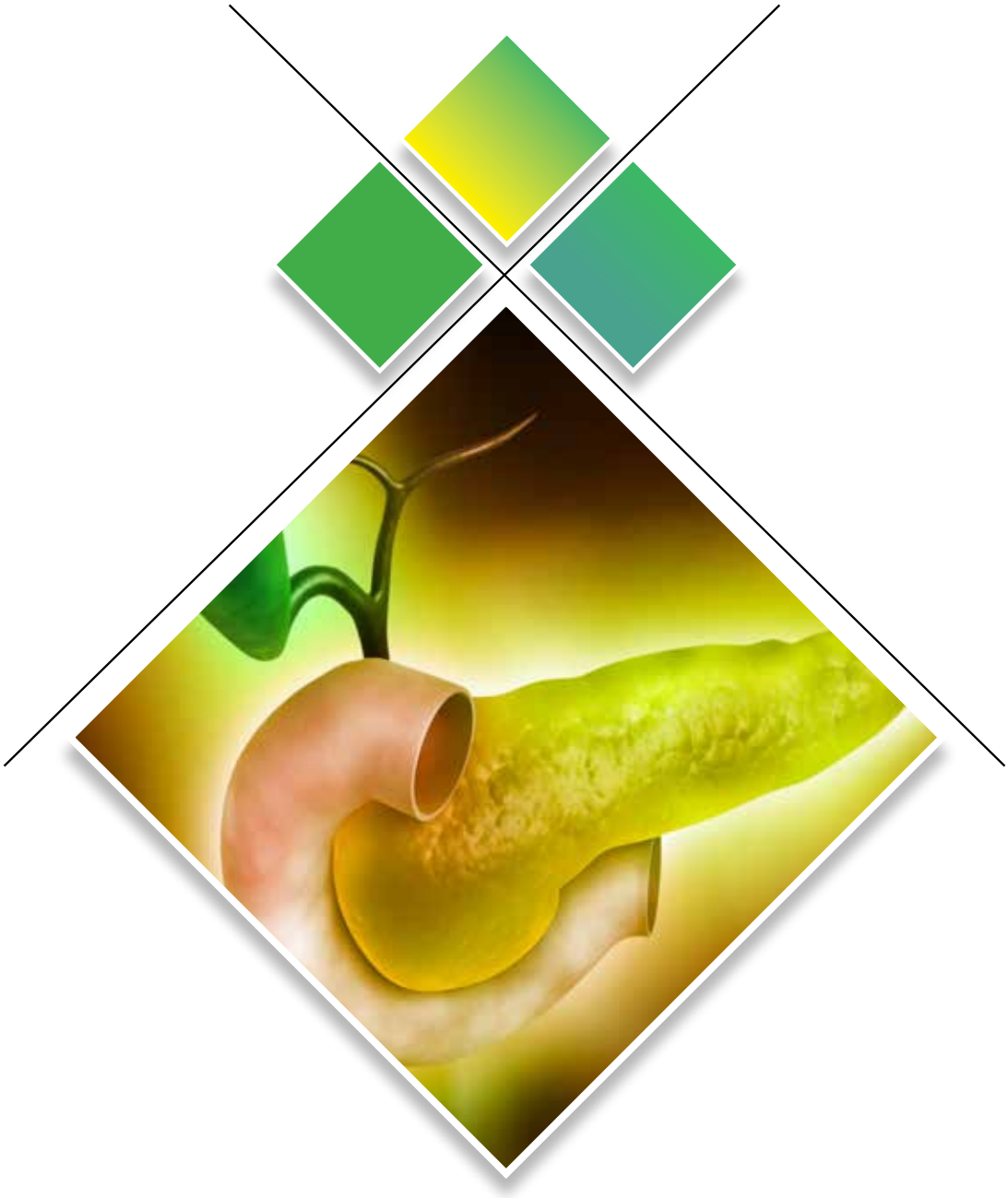
the Pancreas Matters

Continuing Medical Education on all aspects of the pancreas and gastroenterology



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the Pancreas Matters

Editorial

Contents

Editor:	Dr Sean Burmeister
Production Editors:	Ann Lake Publications
	Ann Lake
	Helen Gonçalves
Design:	Jane Gouveia
Enquiries:	Ann Lake Publications
Tel:	011 802 8847
Fax:	086 671 9397
Sponsor:	Abbott
Email:	lakeann@mweb.co.za

Editor: Dr Sean Burmeister
Senior Consultant
Surgical Hepato-Pancreatico-Biliary unit,
Groote Schuur Hospital and Digestive Diseases Centre, UCT Private Academic Hospital

Dear Readers

Welcome to the second edition of the Pancreas Matters for 2023. The journal continues in it's aim to provide up to date reviews of topical issues likely to be encountered by practitioners involved in managing patients with pancreatic disorders. In this issue we tackle effects of antibiotics on the microbial flora resident in the human gut; depression in patients with pancreatic cancer and issues relating to HIV in the workplace.

Recent years have seen an increasing appreciation and interest in the human microbiome and the role it may play in health and disease. The human microbiome represents the genome of the microbial community (bacteria, funghi and viruses) resident within and on a given individual and includes that of both symbiotic and pathogenic organisms. Advances in genomic sequencing and analysis have allowed for a better understanding of the interaction between the microbiome and it's host in the context of health, disease and recovery. The microbiome has been noted to have an impact on human metabolism, nutrition, physiology, defence against pathogens and immune function. The microbiome is highly complex and vast, outnumbering the host's genes by more than 100 times, with many consequently considering the microbiome an organ in it's right. The majority of a host's microbial organisms reside within the gastro-intestinal tract but the effects of imbalances may be felt both locally in the GIT in conditions such as inflammatory bowel disease as well as systemically as in obesity and diabetes. The last almost 100 years has seen the introduction and development of antibiotic use as one of the greatest medical advances during this period. However, the effects of these drugs on human physiology not to mention the microbial environment and it's genetic state is only now becoming better understood. In this issue Dr Peter Barrow, consultant gastroenterologist at the Wits Donald Gordon Medical Centre, reviews some of the current understanding around the effects of anti-bacterials on the gut and it's resident microbiota, including how deleterious effects may be minimised.

Pancreatic cancer remains a feared diagnosis for many reasons. Improvements in outcomes have been slow to arrive and remain worse than for many other malignancies; curative treatment options are complex, challenging and invasive with associated morbidity and even mortality while non-curative or recurrent scenarios may herald a difficult path to the end of life. Frequently the diagnosis may come as a surprise with patients having been relatively asymptomatic until recently or the diagnosis not entertained by previous healthcare practitioners. In this context, news of the diagnosis can come as a devastating bombshell which patients may be poorly prepared for. Treating clinicians, while empathetic, are often focussed on addressing the urgent clinical problem and determining definitive treatment and have often received little formal training in delivering such devastating news. Psychological distress is almost invariable when patients are informed of the diagnosis and may even precede this. Evidence further exists to suggest there may be a physiological link between the disease process itself and the development of depression, which again can precede the development of symptoms and the diagnosis. Consequently these patients are at significant risk of depression and clinicians should actively screen for this as when it develops it may have a significant deleterious effect on quality of life, treatment outcomes and even disease progression. Early involvement of healthcare practitioners when needed can improve outcomes for patients with pancreatic cancer and serious consideration should be given to including them in the treatment team. Gerhard Grundling, clinical psychologist and director of the Clinical Psychology Forum of SA, delves into detail on the clinical picture that aids screening for this co-morbid condition and offers a practical approach to initial management.

HIV remains prevalent in the South African population with current estimates suggesting that between 15 % and 20 % of the population may be affected. While effective anti-viral therapy has transformed this condition into what is essentially a chronic disease, compliance, treatment failure and conditions that can nevertheless occur in immune-competent individuals remain a concern. The impact these and other issues may have on a person's ability to work effectively may cause anxiety in the employee and employer alike. Legislation exists to guide both parties in this regard, in particular emphasising the various responsibilities and rights of employees and the employer as embodied in the Employment Equity Act and HIV code of Good Practice. Elsabe Klinck, well known in medico-legal circles and a regular contributor in numerous fora reviews this legislation as well as other Acts and provides some practical insight by way of case examples.

We trust you will find this latest edition of the Pancreas Matters informative and practically beneficial. We again encourage the readership to approach the publishers with suggested topics that they would like addressed in future editions. Lastly we are indebted to our authors for their time and the publishing team for making it possible for this worthwhile educational resource to continue.

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Microbiome changes in the gut with anti-infectious agents

Dr Peter Barrow
MBBCh, DCH, FCP, Cert. GASTRO
Consultant Gastroenterologist
Wits Donald Gordon Medical Centre
Johannesburg

Over the last decade there has been an "explosion" of interest in the human microbiome. Understanding of the interaction between human health and the bacteria, viruses, parasites and fungi residing in our gastrointestinal system continue to grow.

Helicobacter pylori with its association with digestive diseases including peptic ulcer disease, gastric cancer, mucosa-associated lymphoid tissue lymphoma and "Idiopathic" thrombocytopaenia has highlighted how trying to manipulate at least part of the microbiome can result in beneficial effects.

On the other side of the coin, *Clostridioides difficile* associated pseudomembranous colitis is an example of how altering the microbiome with antibiotics can result in deleterious effects.

In this review I aim to discuss how the use of antibiotics may alter the microbiome and what we may be able to try to do to maintain or restore the health of the microbiome.

THE MICROBIOME

The human body has been estimated to harbour about 100 trillion (100 000 000 000 000) microorganisms, which is approximately 10 fold more than the number of nucleated human cells.[1] Up to 2000 microbial species have been identified within the gastrointestinal tract of "healthy" humans. Among the hundreds of organisms, the four most common are bacteria belonging to the phyla Firmicures, Bateroidetes, Actinobacteria and Proteobacteria. It is now accepted that the commensal microbiota are essential in maintaining homeostasis via production of metabolites that regulate immune responses, mucosal barrier function, suppression of pathogen overgrowth, vitamin and energy source generation. The microbiome has also been shown to "evolve" overtime and in response to environmental factors. This makes it very difficult to define what is a normal microbiome.

Colonisation with "normal" organisms starts shortly after birth and continues throughout life. When an imbalance occurs, it may contribute to a multitude of disorders. The disturbed microbial milieu is termed "dysbiosis". Dysbiosis has been linked to multiple various medical conditions including Irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), *Clostridioides difficile* infection, metabolic syndrome, obesity, non-alcoholic fatty liver disease, various neuro-psychiatric diseases including Parkinson's disease and Alzheimer's, systemic autoimmune diseases and diabetes amongst others.

Figure 1. Illustration of Clostridioides difficile

ANTIBIOTIC EFFECTS

The development of antibiotics is widely regarded as one the greatest medical advances of the 20th century.[2] Worldwide, antibiotic usage continues to increase with an estimated increase by 65 % between 2000 and 2015.

Although often thought to have no major long-term effects, antibiotic usage has now been shown to have several negative effects on the gut microbiota including reduced species diversity, altered metabolic activity and selection of antibiotic resistant organisms. There is also evidence that early childhood exposure to antibiotics can lead to several gastrointestinal, immunologic and neuro-cognitive conditions.

Reduced Diversity

In children, restoration of microbial diversity after antibiotic treatment takes up to 1 month.[3] In adults, antibiotic usage has been shown to alter the balance for at least 180 days.[4] This disruption may lead to an overgrowth of pathogenic bacteria such as *C. difficile*. It should also be noted that reduced diversity does not necessarily mean reduced number of bacteria. Rather, as antibiotic susceptible organisms are eradicated, antibiotic resistant bacteria may multiply and take their place. This can lead to an increase in microbial load even though species diversity is reduced. Treatment with a 7 day course of B-lactam antibiotics actually doubled microbial faecal load and changed the ratio of Bacteroidetes to Fimicutes.[5]

Altered metabolome

The metabolome is the global collection of all low molecular weight metabolites that are produced by cells during metabolism[6] This provides a direct functional readout of cellular activity and may reflect the physiological status of an individual. The effects of antibiotics on the metabolome are less well studied than that on bacterial diversity, but recent studies have highlighted how antibiotics can affect this important system. In mice, low dose antibiotics lead to increase adiposity and disorders of carbohydrate and lipid metabolism.[7] In humans treatment with vancomycin decreased levels of secondary bile acids was shown to decrease peripheral insulin sensitivity.[8] In patients with metabolic syndrome or diabetes, this may worsen their metabolic profile.

Antibiotic Resistance

Worldwide, antibiotic resistance is a significant public health concern. Antibiotic resistance related deaths could reach > 10 million by 2050 as estimated by the WHO.[9] In China, antibiotic usage in livestock has dramatically increased antibiotic resistance. Bacteria have developed a range of processes to elude the effects of antibiotics including protection against uptake through cell membrane changes, developing enzymatic processes to modify or degrade antibiotics or actively removing antibiotics via specialised efflux proteins.[10] In humans, the GUT microbiota contains a pool of antibiotic resistance genes and exposure has been shown to rapidly increase this. Antibiotic resistant GUT bacteria have also been shown to be transferred to children from mothers previously exposed to antibiotics.[11]

CLINICAL COSEQUENCES

Short term

Antibiotics associated diarrhoea (AAD) can occur up to 8 weeks after completion of a course of antibiotics.[12] Under normal circumstances, the intestinal epithelium is maintained by several mechanisms including a thick mucous layer and tight junctions to maintain intestinal integrity. Anti-microbial peptides and secretory IgA

are produced in response to the "normal" gut microbiome. Antibiotic exposure may decrease subsets of normal GUT bacteria and in so doing, decrease the production of the protective mucous layer and disrupt the tight junctions resulting in diarrhoea.

The prevalence of AAD is reported in up to 35% of patients receiving antibiotics. Meta-analysis has indicated that probiotics may be useful for the prevention of AAD esp in children.[13]

A significant proportion of *C difficile* associated diarrhoea is related to antibiotic usage. Risk factors include old age, compromised immunity and hospitalisation. Two meta-analyses in adults and another in children have suggested that probiotics may be helpful, but no firm recommendations were made.[2]

H. pylori eradication therapy with triple or quadruple therapy has been associated with a decrease in Bacteroides and increase in Firmicutes which has been shown to increase bacteria production of short chain fatty acids with may result in increase in metabolic disorders.[14] *H. pylori* eradication strategies that combined probiotics have been shown to have a better adverse event profile and has also been associated with improved effectiveness.[2]

Figure 1. Illustration of Helicobacter Pylori

Long term

Antibiotic usage in childhood has been associated increased development of obesity, asthma allergy and IBD. In a study of children under 2 years of age, the use of macrolide antibiotics was significantly associated with asthma and obesity.[15] Early exposure may also contribute to IBD pathogenesis.[2]

PROTECTION STRATEGIES

The first report of "voluntary" modification of gut microbiotia was described in China with use of human faeces to treat various infections and food poisoning. The use of specific strains of bacteria has only been of clinical interest over the last 50 years. The first use of the term "probiotics" was used by Lilly and Stillwell and was restricted to substances produced by bacteria that promote growth of other bacteria.[17] In 1989, the notion of living microbial organisms emerged.[18] Finally in 2014, the current definition was proposed and considers probiotics to be living microorganisms that must be ingested in sufficient amount to have an effect on health that is not limited to the nutritional effects. Most commercially available probiotics contain species from saccharomyces or lactobacillus genera. These "probiotics" are used because of their ability to withstand the low gastric pH. Protective effects may help in maintaining gut barrier.

Faecal microbial transplantation (FMT) refers to the process of transferring gut microbiota from a healthy individual to another person with a dysbiotic microbiome. Probiotics may be limited by a lack of diversity of the organisms.[1] FMT represents a potentially superior alternative and has emerged as a treatment option for recurrent *C. difficile* infection. It is also being investigated as a novel treatment modality for other disease states including IBS, IBD, non-alcoholic fatty liver disease, obesity, neuropsychiatric illness amougst others. However, at present, is only recommended for treatment *C. difficile* infections. FMT can be done via several routes. The most common are via naso-gastric tube of colonoscopy.

CONCLUSION

Antibiotics are undeniably a major advance in modern medicine but they do come with, often underappreciated, risks. Antibiotics do change the human microbiome and results in decreased microbiome diversity, altered metabolome and increase antibiotic resistance.

Microbia restoration therapies (including use of probiotics and faecal microbial transplantation) remain a major challenge, but represent an exciting future as potential treatment for various conditions and may be a prophylactic option to mitigate the potential side effects from antibiotics. Stool banks, donor stool preparation, donor compensation and cost of donor screening are questions that still need to be answered.

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Screening and treatment of depression in patients with pancreatic cancer

Gerhard Grundling
Clinical Psychologist: Benoni
Director: Clinical Psychology Forum of SA
MD: Glynnview Multi Professional Practice, Glynnview Psychiatric Hospital, Benoni

The diagnosis of a life-threatening disease would generally have a psychological impact on most people. Such a diagnosis will have many implications and would demand various ways to adjust to this reality.

The literature indicates that depression commonly occurs before and after the diagnosis of pancreatic cancer (PC). Increased awareness and screening for depression are important with these patients because the impact would have a negative influence on quality of life as well as on the progression of the illness. Therefore psychological distress should be regarded as a vital sign that has to be identified and treated when it occurs. If neglected, patients would utilise health services and visit emergency health services more, leading to an increased economic burden of pancreatic cancer.[1]

A large population-based study by Seoud T et al indicated that patients diagnosed with pancreatic cancer and depression should be referred to mental health practitioners. This is vitally important because depression that is co-morbid to pancreatic cancer significantly increases the mortality rate of patients. When mental healthcare practitioners are integrated into the treatment team this improves outcomes especially quality of life which is of value to patients suffering from PC.[22]

Relationship between depression and pancreatic cancer

Psychosocial distress is a common occurrence when pancreatic cancer is diagnosed and a substantial number of patients would develop depression. Cancer patients are vulnerable to the medical, psychological, and social factors indicated above, and it is well recognised that depression impacts on quality of life of these patients.

The literature indicates that paraneoplastic limbic encephalitis could be related to the development of depression, and it is also recognised that tumour cells can mediate the production of serotonin antibodies in the central nervous system resulting in depression.[3]

Depression generally occurs before the presentation of pancreatic cancer symptoms. Due to this, it is argued that depression could be related to the disease process and in this regard the bilateral relationship between depression and inflammation has received attention and has been recognised for some time. Cytokines, especially interleukin-6 (IL-6), have received attention, they cross the blood brain barrier and are functionally active. It is postulated that IL-6 (and others) mediate depression through their influence on neuroplasticity, neuro-endocrine function, and the metabolism of neurotransmitters. Studies indicate the presence of higher concentration of IL-6 in plasma of cancer patients – including pancreatic cancer – with depression compared to patients without depression and healthy people.[19]

One of the theories sited in literature is that the relationship between depression and cancer in general may be ascribed to immune (cytokine) dysregulation and that depression could increase the subsequent risk for the development of cancer. This risk seems to be especially important in cancers with a poor prognosis, including pancreatic cancer. It is important to note that there is not agreement or full understanding of the bidirectional relationship and higher incidence of the common co-occurrence and the underlying mechanisms between depression and pancreatic cancer.[3,19,20]

Advances in neuroscience and the concomitant theories have enabled us to better understand illness presentation. In this regard Kalliopi M and co-authors have proposed an integrated theory from the available literature focussing on the role of inflammatory factors, hormonal influences, biochemical factors, and immunological processes leading to depression and anxiety in patients diagnosed with PC.[23] This is presented in **Figure 1** below:

Incidence and presentation

When considering the incidence of depression and anxiety in cancer patients compared to the general population, studies indicate that it is twice as high.[2] When compared with all other tumours of the digestive system, pancreatic cancer patients present with the highest co-occuring rate of major depression.[3] This co-morbid presentation between pancreatic cancer and major depression has been known since the 1930's. In an early study published in 1931 in JAMA, Yaskin indicated that a triad of anxiety, depression and impending doom tend to be present with pancreatic cancer. Since then, researchers have been interested in the incidence and association between depression and pancreatic cancer.[4]

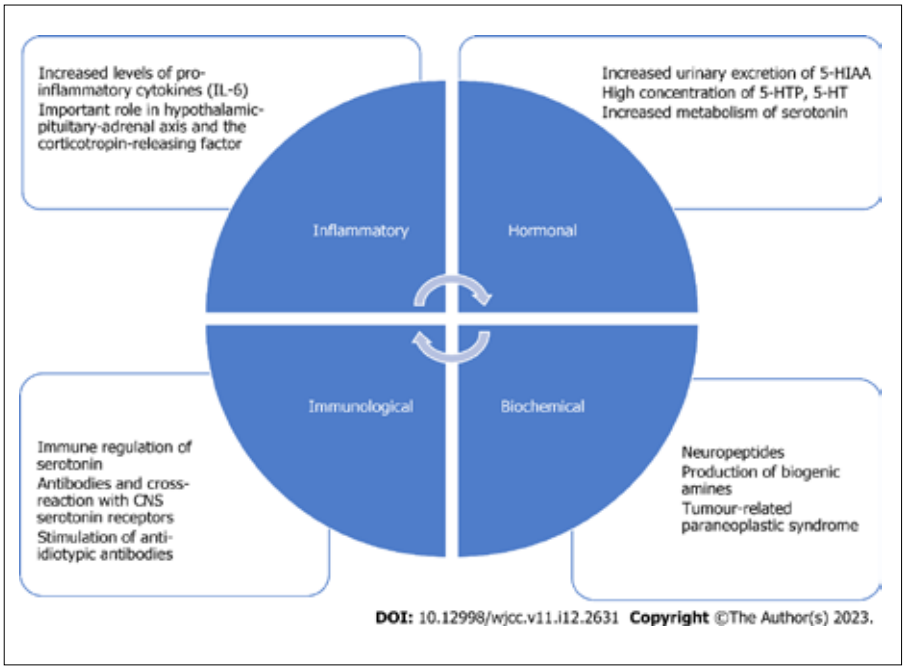

Figure 1. (From Kalliopi M; et al[23])

The prevalence of depression in people with pancreatic cancer has been shown to range from 33 % to 50 %.[4] A study by Fras et al, frequently referenced in the literature regarding pancreatic cancer and depression found that more than half of patients diagnosed with pancreatic cancer reported psychological symptoms up to 43 months before the occurrence of somatic complaints.[6] A study by Holland et al, found that patients with advanced stage pancreatic cancer had more severe depression, severe anxiety and total mood disturbance when compared to patients with other advanced abdominal cancers.[7]

Anxiety has been shown to occur in 48 % of patients with pancreatic cancer and depression.[18]

Pain is a presenting problem in 80 % of patients with pancreatic cancer.[9] It is also known that a bilateral relationship exists between pain and depression, if the one increases so does the other. Levels of anxiety can also impact on mood and pain. In this regard it has been observed that patients awaiting chemotherapy had more severe depression than those awaiting surgery.[9] Due to the high incidence of pain and depression, psychological management should give attention to both.

Clinical outcomes

Depression tends to negatively impact on clinical outcomes in various medical conditions. As a mental health factor depression tends to negatively affect compliance to treatment. Depression causes impairment in judgement and decision-making, leaving patients suffering from depression in a less favourable position to reach treatment outcomes. Depressed patients are less motivated and when patients also experience pathological anxiety avoidant behaviour becomes prominent. To productively access and comply to treatment the identification of and treatment of depression and anxiety is crucial.[26]

Depression has been linked to shorter survival rates for various cancers and more so for PC. Studies show that mortality is 25 % higher for cancer patients with symptoms of depression and 39 % higher for patients diagnosed with depression. Suicide rates are twice as high compared to the general population. PC patients with depression and other mental health conditions receive 20 % to 50 % less surgical interventions and have a worse cancer specific prognosis. Although depression and anxiety are the most common mental health conditions negatively impacting on PC patients, other mental health conditions also have a negative impact. Furthermore, the adverse effect of depression persisted and impacted negatively on long term cancer specific outcomes in PC patients that received treatment and surgical interventions.[26,27]

Research data strongly suggests screening for depression and other mental health conditions to improve short- and long-term outcomes.[32]

Symptoms of depression, screening, and depression types

Knowing the symptoms of depression, is important. This enables the screening, identification, and diagnosis of depression. According to the Diagnostic and Statistical Manual of Mental Disorders 5 (DSM 5) the criteria for the diagnosis of major depression consists of:[8,32]

Five or more symptoms during the same 2-week period and at least one of the symptoms should be either:

1. Depressed mood nearly every day and/ or
2. Loss of interest or pleasure nearly every day.

- Significant weight loss when not dieting or weight gain or decrease or increase in appetite nearly every day.
- Insomnia or hypersomnia nearly every day.
- A slowing down of thought and a reduction of physical movement nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
- Fatigue or loss of energy nearly every day.
- Feelings of worthlessness or excessive or inappropriate guilt nearly every day.
- Diminished ability to think or concentrate, or indecisiveness, nearly every day.
- Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.[8]

As indicated above symptoms include decreased appetite, weight loss and fatigue. These symptoms may be due to the cancer and can then incorrectly be attributed to depression.[10] When diagnosing depression in patients with cancer, attention should be given to psychological and cognitive symptoms such as thoughts of death and suicidal ideation, guilt, worthlessness, impaired concentration, indecisiveness, diminished interest, and diminished pleasure. These symptoms should be used as the basis to diagnose depression in cancer patients.[11]

It is imperative that health practitioners should screen for the presence of depression. Screening should enable practitioners to identify patients with depression at acceptable levels of certainty. In this regard the PHQ9 that is freely available is a good screening tool that is standardised and helps with the diagnosis of depression and gives a clear indication as to the level of severity of depression. It is helpful after diagnosis of depression to repeat the PHQ9 at regular intervals to ascertain the improvement or not of depression. Thus the PHQ9 also functions as an outcome measurement tool for depression.[34,36]

For an initial fast screening of depression, identifying the core symptoms is helpful, namely:[33]

- Sad mood and
- Loss of interest and pleasure

These core symptoms have a positive predictive value of 57 % and a negative predictive value of 98 %. If patients indicate that they do feel sad and experience a loss of interest and pleasure it would be necessary to further investigate for depression and/or refer the patient for diagnosis and management of depression.[15]

Two types of depression would be applicable to patients with PC. The symptomatology is similar[8]

- Major Depression
- Major Depression due to a medical condition.

Choosing the correct antidepressant

Choosing an antidepressant is often difficult as several factors must be considered. What is helpful in this regard is to choose the antidepressant in terms of its specific neurotransmitter action. To know which neurotransmitter is involved, the deconstruction of the DSM 5 criteria can assist.[28]

Serotonergic symptoms include:[28]

- Severe depressed mood,
- Increased or decreased appetite,
- Sleep disturbance,
- Worthlessness and inappropriate guilt,
- Suicidality

Noradrenergic symptoms include:[28]

- Depressed mood,
- Psychomotor agitation or retardation,
- Cognitive symptoms,
- Painful physical symptoms

Dopaminergic symptoms include:[28]

- Depressed mood,
- Anhedonia,
- Cognitive symptoms,
- Psychomotor retardation

A sedative serotonergic or noradrenergic antidepressant can be prescribed if insomnia is a symptom. An activating antidepressant can be prescribed if the patient has diminished drive and energy and needs activation. If weight loss is a problem,

some antidepressants can be of benefit to enhance appetite. Similarly, if sexual side effects are present all the classes of antidepressants have an antidepressant that does not have this side effect. Pain is a common symptom in patients suffering from PC and then antidepressants from the noradrenergic class can be helpful.[28,31,35]

To determine if there could be adverse drug interactions if patients are on other medications, utilising a drug interactions checker such as drugs.com and its applications is valuable.

Referral and follow-up

Literature indicates that referral of patients suffering from PC and depression to a mental health practitioner is preferable because there is a significant difference regarding clinical outcomes between those patients that were referred compared to those that were not referred to a mental health practitioner. Mortality rates were 41.3 % for those patients that were not referred to a mental health practitioner compared to 36.9 % of those that were referred. Interestingly, patients that were referred to a mental health practitioner and received an antidepressant had similar mortality rates. It is thus crucial to ensure that patients are referred to a mental health practitioner.[22]

Once the diagnosis of depression has been made, the severity determined using the PHQ-9, the antidepressant prescribed and the patient referred to a mental health practitioner, the first follow-up appointment by the GP/specialist must be made in two weeks to determine the progress of the patient. At the first follow up visit, the patients' progress must be measured using the PHQ-9 and the patient clinically assessed for improvement and any side effects of the medication. The patient must be encouraged to adhere to taking medication and attending all follow-up consultations. Depending on the measurement of the PHQ-9 the following is relevant:[31,32,36]

- PHQ-9 score below 5 (0-4) indicates that the patient is in remission.
- PHQ-9 score has decreased more than 50 % from the previous score, the patient has had a good response.
- PHQ-9 score has decreased less than 50 % but more than 20 %, the patient has had a poor improvement.
- PHQ-9 score has decreased less than 20 %, it is deemed that the patient had no improvement.

When the PHQ9 indicates a poor improvement or no improvement, then the treatment regime for the depression should be re-evaluated.[36]

Follow up must be scheduled within 2 weeks if any changes to dose or antidepressant have been made, then monthly and eventually 3 monthly.[29]

Conclusion

Depression occurs commonly before and after the diagnosis of PC. There seems to be a bidirectional relationship between PC and depression. Although this relationship is not yet fully understood, recent studies show that screening for and treatment of depression is important because this has a beneficial impact on mortality. Furthermore, early referral to a mental health practitioner should routinely be done as well as to initiate treatment for depression as early as possible. To improve quality of treatment, outcomes measurement of treatment of depression should be initiated to guide the practitioner to adjust treatment regimes when necessary.

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Ethics: Employment and HIV

Ms M.E. Klinck B. Iuris, LLB, BA Hons (German), BA Applied Psychology
Managing Director
Elsabe Klinck & Associates
Johannesburg

Employee and employer concerns

One of the key concerns for employees diagnosed as living with HIV is how safe their jobs are. Apart from the possibility of stigma and discrimination, they are also concerned about what would happen about their health.

Employers, on the other hand, are concerned about the impact of absenteeism on their operations, as well as increased demands on employment social security, such as disability cover and pension/provident funds.

Persons living with HIV also fear discrimination, and that their employment opportunities would be limited. They are also not sure if they have to disclose their status.

Labour legislation covers these issues, as discussed below. Knowing these legal frameworks could go a long way in giving both employers and employees the assurance they need.

The Employment Equity Act, 1998 ("EEA")

The EEA lists HIV as a non-discriminatory ground and includes various protections against discrimination on the basis of HIV (and health in general). The EEA also offers protection in the part of the law governing affirmative action, in that persons living with HIV may claim reasonable accommodation of their condition, as it would fall within the legal definition of a "disability".

The anti-discriminatory protections include:

No unfair discrimination

Employers should take care to not discriminate unfairly, whether in a "direct" or "indirect" fashion. Indirect discrimination occurs where an apparent neutral measure has a disproportionately negative impact on employees living with HIV. For example, a neutral policy relating to sick leave, may have a worse impact on employees living with HIV and requiring more leave. This could also be the case for a family member having to take care of someone living with HIV. An example of direct discrimination may be employment group life insurance, where HIV is excluded, or handled as a dread disease, with benefits limited, or premiums loaded.

The EEA prohibits testing of prospective or existing employees for HIV, unless a Labour Court order has been obtained to approve such testing.

The duty on employers to elimination unfair discrimination, and to take steps towards such elimination.

This would require an analysis by employers as to the aspects of their workplace environments, policies, practices and procedures that might have a discriminatory or exclusionary impact on employees and job applicants. For example, the impact of leave policies, when an employee living with HIV is ill, the social work environment, access to employment benefits, etc. all have to be considered.

Fair discrimination or differentiation

It is possible to differentiate between people on the basis of an inherent requirement of the job. In the context of HIV this would mean that being HIV-negative is an absolute and critical part of the criteria to successfully perform a particular job. It is inconceivable that there could be any such job that requires an HIV negative status. This is in light of the advances in treatment, and even in prophylaxis.

HIV and reasonable accommodation

In terms of affirmative action measures, the annual reports submitted by employers to the Department of Labour, for larger employers, have to indicate that all employment policies and practices have been investigated for possible unfair discrimination. Employers have to specifically indicate whether they have undertaken HIV awareness or similar training, and whether they have a policy on HIV in the workplace.

The HIV Code of Good Practice, 2012

On these matters, the Code of Good Practice on HIV in the Workplace, issued under the EEA, provides valuable guidance to employers on implementing a Workplace HIV Plan and Policy. It should also be kept in mind that the measures an employer must take, are not "once-off" events, and that training, awareness-raising and policies have to be undertaken and reviewed regularly.

An HIV workplace programme must consider the following:

a. *Compliance with legal obligations;*
b. *Management commitment;*
c. *Consultation with relevant stakeholders;*
d. *Development and effective implementation of HIV and AIDS and TB Workplace Policies, Prevention and Wellness Programmes;*
e. *Resources, including human, financial and operational resources must be allocated for the effective development and implementation of policies and programmes;*
f. *Policies and programmes must be informed by the outcomes of research and evidence; and*
g. *Monitoring and Evaluation of HIV and AIDS policies and programmes must be put in place*

The Code refers to the importance of employers having Employee Assistance Programmes (EAPs). It states:

"All workers must have access to affordable health services, social security, insurance schemes or other employment related benefits either through the employer, the State or non-governmental organisations. Programmes of care and support must include measures of reasonable accommodation in the workplace for persons living with HIV or HIV related illnesses."

It also deals with informed consent and confidentiality, making clear that no employee can be forced to disclose their HIV status. Termination of employment on the basis of HIV status is prohibited.

Employers must also, in terms of the Code, design and implement a HIV and AIDS workplace Monitoring and Evaluation Plan.

Reasonable accommodation

Reasonable accommodation means that consideration should be had for the need of such employees to time off to visit their GP, pharmacy or clinic to get their medication and for check-ups. Employees may also need accommodation in either the manner in which sick leave is spread over the three year period, or in having additional sick leave to allow them to fully recover after an opportunistic infection.

Employers with 50 or more employees must implement "reasonable accommodation" measures for persons with disability and HIV. As part of their affirmative action

obligations under the EEA. Employers with less employees have to also accommodate incapacity, or ill health, in terms of Schedule 8 to the Labour Relations Act, 1995. Before dismissing an employee on the basis of incapacity, an employer has to investigate the incapacity, consider the nature and extent to which a person would still be able to do the jobs, as well as whether the employer can reasonably accommodate the employee, or provide alternative employment.

This duty to reasonably accommodate however only extends as far as it imposes "undue hardship". Undue hardship is when there is significant difficulty or expense to the employer and workplace, in the light of the specific situation. For example, if there are only two employees in a particular unit and one is absent quite frequently, the burden on the remaining employee and on the employer to employ a third person to stand in for the absent employee may be too much.

In the case of *Standard Bank of South Africa v the CCMA* the Court considered the nature of the job that the employee that claimed failure of the bank to reasonably accommodate her, held. It also investigated what the employer did, and did not do, in dealing with the employee's disability (or inability to do her previous job). The Court also confirmed the labour law analysis imposed by the Labour Relations Act when dismissal for incapacity is at stake:

In stage one "the employer must enquire into whether or not the employee with a disability is able to perform her work. ... If the employee is unable to perform her work and her injuries are long term or permanent, then the next three stages follow."

In stage two "the employer must enquire into the extent to which the employee is able to perform her work. This is a factual enquiry to establish the effect that her disability has on her performing her work. The employer may require medical or other expert advice to answer this question."

During stage three, "the employer must enquire into the extent to which it can adapt the employee's work circumstances to accommodate the disability. If it is not possible to adapt the employee's work circumstances, the employer must enquire into the extent to which it can adapt the employee's duties. Adapting the employee's work circumstances takes preference over adapting the employee's duties because the employer should, as far as possible, reinstate the employee."

The Court also confirmed that the employer has to take into account relevant factors including "the nature of the job, the period of absence, the seriousness of the illness or injury and the possibility of securing a temporary replacement". Only if no adaptation is possible, the employer must enquire if any other suitable work is available.

Employers should therefore give careful consideration as to the needs of and type of reasonable accommodation required for employees living with HIV, bearing in mind both the EEA and the provisions in the Labour Relations Act prior to dismissing an employee for incapacity-related reasons.

Rights under other laws

Medical schemes may not load premiums of persons living with HIV, and have to fund all diagnoses, treatment and care costs, in full. This also includes the management of complications resulting from HIV, or complications or effects of the treatment of HIV, such as lipodystrophy.

The Promotion of Equality and Prevention of Unfair Discrimination Act, 2000, caters for the possibility of possible unfair discrimination in non-employment sectors on the basis of HIV specifically and health status in general. There is a list of illustrative practices of unfair discrimination, requiring of the state to take measures to address those. The practices include exclusion from educational opportunities, exclusion from health services, insurance, pensions and in the provision of goods and services.

Occupational Health and safety: the Hoffmann case

The Constitutional Court ruled on discrimination on the basis of HIV as long ago as 2000 in the Hoffmann case. It concerned an employee who was refused an appointment as a flight attended for SAA as a result of the employee's pre-employment medical showing he was HIV-positive.

It was argued that employers can actually discriminate against someone on HIV-status, as "HIV" is not listed as a non-discriminatory ground in the South African Constitution. The Constitutional court rejected this argument, stating that the list of grounds in section 9 of the Constitution is not a closed list, and that any ground that displays similar characteristics as those already listed (i.e. where persons experience adverse reactions on that basis, where their dignity is impaired, etc) could claim the protection of the prohibition against unfair discrimination.

Medical grounds were also listed as justifying the discrimination. It was argued that persons living with HIV cannot be vaccinated against yellow fever (a requirement for flight attendants). After examining expert evidence, the Court reached the conclusion that a blanket exclusion of all persons living with HIV is unfair, as vaccination depends on one's CD4. In this case Mr Hoffmann could still be vaccinated against yellow fever.

A third line of argument was about the possible negative impact of employing Mr Hoffmann on the business of SAA. It was alleged that consumers would prefer to not have flight attendance living with HIV and would therefore boycott SAA, leading to financial losses. The Court found that one cannot make the rights of a person dependent on whether others fear or stigmatise them.

Evidence was also presented that other international airline carriers have similar policies to not employ persons living with HIV as flight attendants. This, however according to the Court, could not override the South African Constitution's provisions against unfair discrimination.

Conclusion

The EEA requires of all employers with 50 or more employees to have EE Committees, with specific tasks outlined in the EEA, such as looking into policies and practices, conducting a workforce analysis, looking into barriers to employment for persons from designated groups, etc. The EE Committee becomes the custodian of an HIV workplace policy and oversee issues such as training and awareness campaigns. These could be linked to wellness days, and health and safety analyses undertaken by an employer's Health and Safety Committee. For employers with less than 50 employees, the duty to remove discrimination and to include HIV in the health and safety programme of the workplace, as well as under the Labour relations Act, is still relevant. The recognition and accommodation of HIV in the workplace should be integrated into all aspects of the business, and not be "only an HR issue".

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