

**European Society of Human Reproduction and
Embryology**



COURSE 7

**“Psychological counselling and clinical
management in ART pregnancies”**

**Special Interest Groups
Psychology & Counselling
Early Pregnancy**

**1 July 2007
Lyon, France**

PRE-CONGRESS COURSE 7

Special Interest Groups Psychology/Counselling and Early Pregnancy “Psychological counselling and clinical management in ART pregnancies”

CONTENTS

Program overview p. 1

Speakers' contributions

- Psychological counselling in reproductive medicine: what are issues to be addressed?
L. Hammer - Burns (USA) p. 2
- Social and psychological consequences of ART - *L. Schmidt (DK)* p. 19
- Medical aspects of pregnancy loss and recurring miscarriage
O.B. Christiansen (DK) p. 24
- Emotional aspects of pregnancy loss: the science behind emotions
C. Hammond (UK) p. 29
- Adverse outcome following vanishing twins: lessons to learn – *A. Pinborg (DK)* p. 33
- The impact of multiple preterm births on the family – *J. Denton (UK)* p. 42

PRE-CONGRESS COURSE 7 - PROGRAM

Special Interest Group Psychology and Counselling Special Interest Group Early Pregnancy

Psychological counselling and clinical management in ART pregnancies

Course co-ordinators: P. Baetens (B) and R. Farquharson (UK)

Course co-description: To review psychological counselling and support in its interaction with the clinical management in pregnancies resulting from ART, including multiple pregnancies, pregnancies in older women, early pregnancy failure, social pressure.

Target audience: General medical and psychosocial health care takers

Program

09.00 - 09.30: Psychological counselling in reproductive medicine: what are issues to be addressed?
– **L. Hammer - Burns (USA)**

09.30 - 09.45: Discussion

09.45 - 10.15: Social and psychological consequences of ART - **L. Schmidt (DK)**

10.15 - 10.30: Discussion

10.30 - 11.00: *Coffee break*

11.00 - 11.30: Medical aspects of pregnancy loss and recurring miscarriage – **O.B. Christiansen (DK)**

11.30 - 11.45: Discussion

11.45 - 12.15: Emotional aspects of pregnancy loss: the science behind emotions – **C. Hammond (UK)**

12.15 - 12.30: Discussion

12.30 - 13.30: *Lunch*

13.30 - 14.00: Adverse outcome following vanishing twins: lessons to learn – **A. Pinborg (DK)**

14.00 - 14.15: Discussion

14.15 - 14.45: The impact of multiple preterm births on the family – **J. Denton (UK)**

14.45 - 15.00: Discussion

15.00 - 15.30: *Coffee break*

15.30 - 16.00: Motherhood beyond reproductive age: motivation and medical risks – **M. Camus (B)**

16.00 - 16.15: Discussion

Psychological Counseling in Reproductive medicine: What should be addressed?

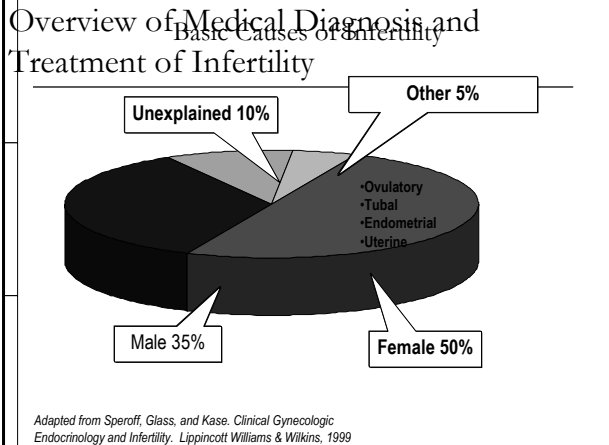
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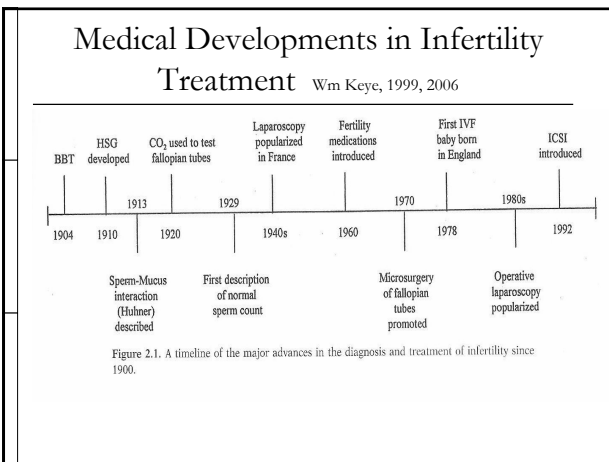
Defining the Role of Counseling in Reproductive Medicine

- Psychological Counseling in Reproductive medicine:
 - What should be addressed?
- Psychological Counseling in Reproductive Medicine:
 - Who should provide it?
 - What does the counselor need to know?
 - What are the important issues that should be addressed by the counselor?
 - How should counseling be provided?

Guidelines on Infertility Counseling

- Graduate degree in mental health profession
 - License to practice
 - Training in medical & psychological aspects of infertility
 - Clinical experience in infertility counseling
 - Continuing education
- Covington & Burns, 1995; ESHRE/PSIG, 1999; BICA, 2007





Overview of Medical Treatment for Genetic Aspects of Infertility

- ❑ Know basics of infertility causes and treatments
- ❑ Understand the role of genetic counseling in infertility
- ❑ Understand—at minimum—the most common medically complicating conditions impacting fertility e.g., cancer, HIV/AIDS, advanced reproductive age

Psychological Impact of Infertility

- ❑ Shock, disbelief, denial
- ❑ Crisis and trauma
- ❑ Grief, mourning, and bereavement
- ❑ Exacerbation of pre-existing psychiatric problem, e.g., depression, anxiety, eating disorders, personality disorder, addiction
- ❑ Isolation and alienation from self and others
- ❑ Financial strain

Psychological Impact of Infertility

- ❑ Crisis of values, religion, and culture
- ❑ Social stigma and shame
- ❑ Potential for marital/sexual problems
- ❑ Conflicts due to gender differences
- ❑ Inadequate or ineffective coping strategies
- ❑ Discordant partner patterns of coping

Psychological Impact of Infertility

- ❑ Anger, jealousy, envy
- ❑ Inability to predict the future
- ❑ Narcissistic wound
- ❑ Out of synch with one's peer group
- ❑ Intergenerational family crisis
- ❑ Decision-making pressures
- ❑ Coming to terms with being a 'patient'

Infertility as a Psychic Trauma

Narcissistic injury effecting:

□ *Self-esteem*

□ *Self-image*

□ *Body image/sexuality*

= Invisible Wound

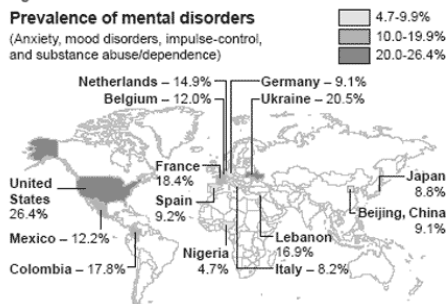
WHO Study: Mental Illness Spans Globe

- 60,463 adults in 14 countries: 10% of people acknowledged mental ailments in > 50% of countries surveyed.
- Most common everywhere except Ukraine were anxiety disorders (including panic attacks, phobias and post-traumatic stress disorder)
- In Ukraine mood disorders including depression most prevalent along with alcoholism
- Range: 26% of Americans to 8% of Italian, only 4.7% of Nigerians acknowledged mental illness – thought to be due to stigma/fear of outsiders

Mental disorders span the globe

According to surveys of 14 countries, the United States has the highest rate of mental illness.

Prevalence of mental disorders
(Anxiety, mood disorders, impulse-control, and substance abuse/dependence)



SOURCE: World Health Organization

AP

Psychological Distress Among Infertility Patients

□ Mood Disorders:

- Significantly greater incidence of anxiety, depression, somatic complaints, and diminished self-esteem in infertile women than infertile men *Wischmann, 1998, Griel, 1997*
- Prevalence of depression comparable to other chronic medical conditions *Domar et al, 1992*
- Increased risk of depression and anxiety when infertility treatment over prolonged period of time. *Anderson et al, 2003*

Psychological Distress Among Infertility Patients

□ Eating Disorders:

- 58% of infertile women with menstrual irregularities had eating disorder *Stewart et al, 1990*

□ Chemical abuse/addiction:

□ Personality Disorders

Psychological Distress Among Infertility Patients with Personality Disorders

- | | |
|-------------------------|--|
| 1. Obsessive/Compulsive | 1. Punishment for letting things get out of control |
| 2. Narcissistic | 2. Attack on autonomy |
| 3. Borderline | 3. Threat of abandonment |
| 4. Dependent | 4. Expected punishment for worthlessness |
| 5. Avoidant | 5. Dangerous invasion of privacy |
| 6. Paranoid | 6. Annihilating assault coming from everywhere outside of self |

Rosenthal et al, 1985

Infertility as a Life Crisis

A crisis is a turning point in life that can present an opportunity for emotional growth, or the danger of increased vulnerability to psychiatric distress.

Infertility is a major life crisis Dunkel-Schetter & Lobel, 1991; Menning, 1985

- ❑ Emotional crisis
- ❑ Social crisis
- ❑ Developmental crisis
- ❑ Medical crisis
- ❑ Ethical, cultural, and/or spiritual crisis
- ❑ Resolution crisis

Losses of infertility

- ❑ Loss of a (potential) relationship
- ❑ Loss of health
- ❑ Loss of status or prestige
- ❑ Loss of self-esteem
- ❑ Loss of self-confidence
- ❑ Loss of security
- ❑ Loss of a fantasy or hope of fulfilling an important fantasy
- ❑ Loss of something or someone of great symbolic value Mahlstedt, 1985

Overwhelming feelings of Loss of Control

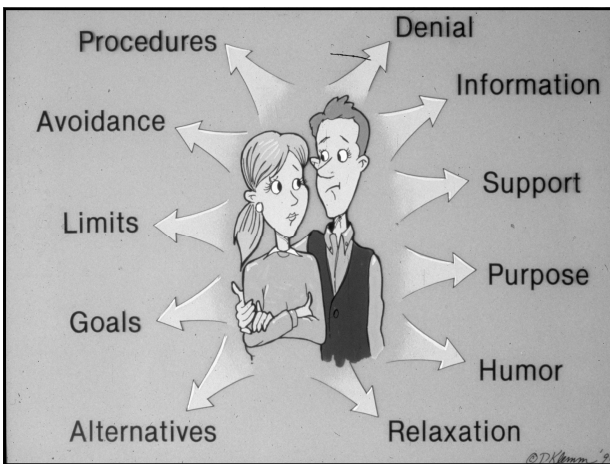
Infertility as Stress

Not experienced in a vacuum:

- ❑ Other life issues
- ❑ Other medical conditions
- ❑ Pre-existing psychological conditions

Infertility as a Stressor

- Infertile women have significantly higher levels of stress than controls *Wright et al., 1991*
- Stress and psychological symptoms of infertility similar to other chronic health problems *Domar, et al., 1993*
- Stress may impact fertility *Domar, et al., 1990*



Cross-cultural Impact of Involuntary Childlessness

- Infertility a crisis in *all cultures*
- Remedies:
 1. Realignment of social relationships
 2. Medical treatment
 3. Spiritual aid: prayer, religious rituals
- Least acceptable solution: social change
 - Remarriage/plural marriage/divorce
 - Adoption/fostering

Rosenblatt et al., 1973

Gender Differences and Infertility

- Men and women respond differently to infertility with men typically responding with less distress except when the infertility diagnosis is male factor.

Men and Infertility

- Men use more avoidant coping (denial, distancing, withdrawal)
- Men with male factor diagnosis: higher levels of anxiety, self-blame, diminished masculinity, and react with more negative emotions Nachtigall et al, 1997; Glover et al, 1998, Connolly et al, 1987; Mikulinear et al, 1998

Women and Infertility

- More likely to seek information and assistance and to access social support
- Less likely to respond negatively to female-factor diagnosis and more likely to 'shield husband' from male-factor diagnosis Petok, 2006
- Experience greater social stigma Hynie & Burns, 2006
- Childbearing more central to women's identity
- Receive the majority of treatment regardless of infertility etiology or treatment
- Report infertility as most upsetting experience in their lives

Impact of Infertility on Couple Relationships/Marriages

- ❑ Communication difficulties
- ❑ Sexual problems
- ❑ Gender differences
- ❑ Loss of control
- ❑ Isolation & alienation from self, partner, and others
- ❑ Financial strain

Impact of Infertility on Couples

- ❑ Ambivalence or unequal investment or different levels of desire for child Lorber, 1987
- ❑ Prolonged treatment increases marital conflict, distancing, divorce/separation Kraft et al, 1987; Benazon et al, 1987; Connolly, Edelman, & Cook, 1987; Lalos et al, 1985
- ❑ Couples in advanced stages of treatment (> 3 years) had lowest levels of marital adjustment Berg & Wilson, 1991
- ❑ Women with moderate amounts of treatment failure reported greater marital distress Boivin et al, 1995

Infertility Counseling with Special Populations

- ❑ 'Reproductive Tourists'....cultural, religious, legal issues
- ❑ Older Patients
- ❑ Secondary Infertility
- ❑ Remarried Couples
- ❑ Gay/Lesbian Couples and Single Women
- ❑ Medically Complicating Conditions
 - Cancer
 - HIV
 - Spontaneous Premature Ovarian Failure
 - Genetic Conditions--PGD
 - Multiple Miscarriage
 - Burns & Covington, 1999

Infertility Options

- Childlessness
- Adoption
- Medical treatment
 - ARTs
 - Third-party reproduction

Counseling Needs of All Infertile Patients

- Information
- Resources
- Time
- A good ear
- Guidance
- Options
- Hope

Childlessness versus Childfree

- Childfree more acceptable in developed countries where
 - Couple can view themselves as a family unit
 - Women have other roles apart from motherhood.
- Childlessness less acceptable if either partner:
 - Believes must have children to be happy, remain married
 - Strong cultural or religious beliefs the necessity of children
 - Family pressure to have children
 - Few roles for women apart from motherhood

Accepting Childfree Life

- Requires redefining identity and life goals to make childlessness acceptable (*accepting unacceptable*)
- Requires acceptance of marital duo as family unit
- Requires finding other means of fostering and generativity.

Forms of Adoption

- **Intrafamilial**
- **Domestic**
 - Agency facilitated (commercial, religious, government)
 - Independent (self-facilitated) with/without professional assistance
 - Agreement with birth parent(s)
- **International**
 - Agency facilitated
 - Birthparents typically unknown
 - Culture of child must be incorporated into new family
 - Health and/or behavioral problems in child
 - Regulations, protocols, and policies of country (e.g., travel to & fro, extended stay in country, BMI, age restrictions, marital status, health status)

Psychosocial Tasks of Adoption After Infertility

- Gather information
 - Address fears and expectations about adoption
 - Educate and assist with realistic expectations
 - Assist with the resolution of feelings about impaired fertility
- Make collaborative decisions as a couple
 - Assist both partners in viewing adoption as acceptable and positive family-building option
 - Facilitate decision-making about adoption
 - Insure decisions are negotiated and without coercion

Infertility Counseling and Assisted Reproductive Technology (ART)

- IVF considered the most stressful of all treatment

- Treatment stress increases with each phase...the most difficult is 2 week waiting period

- Effects of hormones on the psychological experience

Third-Party Reproduction

- Third-Party Reproduction:
 - Donor sperm
 - Donor oocyte (egg)
 - Donor embryo (donated or created)
 - Gestational surrogacy
 - Surrogacy with donated egg/embryo

Infertility Counseling: Psychological Tasks in Third-Party Reproduction

- Acknowledging the individual loss of reproductive capacity and what this means to them individually and as a couple.
- Grieving the assumed and hoped for genetically-shared pregnancy
- Examining the acceptability and suitability of gamete donation/gestational carrier/surrogacy as a family-building alternative for them as individuals and as a couple.

Mahlstedt & Greenfeld, 1989

Infertility Counseling and Third-Party Reproduction

- ❑ Assess ability to provide informed consent and individual emotional stability
- ❑ Assess marital stability
- ❑ Educate about history of treatment, pros and cons of treatment, disclosure issues
- ❑ Determine partner agreement about treatment
- ❑ Assess and assist with outcome: pregnancy or treatment failure

Goals of Infertility Counselor in Third-Party Reproduction

- ❑ Establish positive relationship in which anticipated/ unanticipated problems can be resolved
- ❑ Address psychosocial issues unique to specific family-building alternative (e.g., donated gametes, gestational carrier)
- ❑ Identify conflicts or barriers to impeding or impacting any/all participants.
- ❑ Evaluate unresolved grief, psychopathology, social problems, or other factors that could prevent a positive outcome.
- ❑ Be available to provide ongoing support, education and/or counseling, if desired.



Third-Party Reproduction and Disclosure

- ❑ Recognize laws/policies about disclosure where patient is being treated, where they live, where child will be raised
- ❑ Recognize own professional biases and acknowledged them to patient
- ❑ Provide education, resources, and 'script'
- ❑ Respect individual differences particularly religious, and cultural differences

Goals of Infertility Counseling

- ❑ Restore self-esteem
- ❑ Address narcissistic wounds
- ❑ Bereavement therapy
- ❑ Marital/sexual counseling
- ❑ Screening, guidance, and preparation for treatment
- ❑ Advice, education, and support
- ❑ Assist with decision-making
 - Covington & Burns, 2006

Counseling Treatment Approaches

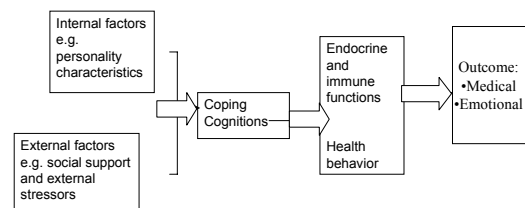
- ❑ Psychodynamic therapy
- ❑ Cognitive/behavioral
- ❑ Marriage and family/sex therapy
- ❑ Group therapy
- ❑ Strategic/solution-focused therapy
- ❑ Crisis intervention
- ❑ Grief counseling
- ❑ Psychopharmacological treatment
- ❑ Complementary medicine approaches (e.g., hypnosis)
- ❑ Behavioral/medicine approaches

Behavioral/Medicine Approach

- Relaxation Techniques
- Improved stress identification and stress management
- Health behavior change and interventions including assistance with
 - Weight management
 - Smoking cessation
 - Cessation of alcohol/drug abuse/addiction

• Verhaak & Burns, 2006

Biopsychosocial Model of Infertility



Multidisciplinary Approach to Infertility Counseling

- Emphasizes 'holistic' approach that integrates medical and psychosocial factors –eliminates historical mind/body split of traditional medicine
- Emphasizes cohesive partnership between all caregivers and patient(s)
- Healthcare givers and patients are equal partners participants in healthcare process

Multidisciplinary Approach to Infertility
Counseling

- ❑ Approach minimizes rigid professional distinctions (but not expertise)
- ❑ All caregivers provide psychological support or counseling (medical caregivers aware of psychosocial aspects of infertility and treatment)
- ❑ Mental health professional educated and trained about medical diagnosis and treatment of infertility

Multidisciplinary Approach to Infertility
Counseling

- ❑ Provides creative and integrating force for improving patient care
- ❑ Collaborative approach improves patient satisfaction and reduces clinical errors
- ❑ Provides arena for evidenced-based research
- ❑ System-based approach enables professional development

Models for Collaborative Reproductive
Healthcare and Infertility Counseling

- ❑ Models of care integrating patient, medical staff, colleague collaboration, and consumer advocacy organizations
- ❑ Infertility Counselor as an independent practitioner
- ❑ Infertility Counselor as an independent practice consultant
- ❑ Infertility Counselor as practice employee
 - Covington, 2006

All Caregivers are Counselors!



Social and psychological consequences of ART

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Learning objectives

At the end of the course, participants are expected to:

Have a general understanding of how infertility and assisted reproduction have an influence on infertile couples' stress, marital benefit, infertility-related communication, coping, and social relationships.

Have knowledge about possible ways of measuring central psychosocial aspects of infertility (fertility problem stress, marital benefit, communication, coping, social relationships)

Lecture summary

Infertility - a chronic stressor and non-event

Infertility is a chronically stressful situation, a non-event transition. Chronic stressors are stressors that develop slowly as continuous and problematic conditions in our social circumstances or social roles. For many couples, infertility and its treatment cause a serious strain on their interpersonal relationships; disturb relationships with other people, cause personal distress including increased anxiety and depressive symptoms, and repeated periods of existential crisis. Despite these strains, infertility is also an experience that can bring the partners closer together and strengthen their marriage.

A review including women in IVF showed that those starting IVF were only slightly different from norm groups. Unsuccessful treatment raised the level of negative emotions. In general, most women proved to adjust well to unsuccessful IVF, although a considerable group showed subclinical emotional problems (Verhaaak et al. 2007).

Many psychological questionnaire based studies on infertility and treatment have used general inventories regarding stress, anxiety, depression and coping. However, it is also of interest to develop instruments aimed at measuring psychosocial aspects of the specific stressor infertility to capture more effectively the strains, communication, and coping associated with this specific low-control stressor.

The following examples of psychosocial measurements are based on the Copenhagen Multi-centre Psychosocial Infertility (COMPI) Research Programme (Schmidt 2006). The programme is conducted in an international, multi-disciplinary research group. The

programme includes a longitudinal cohort of couples starting fertility treatment at one of five clinics in Denmark. Both partners (N=2,812) received three self-administered questionnaire (start of treatment, one-year follow-up, five-year follow-up).

Fertility problem stress

Previous research has shown that infertility causes strain in the personal, marital and social domain (Abbey et al. 1991a; Greil 1997). In COMPI, we measured fertility problem stress using 14 items concerned with the strain related to infertility in these three domains.

Marital benefit

Infertility is also a situation that can bring the partners closer together. In COMPI, we measured whether the infertility has (i) brought the partners closer together and (ii) strengthened their relationship. At baseline, 26% of the women and 21% of the men reported a high marital benefit defined as having agreed strongly to both items.

Communication with partner

Abbey et al. (1991b) showed that spouse interpersonal conflict was related negatively to well-being and spouse support was related positively to well-being. Pasch et al. (2002) studied marital communication in detail and reported that wives wanted to talk more with their partners about trying to have a baby. The husbands' approach to infertility played the vital role in determining the marital outcomes. The authors suggested, "that couples who exhibit poor marital communication have husbands who were not very interested or involved in trying to have a baby" (p. 1246).

In COMPI 27% of the women and 22% of the men reported at start of treatment that they had difficulties in communicating with their partner about infertility and treatment. Longitudinal analyses showed that difficult partner communication among those participants who had not achieved a pregnancy/delivery at a one-year follow-up significantly predicted high fertility problem stress. Further, among men difficult partner communication was a significant predictor of low marital benefit.

Communication with other people

Most infertile people discuss their infertility with other people and generally, more women than men had talked to others (Abbey et al. 1991b, Van Balen and Trimbos-Kemper 1994).

People use different strategies when talking with other people. In COMPI, we identified three different strategies: (i) a secrecy strategy where the infertility experience was not shared with others, (ii) a formal strategy where only formal information was shared, as e.g. date of treatment, number of eggs retrieved, or (iii) an open-minded strategy where both formal information and the emotions regarding the infertility experience were shared with others. At baseline, 8% of the women and 18% of the men used the secrecy strategy, while 74% of the women and 54% of the men used the open-minded strategy. Around 5-8% reported that they always or often had told more to others than they wanted to tell.

In the longitudinal analyses among those participants who had not achieved pregnancy/delivery at one-year follow-up, the infertility-related communication strategies were not a significant predictor of fertility problem stress. However, a comparison of the formal strategy with the open-minded strategy suggested among both women and men an increased risk of high fertility problem stress in all three domains. Further, among men the secrecy communication strategy was a significant predictor of low marital benefit.

Coping

Reviews of the coping literature have often concluded that coping strategies towards managing negative emotions in stressful encounters demonstrate positive associations with maladaptive outcomes (Austefeld and Stanton 2004). However, in response to a low-control situation as infertility it is likely that problem-focused coping strategies aimed at managing the situation actively may have harmful effects, while emotion-focused coping strategy could be adaptive (Terry and Hynes 1998).

In COMPI we developed as recommended by Folkman and Lazarus (1988) and Costa et al. (1996) a coping questionnaire specifically aimed at measuring coping in relation to a specific stressor, here infertility. Items were adapted from: (i) the 66-item Ways of Coping Questionnaire (Folkman and Lazarus 1988), (ii) Folkman's (1997) later revision of the coping model with inclusion of meaning-based coping, and (iii) a previous qualitative interview study among Danish infertile couples (Schmidt 1996). Items were categorized based on their conceptual content: (i) active-avoidance strategies (e.g. avoid pregnant women or children, turning to work to take mind off things); (ii) active-confronting strategies (e.g. show feelings, ask others for advice); (iii) passive-avoidance coping (e.g. hope for a miracle); (iv) meaning.-based coping (e.g. have grown as a person in a good way).

In the longitudinal analyses among those participants who had not achieved pregnancy/delivery at one-year follow-up high use of active-avoidance coping was a significant predictor of high fertility problem stress among both men and women. Among men active-avoidance coping was a significant predictor of low fertility problem stress in the marital domain. Further, among women medium or high use of meaning-based coping predicted significantly low fertility problem stress in the personal and marital domain.

Social relationships

Infertile couples are ready for the transition to parenthood but are not (yet) able to make this transition. Therefore, infertility can be regarded as a non-transition situation in which it is not possible to become parents and not possible to change your own parents into grandparents.

Infertile couples have to cope with the fact, that an increasing proportion of their sisters, brothers, cousins, friends and workmates become parents. Some infertile couples decide to develop close relationships to other people's children, while other couples, to protect themselves, withdraw from social interactions involving children. Some have also experienced unwanted social exclusion, e.g. not being invited to close children's birthdays after family and friends have discovered the couples' infertility (Schmidt 1996).

Miall (1986) investigated infertile women and reported the majority self-labelled themselves as stigmatized and deviant. This happened even without being aware of outside rejection or disapproval.

Women described more benefits and costs than men did when they had spoken to family and friends about their infertility (Abbey et al. 1991b). Mindes et al. (2003) have studied social interactions in a group of women with fertility problems. Based on cross-sectional analyses they reported that infertility-specific unsupportive responses received from others were associated with adjustment problems. However, a longitudinal analyses showed that unsupportive social interactions were only positively associated with depressive symptoms and psychological distress among those women who remained infertile at follow-up.

In COMPI, we studied both supportive and unsupportive social interactions in general and infertility-specific. Around 60-70% reported that they always or often experienced infertility-specific support from family and friends. Around 3-6% experienced often or sometimes negative reactions.

References

Abbey A, Andrews FM and Halman LJ (1991a) Gender's role in responses to infertility. *Psychol Women Q* 15,295-316.

Abbey A, Andrews FM and Halman LJ (1991b) The importance of social relationships for infertile couples' well-being. In Stanton AL and Dunkel-Schetter C (eds) *Infertility. Perspectives from stress and coping research*. New York: Plenum Press, pp.61-86.

Austenfeld JL and Stanton AL (2004) Coping through emotional approach: a new look at emotion, coping, and health-related outcomes. *J Pers Soc Psychol* 68,455-469. ¹⁾

Costa PT, Somerfield MR and McCrae RR (1996) Personality and coping: a reconceptualization. In Zeidner M and Endler NS (eds) *Handbook of coping. Theory, research, applications*. New York: John Wiley & Sons, Inc., pp. 44-61.

Folkman S (1997) Positive psychological states and coping with severe stress. *Soc Sci Med* 45, 1207-1221.

Folkman S and Lazarus RS (1988) *Manual for the Ways of Coping Questionnaire*. Palo Alto: Consulting Psychologists Press.

Greil AL (1997) Infertility and psychological distress: a critical review of the literature. *Soc Sci Med* 45,1679-1704. ²⁾

Miall C (1986) The stigma of involuntary childlessness. *Soc Problems* 33,268-282.

Mindes EJ, Ingram KM, Kliwer W and James CA (2003) Longitudinal analyses of the relationship between unsupportive social interactions and psychological adjustment among women with fertility problems. *Soc Sci Med* 56,2165-2180. ³⁾

Schmidt L (1996) Psykosociale konsekvenser af infertilitet og behandling. [Psychosocial consequences of infertility and treatment. PhD thesis]. Copenhagen: FADL's Press.

Schmidt L (2006) Infertility and assisted reproduction in Denmark. Epidemiology and psychosocial consequences. [Doctoral dissertation]. Copenhagen: University of Copenhagen, Lægeforeningens Forlag or *Dan Med Bull* 53,390-417.*

Terry DJ and Hynes GJ (1998) Adjustment to a low-control situation: reexamining the role of coping response. *J Pers Soc Psychol* 74,1078-1092. ¹⁾

Van Balen F and Trimbos-Kemper TCM (1994) Factors influencing the well-being of long-term infertile couples. *J Psychosom Obstet Gynecol* 15,157-164.

Verhaak CM, Smeenk MJ, Evers AWM, Kremer JAM, Kraaijmaat FW, Braat DDM (2007) Women's emotional adjustment to IVF: a systematic review of 25 years of research. *Hum Reprod* 13, 27-36. ²⁾

- 1) These studies examine emotional coping as well as coping in relation to infertility.
- 2) These studies review psychosocial consequences of infertility and treatment.
- 3) This study examine unsupportive social interactions in relation to infertility.

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Medical aspects of pregnancy loss and recurring miscarriage

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Learning Objectives

- Learn about the statistical associations between medical disorders such as obesity, thromboembolism and autoimmune disease and recurrent pregnancy loss
- Get an overview of theories explaining the associations found
- Learn about how medical disorders affect future pregnancies after recurrent pregnancy loss in terms of maternal and fetal health
- Get orientated about treatments offered to counteract the effect of medical disorders on pregnancy complications

Lecture Summary

Background

Miscarriages and stillbirths can be caused by embryonic/fetal disorders such as aneuploidy and maternal disorders posing harm the fetus or placenta. Embryonic/fetal aneuploidy is a frequent cause of recurrent pregnancy loss (RPL) in women of advanced age (>40 years) and couples with parental chromosome rearrangements whereas it is a more infrequent cause of miscarriage in younger women with multiple miscarriages (four or more) and women with second trimester losses. Maternal disorders suggested to cause RPL are obesity, often associated with polycystic ovary syndrome (PCOS), acquired and hereditary thrombophilic disorders and clinical and subclinical immunologic disorders. The impact of the maternal disorders on RPL is often unclear: there is only consensus that the presence of lupus anticoagulant (LAC) and high and persistent titres of other antiphospholipid antibodies such as anticardiolipin (ACL) are causes of RPL. With respect to obesity, high quality epidemiological studies have documented that it increases the risk of miscarriage in the background population or infertility patients (Wang et al. 2000) but its possible association to RPL still lacks confirmation. Some hereditary thrombophilic factors, especially the Factor V Leiden mutation, have been reported to be associated with RPL in case-control studies (Rey et al. 2003) but their impact on the risk of miscarriage in future pregnancies is poorly documented. The presence of a series of autoantibodies (including LAC and ACL), abnormal natural killer cell activity and abnormal cytokine profiles have been correlated with RPL in many case-control studies but it is still unclear whether we are dealing with abnormalities resulting from repeated exposure to necrotic and inflamed intrauterine fetal tissue or whether they have preceded RPL and thus be causative.

Subjects and methods

The following study was undertaken in 328 consecutive women with RPL defined as at least three first trimester or two second trimester miscarriages to clarify the role of maternal disorders in RPL. The women were admitted to our tertiary centre for RPL investigation and management from 2003-

2007 and all included in this study had normal uterine anatomy and parental chromosomes. Information about previous and present diseases, weight and height and previous reproductive outcome was procured at the first consultation and blood samples were taken.

A full screening for thrombophilic abnormalities, a series of autoantibodies including LAC and ACL, mannose-binding lectin (MBL) and HLA-DR was undertaken in all patients and in addition endocrine investigations were carried out in patients with irregular periods.

The prevalences of the disorders among patients were compared to the corresponding prevalences in normal Danish females with age below 40-44 years when relevant data could be procured from recent publications.

Prevalence of medical disorders in RPL.

We detected significant medical disorders in 115 of the 328 patients = 35.1%. The conditions evaluated to be of significance and their frequencies in patients are shown in table 1. Only disorders that had required medical or surgical treatment were included. In 27 patients (8.2%) two or more disorders were found not including disorders with well-known correlations such as high BMI and PCOS, systemic lupus erythematosus (SLE) and thromboembolism and endometriosis and oophorectomia.

Table 1. Prevalence of medical disorders in 328 consecutive patients with recurrent pregnancy loss (RPL)

Gyn/endocrine disorders	%	Autoimmune disorders	%	Cardiovasc/respiratory disorders	%	Other disorders	%
BMI > 30	6.1	SLE	1.2	Thromboembolism	2.7	Epilepsia	0.9
Irregular periods, BMI < 30	3.4	Inflammatory bowel disease	1.5	Art hypertension	0.9	Psychiatric disease	2.7
PCOS, BMI < 30	3.7	Hyperthyreosis	2.4	Renal disease	0.6	HIV	0.3
Endometriosis	3.6	Hypothyreosis	2.1	Heart disease	1.8	Parasitic disease	0.3
Adrenogenital syndrome	0.3	Multiple sclerosis	0.3	Astma	1.5	Previous cancer	0.6
Oophorectomy	0.9	IDDM	1.2	Other lung disease	0.9		
Hyperprolactinaemia	0.3	Sarcoidosis	0.6	Hypercholesterolaemia	0.3		
NIDDM	0.3	Polyarthritis	2.7				
Conisation	2.7	Psoriasis	1.5				
		Blood disease	1.2				

NIDDM = non-insulin dependent diabetes mellitus; IDDM: insulin dependent diabetes mellitus

The frequencies of 6 disorders in patients could be compared with frequencies in reliable control groups (table 2). The frequencies of three autoimmune diseases and a history of thromboembolism were significantly higher than in controls and the frequency of IDDM was almost significantly

increased. All autoimmune disorders may be found with increased prevalence in RPL but we have only reliable estimates for the prevalence in the normal population for those shown in table 2.

The frequency of BMI > 30 was not different between patients and the normal Danish female population of fertile age. We have no reliable control groups for the prevalence of PCOS and/or irregular menstruations.

In conclusion, autoimmune and thromboembolic disease are associated with RPL but overweight per se is not.

Factors and genes contributing to medical disorders in RPL

With regard to the 9 patients with thromboembolic disorders, five were LAC positive, one was factor V Leiden positive, two were negative for both LAC and other thrombophilic factors and one was LAC (and ACL) negative but not investigated for other thrombophilic factors. LAC and high titres of ACL and factor V Leiden are recognized risk factors for thromboembolism and it is therefore not surprising to find them overrepresented in RPL patients with these disorders. However, it is clear that LAC is the dominant risk factor: five of 11 patients with LAC had had thromboembolic episodes whereas no patient with exclusively ACL without LAC had had such episodes. Only one of 19 RPL patients positive for the Factor V Leiden mutation had had any thromboembolic episodes. It has been suggested that only the carriage of several thrombophilic factors increases the risk of thromboembolism and RPL.

Among the patients with autoimmune disorders 9/40 = 22.5% had MBL < 100 ng/ml compared with 12% in the background population (Kruse et al. 2002) and of the 35 patients who had been HLA typed 17 (48.6%) were positive for the HLA-DR1 and/or HLA-DR3 alleles. In the normal population we would expect 37% to be positive for one of these alleles (Kruse et al. 2004)

Low MBL and the HLA-DR1 and -DR3 alleles have previously been reported to be associated with RPL (Christiansen et al. 1999; Kruse et al. 2004) and confer an increased risk of new miscarriage in these patients (Christiansen et al. 1993). The same immunogenetic factors are also associated with several autoimmune diseases.

It is possible that the endocrine/metabolic disturbances associated with many autoimmune disorders are the causal link between these and RPL. However, since our patients' autoimmune diseases seem to have been optimally treated at the time when the patients miscarried repeatedly and MBL deficiency and HLA-DR1 and -DR3 are also associated with RPL in patients without clinical autoimmune disease it is more likely that the link between autoimmune disease and RPL is due to the carriage of immunogenetic risk factors common for both conditions. Most autoimmune diseases are thought to be polygenic conditions with the combined effect of a series of susceptibility alleles (often related to excessive inflammatory responses) together with environmental factors determining the risk of development of the disease (Baumgart and Carding 2007). HLA alleles are thought to display a major effect on the risk of autoimmune disease whereas other genes each contribute with relatively minor effects.

In conclusion, the RPL patients who had previous thromboembolic episodes or clinical autoimmune disease probably carry more susceptibility genes for thrombophilia or excessive inflammatory response than those without the clinical disorders.

Importance of medical disorders during future pregnancy

In agreement with other studies we found that the presence of the medical disorders in table 1, except for high BMI, decreased the chance of a live birth in the next pregnancy compared with the absence of the disorders. This was in spite of adequate symptomatic treatment of the medical disorders: heparin in case of thrombophilia, insulin, thyroxin og anti-thyroid drugs in case of IDDM or thyroid disease and intravenous immunoglobulin in case of multiple miscarriages. We attribute this decreased prognosis in patients with medical disorders to the presence of a larger

number of susceptibility genes for thrombophilia or excessive inflammation (Christiansen et al. 2006) in patients with clinical disease compared with those without.

With the aforementioned treatments, maternal complications in the next pregnancies were relatively rare. We have seen no new episodes of thromboembolism in our patients with or without previous thromboembolism or thrombophilic factors. Cerebral and renal symptoms are seen quite often in SLE whereas other autoimmune disorders have posed few problems during pregnancy. Some depressive patients need psychiatric support during pregnancy and in one patient with epilepsy the fits became aggravated.

Table 2. Prevalence of selected medical disorders in patients with RPL and Danish female controls below age 40-44

	RPL patients (N = 328)	Controls	OR	P
	%	%		
BMI > 30	6.1	8.1	0.74	NS
Art/Ven thromboembolism	2.7	0.8	3.40	< 0.05
Polyarthritis	2.7	0.1	27.72	< 0.05
IDDM	1.2	0.4	3.02	NS
Hyper-/Hypothyroidism	4.5	2.0	2.31	< 0.05
Inflammatory bowel disease	1.5	0.2	7.60	< 0.05

References

Baumgart DC and Carding SR. (2007) Inflammatory bowel disease: cause and immunobiology. *Lancet*, 369, 1627-1640.

Christiansen OB, Mathiesen O, Husth M, Lauritsen JG, Jersild C and Grunnet N (1993) Prognostic significance of maternal DR histocompatibility types in Danish women with recurrent miscarriages. *Hum Reprod*, 8, 1843-1847.

Christiansen OB, Ring M, Rosgaard A, Grunnet N and Gluud C. (1999) Association between HLA-DR1 and -DR3 antigens and unexplained repeated miscarriage. *Hum Reprod Update*, 5, 249-255.

Christiansen OB, Nielsen HS, Kolte AM. Inflammation and miscarriage. *Sem Fet Neonat Med*, 11, 302-308.

Kruse C, Rosgaard A, Steffensen R, Varming K, Jensenius JC and Christiansen OB. (2002) Low serum level of mannan-binding lectin is a determinant for pregnancy outcome in women with recurrent spontaneous abortion. *Am J Obstet Gynecol*, 187, 1313-1320.

Kruse C, Steffensen R, Varming K and Christiansen OB. (2004) A study of HLA-DR and -DQ alleles in 588 patients and 562 controls confirms that HLA-DRB1*03 is associated with recurrent miscarriage. *Hum Reprod*, 19, 1215-1221.

Rey E, Kahn SR, David M and Shrier I. (2003) Thrombophilic disorders and fetal loss: a meta-analysis. *Lancet*, 361, 901-908.

Wang JX, Davies MJ and Norman RJ. (2000) Obesity increases the risk of spontaneous abortion during infertility treatment. *Obesity Research*, 10, 551-554.

Emotional Aspects of Pregnancy Loss: The Science Behind Emotions

Claudia Hammond
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BBC Radio 4
Lecturer in Social Psychology and Health
Boston University London Programme

Learning Objectives:

- 1) Understanding of possible emotional responses to pregnancy loss
- 2) Knowledge of factors affecting a person's response to pregnancy loss
- 3) Knowledge of effects of pregnancy loss on well-being during a subsequent pregnancy

This presentation is based on in-depth interviews conducted with 8 women for a BBC Radio 4 documentary on emotional responses to miscarriage and on my research on the science of emotions for my book "Emotional Rollercoaster: A journey through the science of Feelings".

The radio documentary "The Miscarriage" can be heard via the BBC website at:
<http://www.bbc.co.uk/radio4/science/pip/pkvru/>

As this is primarily a presentation using audio, I have not included slides. Instead this is a summary of the lecture.

Research on pregnancy loss tends to focus on medical interventions. Before the last ten years there has been little work done on the psychological aspects.

Limitations of current body of literature on psychological responses to pregnancy loss include:

- few controlled studies
- exclusion of those who have experienced considerable distress, but do not merit a psychiatric diagnosis

KEY EMOTIONS INVOLVED IN WOMEN'S RESPONSES TO PREGNANCY LOSS:

- 1) Shock
- 2) Sadness and depression
- 3) Grief

Maker & Ogden (2003) outline a three stage process:

- A. Turmoil
- B. Adjustment
- C. Resolution

- 4) Anxiety
- 5) Fear
- 6) Loss of Hope
- 7) Guilt
- 8) Anger

IMPACT ON PARTNERS:

Within the psychological literature on pregnancy loss women's partners have tended to be neglected. In the few studies which did mention men's responses the expression of anger was more common than the expression of sadness through tears. This finding is reflected across the literature on emotions.

The most comprehensive studies of men's responses were conducted by Martin Johnson. He found that men often found it hard to relate to their partner's grief if the loss had been very early in pregnancy.

PSYCHOLOGICAL IMPACT DURING SUBSEQUENT PREGNANCIES:

Effects can be long-lasting, with raised levels of anxiety throughout the next pregnancy.

Most women report that a subsequent pregnancy reduces feelings of grief, but some symptoms of grief symptoms have been found to be present in most women two years on.

SUMMARY OF HOW HEALTH PROFESSIONALS CAN HELP

- Giving reassurance that these strong feelings are both normal and common
 - Giving reassurance that feeling worse after 6-12 weeks is not unusual (perhaps consider a follow-up appointment during this time)
 - Offer extra support to women who have experienced a particularly severe grief reaction or depression during or after pre or post the birth of a new baby
 - Give women an opportunity to discuss the possible causes of their pregnancy loss and what meaning it had for them
 - Ask both women and their partners how they are feeling and ask them what sort of information and support they would like
-

Key References

Geller, P.A., Kerns, D. and Klier, C.M. (2004) Anxiety following miscarriage and the subsequent pregnancy: A review of the literature and future directions. *Journal of Psychosomatic Research*, 56, 35-45. (This is an extensive, key review of the topic of emotional responses to pregnancy loss).

Hammond, C.A. (2006) *Emotional Rollercoaster: a journey through the science of Feelings*. London: Harper Perennial. (For more detail on specific emotions this consists of nine chapters covering recent research in neuroscience, psychology and sociology with on each of nine emotions).

Janssen, H.J. et al (1996) Controlled prospective study on the mental health of women following pregnancy loss. *American Journal of Psychiatry*, 153, 226-230. (This is one of the few large, controlled studies on the topic).

Johnson, M.P. and Baker, S.R. (2004) Implications of coping repertoire as predictors of men's stress, anxiety and depression following pregnancy, childbirth and miscarriage: a longitudinal study. *Journal of Psychosomatic Gynaecology*, 25, 87-98. (Martin Johnson is one of the few people to have researched men's psychological responses to pregnancy loss).

Klier, C.M., Geller, P.A. and Ritsher, J.B. (2002) Affective disorders in the aftermath of miscarriage: A comprehensive review. *Archives of Women's Mental Health* 5, 129-149. (Another key literature review from Pam Geller and her colleagues.)

Maker, C. and Ogden, J. (2003) The Miscarriage Experience: More than just a trigger to psychological morbidity? *Psychology and Health*, 18(3), 403-415

(A qualitative study which used in-depth interviews to map the detailed emotional responses which are hard to access in the larger quantitative studies)

Ritsher, J.B. and Neugebauer, R. (2002) Perinatal Bereavement Grief Scale: Distinguishing Grief From Depression following miscarriage. Assessment 9 (1), 31-40. (Interesting discussion of the differences between grief and depression after pregnancy loss.)

ADVERSE OUTCOME FOLLOWING VANISHING TWINS: LESSONS TO LEARN



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SIG Early Pregnancy, ESHRE 2007

INTRODUKTION

- 4% of a birth cohort is born after IVF
- 25% twin pregnancies after IVF
- IVF singletons have poorer obstetric outcome than spontaneously conceived singletons

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Obstetric outcome in IVF singletons

OR (95%CI)	Helmerhorst	Jackson
	<i>Br Med J, 2004</i>	<i>Am J Obs Gyn, 2004</i>
No	5.361	12.283
<2500 g	1.7 (1.5-1.9)	1.8 (1.4-2.2)
<1500 g	3.0 (2.1-4.4)	2.7 (2.3-3.1)
<37 weeks	2.0 (1.8-2.3)	2.0 (1.7-2.2)
<32 weeks	3.3 (2.0-5.3)	-
SGA	1.4 (1.2-1.7)	1.6 (1.3-2.0)
Mortality	1.7 (1.1-2.6)	2.2 (1.6-3.0)

IVF SINGLETONS

Misdannelser

Number needed to harm (NNTH)

Studies	Alle	Selected
n	15	6
OR (95%CI)	1.3 (1.2-1.5)	1.4 (1.2-1.5)
1%	333	250
2%	167	125
3%	111	83
4%	83	62

(Hansen, Hum Reprod Update, 2004)

IVF SINGLETONS

Cerebral parese

OR (95%CI)	Lidegaard Hum Rep 2005	Strömberg Lancet 2002
IVF singletons	1.8 (1.2-2.8)	2.8 (1.3-5.8)

IVF/ICSI ENKELTFØDTE - STØRRE RISIKO?

- **Subfertilitet**
 - Neonatal mortalitet: Draper Lancet 1999; Basso BMJ 2005
 - Pretermaturitet og lav fødselsvægt: Henriksen OG 1997, Pandian HR 2001, Basso HR 2003
 - Misdannelser: Zhu BMJ 2006
- **Antal gestationssække**
 - Dickey, Am J Obstet Gynecol 2002
 - Schieve, NEJM 2004
 - Lancaster, ESHRE 2004
- **IVF/ICSI metoder**

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Infertility and adverse outcome

- **Infertility correlates with adverse outcome**
(Henriksen Obstet Gynecol 1997, Pandian HR 2001, Basso HR 2003)

- **TTP >12 months and preterm birth**
(Basso HR 2003)

Primiparas: Untreated OR 1.4 (1.1-1.7)

Multiparas: Untreated OR 1.6 (1.2-2.1)

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Infertility and mortality

- **TTP >12 months and perinatal deaths**
(Draper, Lancet 1999)

– No treatment AOR 3.3 (1.6-6.8)

– Treatment AOR 2.7 (1.5-4.7)

- **TTP >12 months and neonatal deaths**
(Basso, BMJ 2005)

– No treatment AOR 3.3 (1.5-7.5)

– Treatment AOR 2.3 (0.9-5.8)

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DEATH OF A CO-TWIN

- *Petterson B, BMJ 1993*

Survivors 1 year 96.2/1000

Live born twins 6.4/1000

Live born singletons 1.6/1000

Intrauterine death of a co-twin is associated with a 10% greater risk of cerebral palsy

- *Pharoah and Adi, Lancet 2000*

The risk of cerebral impairment of the live-born co-twin of a fetus that died in utero: 20% (95% CI 16-25)

- *Pharoah and Cooke, Dev Med Child Neu 1997*

“A hypothesis for the aetiology of cerebral palsy – the vanishing twin”

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Vanishing twins in IVF singletons Methods

- Retrospective Danish cohort study 1995-2001
- Multi-centre study (11 fertility clinics)
- 72% of all IVF/ICSI cycles in Denmark
- Singleton and twin pregnancies 8 weeks
- The Medical Birth Registry and The National Patient Registry

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COHORTS



Cohort	n	
Singleton	5237	
Twins	3678	
Survivor	642	
Early (<8 weeks)	424 (66%)	} Singleton survivors 10.4% (611/5848)
Intermediate (≥8 weeks)	187 (29%)	
Late (stillborn)	31 (5%)	

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Consequences of vanishing twins in IVF/ICSI (Hum Reprod 2005, 20; 2821-9)

	Survivors	Singletons	p-value
n	642	5237	
Birth weight, g	3264 ± 795	3442 ± 662	<0.001
Gestational age	38.9 ± 3.4	39.5 ± 2.6	<0.001
NICU, days (mean)	15.5	11.4	0.01
NICU, >7 days (%)	46.5%	38.5%	0.05
n (per 1000)			
Mortality <1 år	10 (15.6)	24 (4.6)	0.001
Neu. sequelae	11 (17.1)	95 (18.1)	0.9
Cerebral palsy	5 (7.8)	22 (4.2)	0.2

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Consequences of vanishing twins in IVF/ICSI
(Hum Reprod 2005, 20; 2821-9)

Outcome	OR (95%CI)*
BW <2500g	1.7 (1.2; 2.2)
BW <1500g	2.1 (1.3; 3.6)
GA<37 weeks	1.3 (1.0; 1.7)
GA<32 weeks	2.3 (1.4; 4.0)
Neu. sequelae	0.8 (0.4; 1.6)
Cerebral palsy	1.9 (0.7; 5.2)

*OR adjusted for age, parity and treatment method

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VANISHING TWINS
"Time of vanish"



	Early (<8.weeks)	<i>p</i>	Intermediate (≥8.weeks)	<i>p</i>	Late (Stillborn)
Live born, n	424		187		31
Birth weight	3365±695	<0.001	3185±867	<0.001	2178±940
Gestational age	39.4±2.6	<0.001	38.5±4.1	<0.001	34.3±4.8
Mortality <1 year (per 1000)	1 (2.4)	<0.001	8 (42.8)	0.8	1 (32.3)

(Hum Reprod 2005, 20; 2821-9)

VANISHING TWINS
Neurological sequelae



	Early (<8 wks) (N=424)	Intermediate (≥8 wks) (N=187)	Late (stillborn co-twin) (N=31)	Spearman correlation (<i>r</i>)*	<i>P</i>
No. (per 1000)					
Cerebral palsy	3 (7.1)	2 (10.7)	0	-0.008	0.85
Neurological sequelae	4 (9.4)	5 (26.7)	2 (64.5)	-0.09	0.022
All neurological diagnoses	14 (33.0)	15 (80.2)	3 (96.8)	-0.109	0.006

*Spearman correlation coefficient (*r*) for ordinal data

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Vanishing twins & SGA



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Vanishing twins and IUGR

- Crowding of gestational sacs
- Lack of appropriate sites for implantation
- Vaginal bleeding

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Small for gestational age (SGA)

- Small for gestational age
= Birth weight <10th percentile
- Term infants (>37 weeks) with
birth weight <2500 g



SIG Early Pregnancy, ESHRE 2007

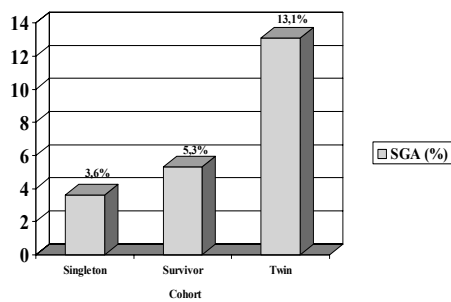
SGA in IVF singletons after a vanishing twin

N (%)	SGA		non-SGA	All
Singletons	186 (3.6%)		5012 (96.4%)	5198 (100%)
Survivors	33 (5.3%)	$p=0.04$	592 (94.7%)	625 (100%)
<8 wks	16 (3.8%)	$r = -0.1$	402 (96.2%)	418 (100%)
≥8 and <22 wks	14 (7.7%)		169 (92.3%)	183 (100%)
≥22 wks	3 (12.5%)		$p<0.02$	21 (87.5%)

SGA = small for gestational age
 r = Spearman correlation coefficient

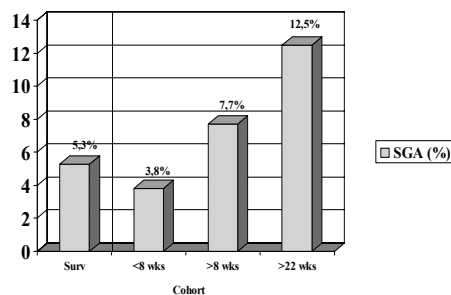
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SGA (%) in IVF singletons



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SGA (%) in IVF singletons



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SGA in IVF singletons after a vanishing twin

- SGA in the survivor cohort OR 1.5 (95%CI 1.03; 2.20) (p=0.04)
- SGA babies increased with increasing gestational age at onset of vanish ($r = -0.1$, $p < 0.02$)
- In multiple logistic regression vanish of co-twin was the only predictor of SGA OR 2.1 (95%CI 1.0; 4.3) (Maternal age, parity, child gender)

SIG Early Pregnancy, ESHRE 2007

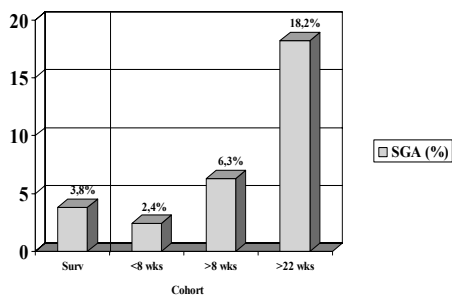
Low birth weight (<2500g) in term singletons after a vanishing twin

N (%)	LBW (<2500g)		NBW (>2500g)	All
<i>Singletons</i>	108 (2.3%)		4624 (97.7%)	4732 (100%)
<i>Survivors</i>	21 (3.8%)	$p < 0.03$	528 (96.2%)	549 (100%)
<8 wks	9 (2.4%)	$r = -0.12$ $p < 0.01$	371 (97.6%)	380 (100%)
≥8 and <22 wks	10 (6.3%)		148 (93.7%)	11 (100%)
≥22 wks	2 (18.2%)		9 (81.8%)	24 (100%)

r = Spearman correlation coefficient
LBW = Low birth weight
NBW = Normal birth weight

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Birth weight <2500g in term IVF singletons



SIG Early Pregnancy, ESHRE 2007

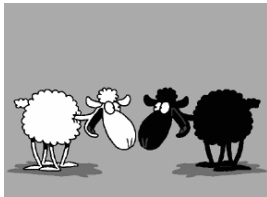
TAKE HOME MESSAGES



- Vanishing twins are seen in 10% of IVF singletons
- SGA ↑ prematurity ↑ LBW ↑ Mortality ↑
- The higher risk the higher gestational age at “vanish”
- Vanishing twins are one of the reasons for the poorer outcome in IVF singletons

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Another argument for elective single embryo transfer



SIG Early Pregnancy, ESHRE 2007

The Impact of Multiple Preterm Births on the Family

Jane Denton
Director, Multiple Births Foundation

Psychological counselling and clinical management in ART pregnancies

1 July 2007
ESHRE LYON



The Impact of Multiple Preterm Births on the Family

Learning objectives:

- To understand the risks and complications of multiple pregnancies
- To understand the impact of multiple births on the family
- To be aware of all the information about the implications of multiple births which people should understand before commencing fertility treatments



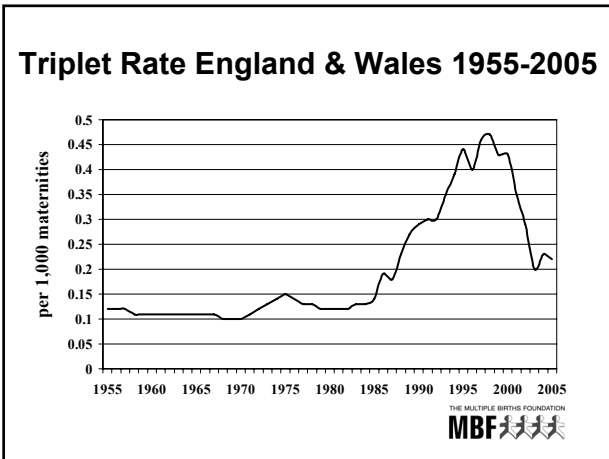


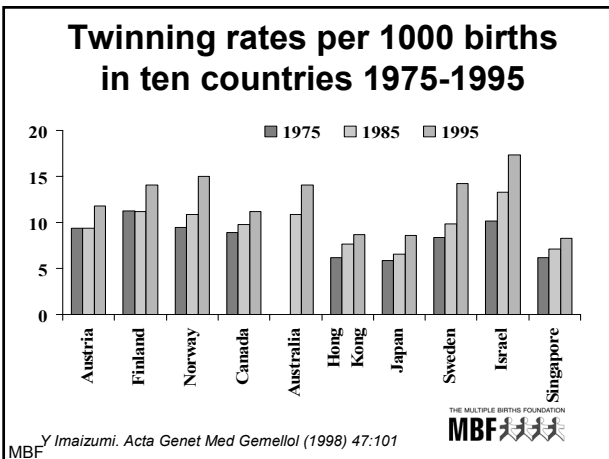


Risk of preterm birth

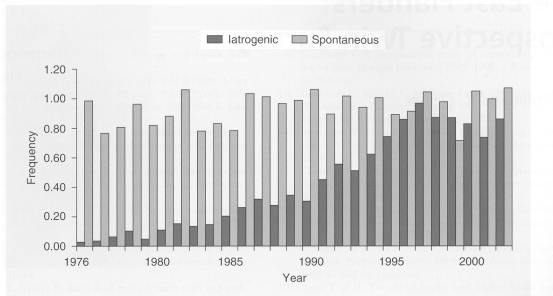
- twins 50%
- triplets 90%

THE MULTIPLE BIRTHS FOUNDATION
MBF 人々人々





Yearly frequencies of spontaneous and iatrogenic twin pregnancies



East Flanders Prospective Twin Survey (1976-2002)



Risks of Multiple Pregnancy

Mother:

Miscarriage, Hypertensive disorders, Anaemia, Haemorrhage, Caesarean section

Babies:

Preterm birth, Fetal growth restriction, Monochorionicity



Outcome in spontaneous and ART twins

	Spontaneous	ART
Maternal age (years)	29.2 (4.1)	32.3 (3.9)
Gestation (weeks)	35.4 (3.8)	34.9 (4.0)
Birthweight (grams)	2319 (663)	2250 (686)

Lambalk and van Hooff. *Fertil Steril* (2001) 75:731



MBF

Perinatal factors



	Birthweight < 1500g %
Singletons	0.7
Twins	9.0
Triplets	28.4
Quads	52.3

UK Triplet Study (1990)



Placentation of twins



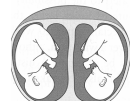
**Monozygotic
or Dizygotic**

Separate
placenta
2 chorions
2 amnions



Monozygotic

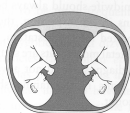
Single
placenta
1 chorion
2 amnions



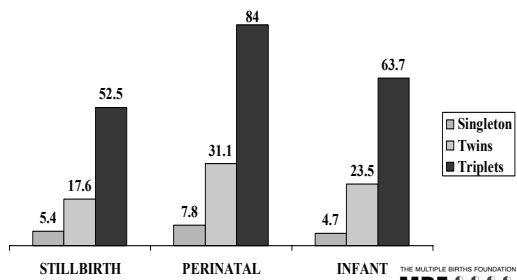
Fused
placenta
2 chorions
2 amnions



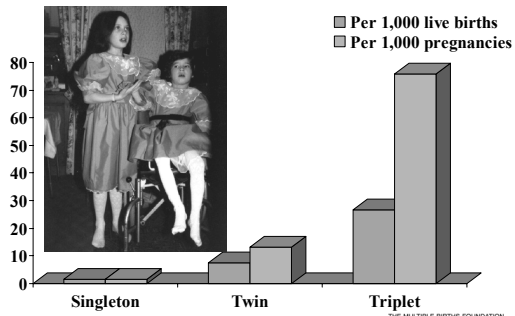
Single
placenta
1 chorion
1 amnion



MORTALITY IN MULTIPLE BIRTHS England and Wales 2003 per 1,000 births



Prevalence of cerebral palsy Western Australia 1980-1989



Petterson et al. *BMJ* (1993) 307:1239-43



MBF

Consequences of Multiple Pregnancy

Maternal

- 6x risk of pregnancy complications
- 3x maternal mortality

Fetal

- 7x risk of neonatal death
- 4x perinatal death
- 5x risk of cerebral palsy
 - 17x for triplets and higher
- 2x risk of disability
 - 3x for triplets and higher



Development of Twins

Environmental factors:

- psychological health of parents
- increased stress for parents
- reduced attention
- decreased breast feeding

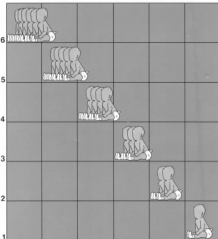
Twinning issues:

- shared experience/identity
- language development



Impact on the families

THREE, FOUR AND MORE



A Study of Triplet and Higher Order Births
HBSO

- Practical
- Emotional
- Financial
- +/-
- Bereavement
- Disability



“In the first 12 months of their life I didn’t go out. My husband did my supermarket shopping. I shopped for clothes by post.”

“In the last 2 ½ years my wife has only had one day off from looking after the children - for her grandmother’s funeral.”

UK triplet study 1990



“I am here to manage with practical problems and to maintain order... that’s all.”

“From time to time, when I can, I play with them... it is not every day, it is not often.”

“I feel sometimes that they are on their own, as if they were abandoned.”

Garel et al. Psychological consequences of having triplets. Fertil Steril. (1997) 67, 116-1165



Impact on the Families

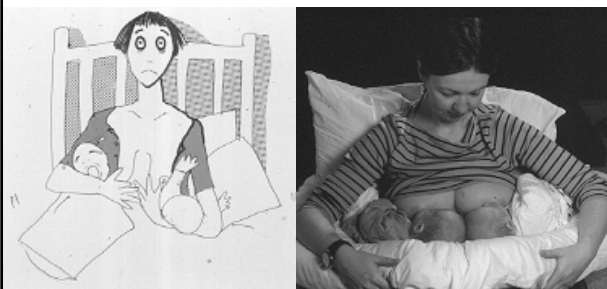
AMBA
Mothers of 6 month old triplets
(74 families)

Babies and housework = 197.5 hours pw
(hours in week = 168)

Australian Multiple Births Association 1984







Tamba Membership Survey 2004

“I am an experienced parent ... but nothing prepared me for the sheer exhaustion of being a twin mum”

“More information should be available to everyone while pregnant about the impact twins have on your life”



Psychological impact on parents of twins

Increased:

- Anxiety over health of babies
(*perinatal complications, cerebral palsy*)
- Difficulties in mother-infant relationship
- Maternal fatigue, isolation, depression
- Financial worries
- Developmental problems in twins
- Behaviour problems in siblings
- Marital stress
- Child abuse



Comparison of Prevalence of Depression in Mothers of Twins and Mothers of Singletons

Conclusion: Mothers of twins are more likely to experience depression. This suggests a relation between the additional and exceptional stresses that twins present and the mother's motional wellbeing.

Thorpe et al BMJ (1991) 302:875-8



Language Development in Twins



- Triadic communication
- Reduced eye contact
- Reduced dialogue with mother
- Poor model
- Reinforcement of errors

*Twins Language Development,
Thorpe (2006)*

Early Human Development 82:387-395



Relationships in multiples – negative aspects

- Domination
- Dependency
- Rivalry
- Jealousy
- Collusion
- Exclusiveness



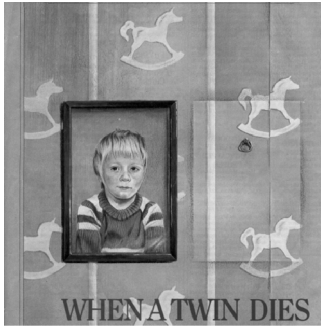
Disability – Challenges for Parents



- Coping with different needs for each child
- Constant reminder
- Bonding difficulties
- Healthy child – guilt, jealousy
- Disabled child – frustration, jealousy
- Insufficient time for either child



Bereavement



Parents:

- Conflicting emotions
- Loss of special status
- Bonding difficulties

Surviving Twin:

- Mixed/confusing emotions
- Guilt
- Fear
- Anger

THE MULTIPLE BIRTHS FOUNDATION
MBF

Child abuse

10% victims multiple births

Rarely both

Disadvantaged child affected

Tanimura M et al. Lancet (1990) 336:1298

THE MULTIPLE BIRTHS FOUNDATION
MBF



**Siblings
behaviour problems**
2-5 yrs – x3
8-11yrs – x6

Hays et al. Aus J Early Child (1997) 13:25-28

THE MULTIPLE BIRTHS FOUNDATION
MBF

Parenting ART Twins

Parenting stress greater in IVF group

Cook et al. Hum Reprod (1998)

No differences between ART and spontaneous twins

Colpin et al. Hum Reprod (1999)

Parenting and marital stress greater for all twins

Pinborg et al. Hum Reprod (2003)

Severe parenting stress for mothers

22% twins

5% singletons

Glazebrook et al. Fertil Steril (2004)



Parenting ART Twins

“The significant psychosocial risks associated with each increase in the number of ART multiple birth children include difficulty in providing basic material needs for their families, lower QOL, and increases in social stigma and maternal depression. The identification of these risks can provide useful information in counseling those seeking fertility treatment, who may underestimate the difficulties involved in raising multiple birth children.”

Ellison et al. Fertil Steril (2005) 83: 1422-1428



The goal:

The uneventful live birth to a fit woman, of a single, healthy baby.

Evers. ESHRE Taskforce on Risks and Complications in ART (2002)



The Impact of Multiple Preterm Births on the Family

Learning objectives:

- To understand the risks and complications of multiple pregnancies
- To understand the impact of multiple births on the family
- To be aware of all the information about the implications of multiple births which people should understand before commencing ovarian stimulation for fertility treatments





Guidelines: for professionals

1. Facts about Multiple Births
2. Multiple Pregnancy
3. Special Needs
4. Bereavement
5. The First Five Years and Beyond

by: E Bryan, J Denton, F Hallett

The Multiple Births Foundation

www.multiplebirths.org.uk