Nutrition & Integrative Approaches to Infertility

Improving Patient Experience & Outcomes

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This Session

Explores psycho-social impacts of female infertility & the lived experience of fertility treatment

Consider the impact on pregnancy & pregnancy related problems & therapeutic relationship

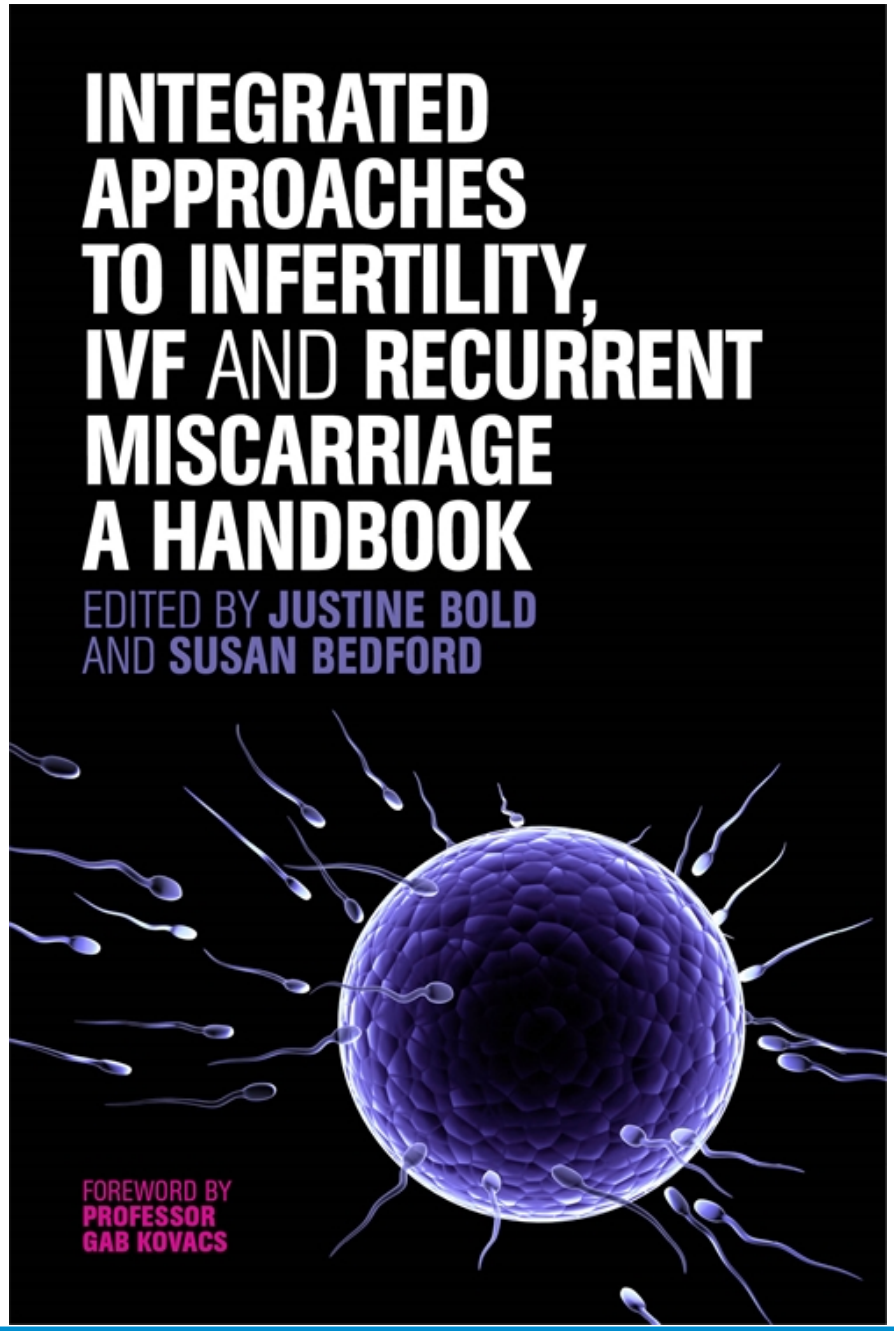
Consider the evidence for & benefits of wider integrative approaches

Contents

- Infertility overview
  - Psychosocial impacts
  - Lived experience
  - Recurrent pregnancy loss
  - Immune mediated infertility
  - Unexplained infertility
- Challenges of managing past experience in therapeutic relationship especially re. pregnancy related problems
- Integrative approaches
  - Psychotherapeutic treatments e.g. CBT, mindfulness
  - Nutritional support, weight management, Coeliac disease
    - Nutritional management of endometriosis and PCOS
  - Lifestyle advice, smoking cessation
- Questions

Introduction

- Senior Lecturer
  Allied Health & Applied Social Sciences
- Work on Nutrition postgraduate programmes
- Research interests @ infertility, mental health, food allergy, auto-immunity, gluten, coeliac disease, non-coeliac gluten sensitivity
- Edited book on infertility published in 2016
- Personal experience of infertility - after several fertility treatment twins born in 2013



Service user experience throughout text

'their stories, their words'

Some anonymised

Some have given permission for names to be included

Approach linked to my doctoral research & new project on mental health

Infertility Overview

- Infertility - ***involuntary*** childlessness
- Broad general definition
  - A couple is defined as infertile if they haven't conceived after a year of regular intercourse without using contraception
- 10% global prevalence (Kalinarta et al., 2011)
- UK statistics
  - @ 1 in 7 heterosexual couples in Britain have difficulty conceiving (HFEA 2014)
  - In UK 40% cases involve both male and female factors (NICE 2013)

Impacts of Infertility

- Health related quality of life is severely reduced in patients experiencing infertility (Rashidi *et al.,* 2008).
- 1 in 6 seek fertility treatment (Jenkins, Fleming and Brown 2005)
  - Consistent with data from Cahill and Wardle (2002)

Psychosocial Impacts

- Fertility often viewed as essential part of female identity (Kalinarta et al., 2011)
- ‘Socially unacceptable, culturally taboo and invisible’ (Allan 2007)
- Pregnancy loss still a taboo (Bansen & Stevens 1992)
- Isolating & stigmatising (Whiteford & Gonzalez 1995)
- Effects similar to a bereavement (Christie 1997)

Lived Experience of Fertility Treatment

- Women experience high levels of guilt, distress and frustration (Reid and Alfred 2013)
- Negative impacts on self esteem, relationships and sex life (Wishmann et al 2014)
- The experience is particularly ‘devastating’ for women (Griel 1997)
- Life is disrupted and ‘on hold’ (Cunningham 2014)
- Social withdrawal might be a coping mechanism (Jansen & Sainte Onge 2015)
- It’s a ‘lonely’ journey (Reid and Alfred 2013, Allan 2007)

Lived Experience

- Women report treatment is one of the most stressful experiences (Cousineau and Domar 2007)
  - It's also invasive, costly and uses hormone based medication
- Those undergoing treatment report high levels depression and anxiety (Chiaffarino et al 2011)
- Researchers working with women 4 years after unsuccessful treatment document that women report
  - 'Existential challenges to their sense of self-identity and meaning and purpose of life' (McCarthy 2008)

Harvard Mental Health Letter {http://www.health.harvard.edu/newsletters/harvard_mental_health_letter/2009/may}

The psychological impact of infertility and its treatment

Summary points

- The relatively recent focus on physical causes of infertility means that its psychological impact may be overlooked.
- Medication side effects, money worries, and uncertain outcomes all contribute to infertility-related stress.
- For additional information and resources about dealing with the stress of infertility, visit www.health.harvard.edu/mentalextra {http://www.health.harvard.edu/mentalextra}.

Stress of infertility and interventions

Individuals who learn they are infertile often experience the normal but nevertheless distressing emotions common to those who are grieving any significant loss — in this case the ability to procreate. Typical reactions include shock, grief, depression, anger, and frustration, as well as loss of self-esteem, self-confidence, and a sense of control over one's destiny.

Relationships may suffer — not only the primary relationship with a spouse or partner, but also those with friends and family members who may inadvertently cause pain by offering well-meaning but misguided opinions and advice. Couples dealing with infertility may avoid social interaction with friends who are pregnant and families who have children. They may struggle with anxiety-related sexual dysfunction and other marital conflicts.

There are about 40 ways to treat infertility. About 85% to 90% of patients are treated with conventional methods, including advice about timing of intercourse, drug therapy to promote ovulation or prevent miscarriages, and surgery to repair reproductive organs. Only about 3% of patients make use of more advanced assisted reproductive technology such as in vitro fertilization (IVF). While medical interventions offer much-needed help and hope, studies suggest that they may also add to the stress, anxiety, and grief that patients are already experiencing from infertility itself.

Pregnancy Loss

- Pregnancy loss after fertility treatment is a taboo (Freda Devine and Semelsberger 2003)
- Major depression develops after pregnancy loss more commonly in childless women (Neugebauer et al 1997)
- Study in news recently linking miscarriage to post traumatic stress disorder (PTSD)

BBC News

2/11/16

Health

Miscarriage can trigger post-traumatic stress disorder

2 November 2016 | Health 18

NICOLE MARTIN

Women who have recently had a miscarriage are at risk of developing post-traumatic stress disorder, doctors at Imperial College London have said.

Freda MC, Devine KS Semelsberger C **(**2003) '**The lived experience of miscarriage after infertility'.** MCN Am J Matern Child Nurs.Jan-Feb;28(1):16-23

Phenomenology - interviews with 8 women ***Excerpt From Abstract***

Results

"Themes included : going back to "square one," an inner struggle between hope and hopelessness for future fertility, running out of time, anger/frustration, lack of understanding by others, guilty feelings, feeling alone/numb with their grief, and gaining strength from adversity".

Clinical implications

"This study provides a first glimpse of women who miscarry after infertility treatments, and demonstrates that they feel profoundly alone, and grieve intensely. They worry that they caused the miscarriage, and find it difficult to hope that they will ever become pregnant again. Several women described being hospitalized for their miscarriage on postpartum units. This was unbearable for them, and should remind all of us in healthcare that this type of unthinking treatment of women who miscarry after infertility is not acceptable"

Recurrent Pregnancy Loss

- Important to think about the impact of RPL within wider context of infertility experience
- Medically referred to RSA - recurrent spontaneous abortion
- Investigations in UK after 3 losses
- Aspirin, heparin, steroids, progesterone and main stay of conventional treatment options (but new treatments trialed with anti-malarials)

Unexplained Infertility (UI)

- Difficult for patients to deal with unexplained diagnosis

- Often other conditions are misdiagnosed as UI
  - Particularly endometriosis
  - Tubal problems (especially distal and peritubal disease)
  - Premature ovarian ageing
  - Immunological infertility

    (Gleicher and Barad 2006)

Unexplained infertility @ 30% cases

Obstet Gynecol Surv. 2014 Feb;69(2):109-15.Definition and epidemiology of unexplained infertility.Gelbaya TA1, Potdar N1, Jeve YB2, Nardo LG3.

- Abstract "**The diagnosis of unexplained infertility can be made only after excluding common causes of infertility using standard fertility investigations, which include semen analysis, assessment of ovulation, and tubal patency test**. These tests have been selected as they have definitive correlation with pregnancy. **It is estimated that a standard fertility evaluation will fail to identify an abnormality in approximately 15% to 30% of infertile couples**. The reported incidence of such unexplained infertility varies according to the age and selection criteria in the study population. We conducted a review of the literature via MEDLINE. Articles were limited to English-language, human studies published between 1950 and 2013. Since first coined more than 50 years ago, the term unexplained infertility has been a subject of debate. Although additional investigations are reported to explain or define other causes of infertility, these have high false-positive results and therefore cannot be recommended for routine clinical practice. **Couples with unexplained infertility might be reassured that even after 12 months of unsuccessful attempts, 50% will conceive in the following 12 months and another 12% in the year after.**

Immune Mediated Infertility

- Controversial area (peripheral versus uterine NK cells, testing)
  - High Natural Killer cells may be problematic
    - Elevations in NK cell activity linked to RSA (Yamada 2003)
    - CD56 NK cells cells linked to IVF failure & RSA (Karami et al 2012)
- A few private clinics investigate this in UK
- NHS management
  - Antiphospholipid syndrome or Hughes Syndrome
  - Other autoimmune thyroid problems

Challenge of Managing Past Experiences

- Women with IVF pregnancies have high levels of anxiety in pregnancy and experience anxiety about survival of baby in childbirth (McMahon 1997)
- Challenges in therapeutic relationships especially @ pregnancy related problems
  - Patience & understanding
  - Sensitivity
  - Ways to manage anxiety

Case History Example

- Female diagnosed with unexplained infertility, trying to conceive for many years
  - Had history of two pregnancy losses including one second trimester loss
  - Some endometriosis ablated but fallopian tubes OK, hormone profiles normal, ovarian reserve healthy for age
- Male factor fertility issue for partner
- After ICSI fertility treatment and two further miscarriages, tests confirm antiphospholipid syndrome
  - Heparin, aspirin to support pregnancy – risk of miscarriage, still birth, premature delivery with this condition

Case History Example

- Gets pregnant again
- Has sub chorionic haematoma and bleeding until 17 weeks
- Also develops carpel tunnel syndrome in both wrists causing severe pain into lower arms
- Main problem is pain & disturbed sleep
- Anxiety is also an on-going problem
- Preterm premature rupture of membranes @ 30 weeks (though suspects leaking fluid earlier)
    - Anxiety from this point is very severe
    - Carpel tunnel is an on-going problem
    - Sleep disturbance continues
    - Baby eventually born @ 30 weeks, some complications from lack of amniotic fluid
    - NICU

Integrative Approaches

- Patient-centred care
  - Focuses on the individual patient's wellbeing (Gameiro, Canavarro and Boivin 2013)
- Think about benefits in previous case study
  - Whole person approach
    - Emotional support vital, 4 pregnancy losses including second trimester loss, infertility for many years, then NICU
  - Optimal nutritional status/weight can help normalise hormones and gives better chance of conception/successful pregnancy (Kennedy and Griffin 1998)
- Consider all of this against trends for child bearing later in life when fertility naturally declines

Integrative Approaches

- Psychotherapeutic support
  - Counselling & Cognitive Behavioural Therapy (CBT)
  - Mindfulness
- Nutritional support to medical treatments
  - Healthy eating
  - Alcohol / caffeine
  - Gluten & coeliac disease
  - Nutritional support for Endometriosis and PCOS
  - Weight management
- Lifestyle
  - Smoking cessation / exercise

Psychotherapeutic Support

- Many authorities agree that prioritisation is needed in developing optimal standards of care in infertility and beyond
  - Beyond = miscarriage, pregnancy, NICU
- Psychotherapy reduces stress of infertility (de Liz and Strauss 2005)
- In women awaiting fertility treatment CBT has beneficial effects on stress hormone response and associated cardiovascular parameters (Facchinetti et al, 2004)

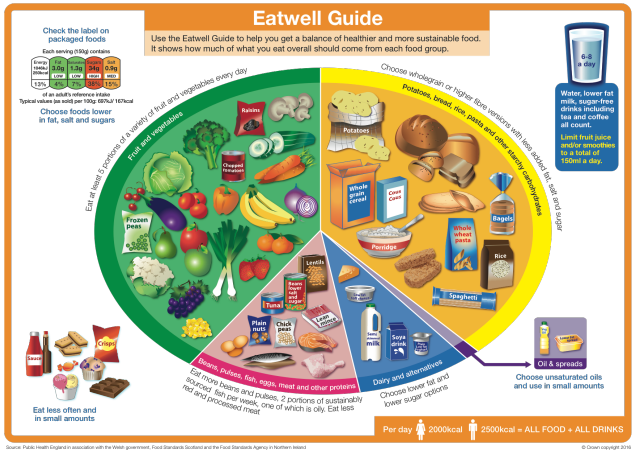
Psychotherapeutic Support

- CBT – talking therapy (aims to change thinking and behaviour)
- CBT ranked better than other psychotherapeutic options by Mitsi and Efthimiou (2014) and they reported it enhanced pregnancy rate
    - However questions around methods in literature
- CBT helps manage stress through fertility treatment and associated anxiety and depressive symptoms (Tarabusi, Volpe and Facchinetti 2004)

Mindfulness and Hypnotherapy

- Some evidence hypnotherapy may improve treatment outcomes (Levitas et al 2006)
- Mindfulness group programme shown to reduce depressive symptoms, shame and sense of entrapment and defeat
    - Attendance was for @ 2 hours of group sessions across 10 weeks

Nutritional Support



- Healthy Eating
  - Overall energy balance and weight
  - Nutritional adequacy – Eat Well Guide
  - Nutrient dense foods - 5 a day/fibre 30g a day
    - Macronutrients - protein & essential fats
      - Omega 3 especially (DHA)
    - Key micronutrients
      - Folic acid, B12, zinc, iron, Vit D, iodine, selenium

Nutritional Support

- Diet and Fertility/ART success
  - A prospective study found diet higher in monounsaturated fats rather than trans fats, increased vegetable rather than animal protein, high fat over low fat dairy and decreased glycemic load and increased iron and multivitamins had reduced infertility owing to ovulatory problems (Chavarro et al 2007)
  - Study in Holland – found a diet with 4 slices of whole-wheat bread or other wholegrain cereals daily, mono or poly unsaturated fats, 200g vegetables every day, two or more pieces of fruit a day, and meat (<3 times weekly) and fish 1 a week increased chance of pregnancy in those undergoing IVF (Twigt et al, 2012)

Nutritional Support

- Alcohol and caffeine – moderate intakes
  - Within recommended levels
- Healthy eating might help weigh maintenance, or slight weight loss enough to put someone into normal BMI range
- Plan for weight loss if weight is issue affecting hormonal balance (PCOS)
- Nutritional approaches for supporting conception
- Pre-conceptual care
- Both partners

Caffeine

- Caffeine linked to miscarriage, still birth, low birth weight
- Recommended intake in pregnancy is 200mg a day in UK
  - Approx. 2 small cups instant coffee a day
- Remember other sources of caffeine
    - Tea
    - Colas
    - Caffeine drinks
    - Chocolate/hot chocolate
    - Green tea
  - Some studies link caffeine to reduced IVF success (Al-Saleh 2010)

Eur J Epidemiology. 2014 Sep 2. Caffeine intake during pregnancy and adverse birth outcomes: a systematic review and dose-response meta-analysis. Greenwood DC1, Thatcher NJ, Ye J, Garrard L, Keogh G, King LG, Cade JE.

Abstract

"**Caffeine is commonly consumed during pregnancy, crosses the placenta, with fetal serum concentrations similar to the mother's, but studies of birth outcome show conflicting findings.** We systematically searched Medline and Embase for relevant publications. We conducted meta-analysis of dose-response curves for associations between caffeine intake and spontaneous abortion, stillbirth, preterm delivery, low birth weight and small for gestational age (SGA) infants. Meta-analyses included 60 unique publications from 53 cohort and case-control studies. **An increment of 100 g caffeine was associated with a 14 % (95 % CI 10-19 %) increase in risk of spontaneous abortion, 19 % (5-35 %) stillbirth, 2 % (-2 to 6 %) preterm delivery, 7 % (1-12 %) low birth weight**, and 10 % (95 % CI 6-14 %) SGA. There was substantial heterogeneity in all models, partly explained by adjustment for smoking and previous obstetric history, but not by prospective assessment of caffeine intake. There was evidence of small-study effects such as publication bias. **Greater caffeine intake is associated with an increase in spontaneous abortion, stillbirth, low birth weight, and SGA, but not preterm delivery**. There is no identifiable threshold below which the associations are not apparent, but the size of the associations are generally modest within the range of usual intake and are potentially explained by bias in study design or publication. There is therefore insufficient evidence to support further reductions in the maximum recommended intake of caffeine, but maintenance of current recommendations is a wise precaution".

Alcohol



- Alcohol damaging to reproductive health in both men and women and reduces ART success (NICE 2012, HEFA 2010)
  - But mechanisms not fully understood
- In women there is some evidence it may reduce Follicle Stimulating Hormone reducing folliculogenesis and ovulation
  - IN ART studies show fewer eggs at egg collection and lower pregnancy rates with alcohol intake (Klonoff-Cohen, Bleha, Lam-Kruglick 2002)

Weight Management

- Obesity and body fat distribution affects hormonal balance in women
  - Central adiposity associated with higher testosterone production (Kirschner et al 1990)
  - Linked to Polycystic Ovarian Syndrome
- Obesity reduces ART success
- But low BMI can also reduce sex hormone levels, ovulation and menstruation (Wentz 1980)

Weight Management

- If patient is experiencing infertility there may be comfort eating
- Weight loss can be challenging if stressed
- Trick is to find what works for person
    - Of particular interest to me in terms of ease and success are approaches advocated by intermittent fasting
        - 5 - 2 and also use of overnight fasting 3-4 x a week, eat evening meal and then nothing until early lunch the next day

Gluten and coeliac disease (CD)

- Gluten is the protein in grains such as wheat, barley, rye and spelt
- Coeliac disease is an auto-immune enteropathy associated with damage to the small intestine and malabsorption
    - Villous atrophy and symptoms such as bloating, abdominal pain
    - Iron deficiency anaemia, B12 deficiency and anaemia, osteomalacia and osteoporosis
- Current guidelines don't recommend screening of women with fertility problems for coeliac disease
    - BUT numerous associations in literature with sub fertility infertility, miscarriage and other pregnancy complications

Gluten and coeliac disease

- Prevalence of coeliac disease is women with infertility is higher than general population where it affects @ 1% of the population
  - Estimates of 4-8% prevalence in women with infertility in Europe (Fortunato et al, 2014)
  - Particularly with women with unexplained infertility (Singh et al, 2016)
- Women with endometriosis have higher risk of CD

Non coeliac gluten sensitivity (NCGS)

- Controversial BUT now recognised as distinct clinical entity
  - Exact pathophysiology and mechanisms not yet understood
  - Newest research links it to systemic inflammation (Uhde et al 2016)
- Intolerance to gluten without coeliac disease
  - Symptoms such as abdominal pain, bloating, brain fog, fatigue, depression (Capili et al, 2014)
  - But no damage to lining of the small intestine (Sapone et al 2011)

Non coeliac gluten sensitivity

- Undertaken a research project on this over summer 2016 for BBC2 Trust Me I'm A Dr
  - Assessing immune response and gastrointestinal symptoms in gluten exclusion and challenge
  - Writing up full results for publication presently but preliminary results presented in TV programme and on BBC website
- Iron, folic acid Vitamin D B12 deficiency all associated with NCGS (Bold and Rostami 2015)

Non coeliac gluten sensitivity

Active area of research

Published case report written with gastroenterologist

Gastroenterology and Hepatology From Bed to Bench.

CASE REPORT

Non-coeliac gluten sensitivity and reproductive disorders

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ABSTRACT

An association between coeliac disease and fertility disorders is well recognised in the current literature, but the information related to non-coeliac gluten sensitivity (NCGS) and infertility is lacking. This case highlights a possible role of treating NCGS in the reversal of infertility.

Keywords: Irritable bowel syndrome, Non-celiac gluten sensitivity, Infertility, Reproductive disorders, Gluten.
(Please cite as: **Bold J, Rostami K. Non-coeliac gluten sensitivity and reproductive disorders. Gastroenterol Hepatol Bed Bench 2015;8(4):294-297).**

Introduction

Coeliac disease may impair the reproductive life of affected women, eliciting delayed puberty, infertility, amenorrhea and precocious menopause. Clinical and epidemiological studies show that female patients with coeliac disease are at higher risk of spontaneous abortion, low birth weight of the newborn, reduced duration of lactation (1), polycystic ovarian syndrome and endometriosis (2, 3). No adequate studies are available on the non-coeliac gluten sensitivity (NCGS) and fertility disorders. Although iron, folic acid, vitamin D and B12 deficiency have been reported in a proportion of NCGS patients (4, 5). It is unclear whether other gluten related disorders like NCGS could induce malabsorption and deficiency of factors essential for organogenesis, e.g. iron, folic acid and vitamin B12. The overall impression is that patients with NCGS may also be a group particularly susceptible to reproductive abnormalities; however, the pathogenesis of NCGS-related reproductive disorders still awaits clarification. This case highlights the possible association between fertility disorders and NCGS.

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Case Report

We present a patient who commenced Assisted Reproduction Treatment (ART) after trying to conceive unsuccessfully for four years. At the time of initial presentation to her general practitioner, she was in her late thirties and had a history of irritable bowel syndrome (IBS) after a Campylobacter jejuni infection and many drug allergies, asthma and a history of miscarriage, but overall was in good health. She reported her IBS was well controlled if she avoided dairy products. The patient in this case study did not have a formal investigation or diagnosis of lactose intolerance, but it maybe that she had developed this after infection as ingestion of dairy foods caused her discomfort with bloating, abdominal distension and diarrhoea. Gastroenteritis may result in gluten or lactose intolerance and IBS is not an appropriate diagnosis in such cases (6).

Endometriosis

- Affects around 2 million women in the UK (Adamson et al 2010)
- Has been reported as the primary symptom of CD when classical symptoms were absent
- Also interesting that IBS is frequently seen as co-morbidity (Ek et al 2015)
    - We now know a portion of IBS sufferers are gluten sensitive) – more research needed on possible role of NCGS
- Support @ healthy eating, nutritional adequacy & consider CD/NCGS

Polycystic Ovarian Syndrome

- Strategy @ healthy eating for weight loss and to help support the balancing of hormones
- Gradual weight loss – long term behaviour change (healthy eating for life)
    - Maybe on medication such as metformin
    - Key dietary support @ snacking and free sugars
    - If have diabetes type II work with diabetic team
- Exercise key in management and helps normalise hormones and improve insulin sensitivity
- May be issues @ self-esteem requiring psychotherapeutic support

Smoking Cessation

- Smoking reduces fertility in both sexes, taking longer for smokers to conceive (Shiverick 2011)
- In women having ART it is associated with adverse impacts on ovarian function (Voorhis et al 1996)
- Reduces live birth outcome (Klonoff-Cohen, Marrs and Yee 2001)
- Remember may be used to relieve stress
- Signpost to local smoking cessation support services

Questions

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