PRE-CONGRESS COURSE 7

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

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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
Basic Causes of Infertility

- Ovulatory
- Tubal
- Endometrial
- Uterine

Male 35%
Female 50%
Other 5%
Unexplained 10%

Adapted from Speroff, Glass, and Kase. Clinical Gynecologic Endocrinology and Infertility. Lippincott Williams & Wilkins, 1999

Medical Developments in Infertility Treatment

Overview of Medical Diagnosis and Treatment of Infertility

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

Adapted from Speroff, Glass, and Kase. Clinical Gynecologic Endocrinology and Infertility. Lippincott Williams & Wilkins, 1999
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 disorders/dependence)

- Netherlands – 14.9%
- Belgium – 12.0%
- France – 10.4%
- Spain – 8.2%
- Germany – 9.1%
- Ukraine – 20.9%
- Poland – 9.0%
- Italy – 8.2%
- Mexico – 12.2%
- Colombia – 17.8%
- Japan – 8.6%
- Korea, China – 5.1%
- Nigeria – 4.7%
- United States – 26.4%

SOURCE: World Health Organization
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. (Corner et al., 1992)
  - Increased risk of depression and anxiety when infertility treatment over prolonged period of time. (Anderson et al., 2003)

- **Eating Disorders:**
  - 58% of infertile women with menstrual irregularities had eating disorder. (Stewart et al., 1990)

- **Chemical abuse/addiction:**

- **Personality Disorders**
  1. Obsessive/Compulsive
  2. Narcissistic
  3. Borderline
  4. Dependent
  5. Avoidant
  6. Paranoid
  - Punishment for letting things get out of control
  - Attack on autonomy
  - Threat of abandonment
  - Expected punishment for worthlessness
  - Dangerous invasion of privacy
  - 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. Petos, 2005
- Experience greater social stigma. Myers & 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 \( \text{Lorber, 1987} \)
- Prolonged treatment increases marital conflict, distancing, divorce/separation \( \text{Kraft et al., 1987; Dennis et al., 1987; Coffey, Edelman, & Cook, 1987; Labos et al., 1985} \)
- Couples in advanced stages of treatment (\( > 3 \) years) had lowest levels of marital adjustment \( \text{Berg & Wilson, 1991} \)
- Women with moderate amounts of treatment failure reported greater marital distress \( \text{Boivin et al. 1995} \)

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
- Internal factors e.g. personality characteristics
- External factors e.g. social support and external stressors
- Coping/Cognitions
- Endocrine and immune functions
- Health behavior
- Outcome: Medical, Emotional

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!
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 (Austenfeld 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


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.

* Send e-mail to L.Schmidt@pubhealth.ku.dk to receive the published thesis.
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 oophorectomy.

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

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

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 trombophilic 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

<table>
<thead>
<tr>
<th></th>
<th>RPL patients (N = 328)</th>
<th>Controls</th>
<th>OR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &gt; 30</td>
<td>%</td>
<td>%</td>
<td>0.74</td>
<td>NS</td>
</tr>
<tr>
<td>Art/Ven thromboembolism</td>
<td>2.7</td>
<td>0.8</td>
<td>3.40</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Polyarthitis</td>
<td>2.7</td>
<td>0.1</td>
<td>27.72</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>IDDM</td>
<td>1.2</td>
<td>0.4</td>
<td>3.02</td>
<td>NS</td>
</tr>
<tr>
<td>Hyper-/Hypothyroldism</td>
<td>4.5</td>
<td>2.0</td>
<td>2.31</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>1.5</td>
<td>0.2</td>
<td>7.60</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

References


Emotional Aspects of Pregnancy Loss: The Science Behind Emotions

Claudia Hammond
Broadcaster
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


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

ADVERSE OUTCOME FOLLOWING VANISHING TWINS: LESSONS TO LEARN

Anja Pinborg
Fertility Clinic, Rigshospitalet, University of Copenhagen, Denmark

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

<table>
<thead>
<tr>
<th></th>
<th>Helmerhorst</th>
<th>Jackson</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>5.361</td>
<td>12.283</td>
</tr>
<tr>
<td>&lt;2500 g</td>
<td>1.7 (1.5-1.9)</td>
<td>1.8 (1.4-2.2)</td>
</tr>
<tr>
<td>&lt;1500 g</td>
<td>3.0 (2.1-4.4)</td>
<td>2.7 (2.3-3.1)</td>
</tr>
<tr>
<td>&lt;37 weeks</td>
<td>2.0 (1.8-2.3)</td>
<td>2.0 (1.7-2.2)</td>
</tr>
<tr>
<td>&lt;32 weeks</td>
<td>3.3 (2.0-5.3)</td>
<td>-</td>
</tr>
<tr>
<td>SGA</td>
<td>1.4 (1.2-1.7)</td>
<td>1.6 (1.3-2.0)</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.7 (1.1-2.6)</td>
<td>2.2 (1.6-3.0)</td>
</tr>
</tbody>
</table>
### IVF SINGLETONS
#### Misdannelser

**Number needed to harm (NNTH)**

<table>
<thead>
<tr>
<th>Studies</th>
<th>Alle</th>
<th>Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1.3 (1.2-1.5)</td>
<td>1.4 (1.2-1.5)</td>
</tr>
<tr>
<td>1%</td>
<td>333</td>
<td>250</td>
</tr>
<tr>
<td>2%</td>
<td>167</td>
<td>125</td>
</tr>
<tr>
<td>3%</td>
<td>111</td>
<td>83</td>
</tr>
<tr>
<td>4%</td>
<td>83</td>
<td>62</td>
</tr>
</tbody>
</table>

(Hansen, Hum Reprod Update, 2004)

---

### IVF SINGLETONS
#### Cerebral paresis

<table>
<thead>
<tr>
<th>OR (95%CI)</th>
<th>Lidegaard</th>
<th>Strömberg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hum Rep 2005</td>
<td>Lancet 2002</td>
</tr>
<tr>
<td>IVF singletons</td>
<td>1.8 (1.2-2.8)</td>
<td>2.8 (1.3-6.8)</td>
</tr>
</tbody>
</table>

---

### IVF/ICSI ENKELTFØDTE
- **STØRRE RISIKO?**
  - **Subfertilitet**
    - Neonatal mortality: Draper Lancet 1999; Basso BMJ 2005
    - Misdannelser: Zhu BMJ 2006
  - **Antal gestationssække**
    - Schieve, NEJM 2004
    - Lancaster, ESHRE 2004
  - **IVF/ICSI metoder**

SIG Early Pregnancy, ESHRE 2007
Infertility and adverse outcome

- Infertility correlates with adverse outcome

- TTP >12 months and preterm birth
  (Basso NR 2003)
  - Primiparas: Untreated OR 1.4 (1.1-1.7)
  - Multiparas: Untreated OR 1.6 (1.2-2.1)

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)

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"
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

Cohorts

<table>
<thead>
<tr>
<th>Cohort</th>
<th>n</th>
<th>Singleton survivors</th>
<th>Singleton survivors %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singleton</td>
<td>5237</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Twins</td>
<td>3678</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survivor</td>
<td>642</td>
<td>424 (66%)</td>
<td>10.4% (611/5848)</td>
</tr>
<tr>
<td>Early (&lt;8 weeks)</td>
<td>424</td>
<td>244 (57%)</td>
<td></td>
</tr>
<tr>
<td>Intermediate (&gt;8 weeks)</td>
<td>187</td>
<td>107 (57%)</td>
<td></td>
</tr>
<tr>
<td>Late (stillborn)</td>
<td>31</td>
<td>20 (65%)</td>
<td></td>
</tr>
</tbody>
</table>

Consequences of vanishing twins in IVF/ICSI

<table>
<thead>
<tr>
<th></th>
<th>Survivors</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>642</td>
<td>5237</td>
</tr>
<tr>
<td>Birth weight, g</td>
<td>3264 +795</td>
<td>3442 + 662</td>
</tr>
<tr>
<td>Gestational age</td>
<td>38.9 +3.4</td>
<td>39.5 +2.6</td>
</tr>
<tr>
<td>NICU, days (mean)</td>
<td>15.5</td>
<td>11.4</td>
</tr>
<tr>
<td>NICU, &gt;7 days (%)</td>
<td>46.5%</td>
<td>38.5%</td>
</tr>
<tr>
<td>Mortality &lt;1 yr</td>
<td>10 (15.6)</td>
<td>24 (4.6)</td>
</tr>
<tr>
<td>Neu. sequelae</td>
<td>11 (17.1)</td>
<td>95 (18.1)</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>5 (7.8)</td>
<td>22 (4.2)</td>
</tr>
</tbody>
</table>
Consequences of vanishing twins in IVF/ICSI
(Hum Reprod 2005, 20; 2821-9)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>OR (95%CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW &lt;2500g</td>
<td>1.7 (1.2; 2.2)</td>
</tr>
<tr>
<td>BW &lt;1500g</td>
<td>2.1 (1.3; 3.6)</td>
</tr>
<tr>
<td>GA&lt;37 weeks</td>
<td>1.3 (1.0; 1.7)</td>
</tr>
<tr>
<td>GA&lt;32 weeks</td>
<td>2.3 (1.4; 4.0)</td>
</tr>
<tr>
<td>Neu. sequelae</td>
<td>0.8 (0.4; 1.6)</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>1.9 (0.7; 5.2)</td>
</tr>
</tbody>
</table>

*OR adjusted for age, parity and treatment method

VANISHING TWINS
"Time of vanish"

<table>
<thead>
<tr>
<th>Time of vanish</th>
<th>Early (&lt;8 wks)</th>
<th>Intermediate (&gt;8 weeks)</th>
<th>Late (stillborn)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live born, n</td>
<td>424</td>
<td>187</td>
<td>31</td>
</tr>
<tr>
<td>Birth weight</td>
<td>3360±655</td>
<td>2189±687</td>
<td>2179±940</td>
</tr>
<tr>
<td>Gestational age</td>
<td>39±2.6</td>
<td>38.5±2.1</td>
<td>34±2.8</td>
</tr>
<tr>
<td>Mortality &lt;1 year (per 1000)</td>
<td>1 (2.4)</td>
<td>0 (0.01)</td>
<td>1 (32.3)</td>
</tr>
</tbody>
</table>

(Vanishing twins, ESHRE 2007)

VANISHING TWINS
Neurological sequelae

<table>
<thead>
<tr>
<th>Time of vanish</th>
<th>Early (&lt;8 wks)</th>
<th>Intermediate (&gt;8 wks)</th>
<th>Late (stillborn)</th>
<th>Spearman correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurological sequelae</td>
<td>(N=424)</td>
<td>(N=187)</td>
<td>(N=31)</td>
<td>(r)*</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>5 (7.1)</td>
<td>2 (10.7)</td>
<td>0</td>
<td>-0.008</td>
</tr>
<tr>
<td>Neuropathological</td>
<td>4 (5.4)</td>
<td>0 (26.7)</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>All neurological diagnoses</td>
<td>14 (33.0)</td>
<td>15 (80.2)</td>
<td>3 (96.9)</td>
<td>-0.109</td>
</tr>
</tbody>
</table>

*Spearman correlation coefficient for ordinal data
Vanishing twins & SGA

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

Small for gestational age (SGA)

• Small for gestational age
  = Birth weight <10th percentile
• Term infants (>37 weeks) with birth weight <2500 g
SGA in IVF singletons after a vanishing twin

<table>
<thead>
<tr>
<th>N (%)</th>
<th>SGA</th>
<th>non-SGA</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singletons</td>
<td>186 (3.6%)</td>
<td>5012 (96.4%)</td>
<td>5198 (100%)</td>
</tr>
<tr>
<td>Survivors</td>
<td>33 (5.3%)</td>
<td>p=0.04</td>
<td>592 (94.7%)</td>
</tr>
<tr>
<td>&lt;8 wks</td>
<td>16 (3.8%)</td>
<td>p=0.02</td>
<td>402 (96.2%)</td>
</tr>
<tr>
<td>≥8 and &lt;22 wks</td>
<td>14 (7.7%)</td>
<td>p=0.02</td>
<td>169 (92.3%)</td>
</tr>
<tr>
<td>≥22 wks</td>
<td>3 (12.5%)</td>
<td>p&lt;0.02</td>
<td>21 (87.5%)</td>
</tr>
</tbody>
</table>

SGA = small for gestational age
r = Spearman correlation coefficient

The table above shows the percentage of SGA in IVF singletons after a vanishing twin. The percentages are categorized by the gestational age of the survivors. The data shows that the percentage of SGA is higher in the group with a gestational age of ≥22 wks compared to those with a gestational age of <8 wks and ≥8 and <22 wks.
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)

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

<table>
<thead>
<tr>
<th></th>
<th>LBW (&lt;2500g)</th>
<th>NBW (&gt;2500g)</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survivors</td>
<td>21 (3.8%)</td>
<td>528 (96.2%)</td>
<td>549 (100%)</td>
</tr>
<tr>
<td>&lt;8 wks</td>
<td>9 (2.4%)</td>
<td>371 (97.6%)</td>
<td>380 (100%)</td>
</tr>
<tr>
<td>≥8 and &lt;22 wks</td>
<td>10 (6.3%)</td>
<td>148 (93.7%)</td>
<td>158 (100%)</td>
</tr>
<tr>
<td>≥22 wks</td>
<td>2 (18.2%)</td>
<td></td>
<td>11 (100%)</td>
</tr>
</tbody>
</table>

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

Birth weight <25000g in term IVF singletons
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

Another argument for elective single embryo transfer
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

Page 42
Risk of preterm birth
• twins 50%
• triplets 90%

Triplet Rate England & Wales 1955-2005

Twinning rates per 1000 births in ten countries 1975-1995
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

<table>
<thead>
<tr>
<th></th>
<th>Spontaneous</th>
<th>ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (years)</td>
<td>29.2 (4.1)</td>
<td>32.3 (3.9)</td>
</tr>
<tr>
<td>Gestation (weeks)</td>
<td>35.4 (3.8)</td>
<td>34.9 (4.0)</td>
</tr>
<tr>
<td>Birthweight (grams)</td>
<td>2319 (663)</td>
<td>2250 (686)</td>
</tr>
</tbody>
</table>

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

Fused placenta
2 chorions
2 amnions

Monozygotic

Single placenta
1 chorion
2 amnions

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

Singletons
Twins
Triplets

STILLBIRTH
PERINATAL
INFANT
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

- 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.”

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 emotional wellbeing.

Language Development in Twins

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

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

Child abuse

10% victims multiple births
Rarely both
Disadvantaged child affected


Sibling behaviour problems
2-5 yrs – x3
8-11yrs – x6

Parenting ART Twins

Parenting stress greater in IVF group


No differences between ART and spontaneous twins


Parenting and marital stress greater for all twins


Severe parenting stress for mothers

22% twins
5% singletons


“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.”


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