CHILDREN WITH OESOPHAGEAL ATRESIA

A BIOPSYCHOSOCIAL FOLLOW UP STUDY

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ERRATA

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THE PAPERS ON WHICH THE THESIS IS BASED

I. Faugli A, Aamodt G, Bjørnland K, Emblem R, Diseth TH. Assessment of early mother-child relation in infants with oesophageal atresia. Nordic Journal of Psychiatry 2005; 59: 498-503.

II. Faugli A, Emblem R, Veenstra M, Bjørnland K, Diseth TH. Does esophageal atresia influence the mother-infant interaction? Journal of Pediatric Surgery, 2008 in press.

III. Faugli A, Emblem R, Bjørnland K, Diseth TH. Mental health in infants with esophageal atresia. Infant Mental Health Journal, 2008 in press.

IV. Faugli A. Bjørnland K, Emblem R, Nøvik TS, Diseth TH. Mental health and psychosocial functioning in adolescents with esophageal atresia. Journal of Pediatric Surgery, 2008 submitted.

1.   Introduction

This study was conducted to advance the holistic understanding of children with OA and their families' situation.

The study was based on collaboration between Section for Child and Adolescent Psychiatry and Section for Paediatric Surgery at Rikshospitalet University Hospital, Norway. The study comprises a survey of two groups of children with oesophageal atresia (OA); one group born 1999-2002 (infants), and another born 1986-1990 (adolescents). In the infant group (paper I-III) we assessed parent-child interaction and parents' experiences nurturing a child with OA and studied mental health and psychomotor development in the infants. This part of the study makes baseline for a future prospective study of children with OA. In the adolescent group (paper IV) we explored mental health and psychosocial functioning in adolescents with OA and their parents' experiences.

Improved medical treatments for children with chronic illness have resulted in better survival rates as well as more morbidity and use of medical resources by ill children. Increasingly, interest is being directed at the implications of illness for the child's psychiatric adjustment. However, little focus has been on mental health of babies born with defects and chronically ill infants.

As I started working as a child psychiatric consultant at the Section for Paediatric Surgery at Rikshospitalet University Hospital (1998), I had experience from an infant mental health centre, were I was trained in parent-child interaction evaluations and early interventions. Thus, the infant patients in the neonatal intensive care unit and the paediatric surgery ward and their parents immediately captured my interest. However, I found it difficult to answer parents of new-borns with congenital anomalies when they asked

about the short and long-term effects of a serious medical condition and invasive treatment procedures on mental health and psychosocial functioning. The type of defects and treatment procedures were very different and the research on this field was scarce.

My interest in OA in particular was aroused by a four year old girl with OA who refused eating. She and her parents were referred to the Section for Child and Adolescent Psychiatry for relationship difficulties. Their experiences with paediatric health services reflected helplessness and poor knowledge of infant mental health and parent-child interaction among health care professionals. The complex and challenging situation for the young girl and her family, made me comprehend the urgent need of more knowledge about this illness and its impact on development of mental health and psychosocial functioning. In collaboration with the paediatric surgeons gradually the plans of a follow-up study of children with OA evolved.

Child development is not determined solely by the environment or by genetics. In accordance with Friedman and Chase-Lansdale we view development as a transactional process, as interplay between the child's inherent predispositions (e.g. gender, temperament, genes, physical health) and the environment (e.g. caregivers, family, society, peers) (1). Biopsychosocial models recognize the importance of both intrinsic and extrinsic factors (2). Thus, we chose a biopsychosocial model for this study.

1.1 Biological; physical health

The impact of chronic paediatric illnesses on child development has been well-recognized (3-7). In general, children with chronic illnesses or birth defects appear to have about twice the risk of healthy children for developing a secondary emotional handicap or psychosocial maladjustment (3;8).

However, the majority of children with severe paediatric illnesses are extremely resilient (9). Nevertheless, in those paediatric patients with a comorbid psychiatric illness, appropriate recognition and prompt intervention are critical (3).

In those children who have got a psychiatric disturbance, the thesis has been developed that their severe paediatric illness may have contributed to a risk factor to the development of their psychopathology. Even sensitive paediatric care, involves a spectrum of illness-related challenges that are appropriately categorized as risk factors for early developmental psychopathology (3). Repeated hospital admissions and surgery in early childhood may have long-term effects on emotional and behavioural adjustment (10-19). Early experience is particularly important because learning proceeds more efficiently along established synaptic pathways (20). Traumatic experiences related to symptoms or treatment may create enduring alterations in the neurotransmitter and endocrine systems that mediate stress response, possible increasing the risk of mental illness later in life (2; 21; 22). Following surgical repair of life-threatening congenital anomalies, many children may be left with inadequately functioning internal organs and chronic physical health problems. Since repair of anomalies generally begins in the early days or months of life, these children are perceived to be "different" from birth, and, in common with children with chronic illness, this places them at an increased risk for psychosocial maladjustment (11).

Risk factors for psychosocial sequels of children with chronic illness or birth defects may be related to the nature and severity of the medical condition, gender, low birth weight, hospitalisation, psychological responses of mother, self-esteem, school functioning, and family strain (8;23-25).

1.1.1 Oesophageal atresia

Oesophageal atresia is a major congenital anomaly embracing a clinically heterogeneous group of patients concerning seriousness of the medical condition, additional malformations and complications. Oesophageal atresia is a relatively common congenital malformation, with a prevalence of approximately one in 2500 births (26).

The aetiology of OA is likely to be multifactorial and remains unknown, however, key developmental processes that may be disturbed during embryogenesis are identified (27). A disturbance during the tracheooesophageal organogenesis is likely to cause defects. The molecular mechanisms that underlie the defects is supposed to be loss of function mutations of a key developmental gene and members of its signalling cascade (27;28). A blind upper oesophageal pouch with lower tracheooesophageal fistulae is the most common among these defects (Figure 1) (29). The motility of the oesophagus is always affected in OA.
The trachea is also abnormal in OA. The abnormality consists of an absolute deficiency of tracheal cartilage and an increase in the
length of the transverse muscle in the posterior tracheal wall. When severe, these abnormalities result in tracheomalacia (27).

Successful repair of OA depend on surgical techniques and methods of caring for the critically ill infant. All infants with OA need surgery during their first living days, and if possible, primary surgery with oesophageal anastomoses is the preferable treatment (30). Associated anomalies are observed in about 50 % of patients with OA. The most frequent are cardiovascular, anorectal, genitourinary, gastrointestinal and vertebral/skeletal anomalies (27;31). Low birth weight (below 1500 g) combined with cardiac anomaly is associated with a poor prognosis, otherwise the survival is 98 % (32).

Figure 1. The most common type of oesophageal atresia with a blind upper oesophageal pouch and a lower tracheooesophageal fistula.
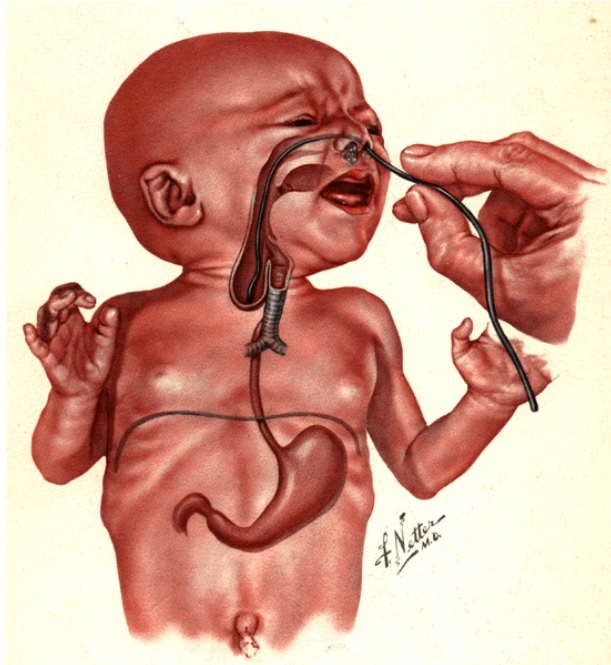
There are several ways to classify the seriousness of oesophageal atresia (32-37). In the present study we chose the Montreal classification (34) because this was used by others assessing mental health and psychosocial functioning in school children with OA (38). Patients with either life-threatening anomalies or both major anomalies and ventilator dependence were in the high risk class.

Following initial surgery, complications of the condition and its surgery are anastomotic stricture, postoperative pulmonary complications, recurrent fistula and gastrooesophageal reflux (GOR) (32;37;39). Feeding difficulties

and respiratory problems are frequent during infancy and early childhood; whereas dysphagia, food impaction and gastrooesophageal reflux (GOR) are common later (27;40;41). Oesophageal dysmotility, GOR and anastomotic stricture are the principal reasons for feeding problems (40). Additional operations and dilatations of oesophagus may be required during the first years of life. Surgical interventions may also be required in older children and adolescents (42).

1.2 Psychological; Parent-child relationship/Mental health

1.2.1 Parent-child relationship

Very early in life, the parent and child develop a reciprocal relationship, vocalising back and forth, gazing at one another, and enjoying interchanges of smiling and cuddling. This experience provides an early relational platform for early attachment processes (43) The central premise in attachment theory is that the need for human contact, reassurance, and comforting in the face of illness, injury, and threat is a normal response throughout the life span. The need is especially prominent early in development when physical and emotional survival depends on the care giving relationship (44). Much of the early parent-infant interaction is centred on feeding, and there is a close intimacy between mother and child that emerges while the baby suckles.
The mother-child relationship provides a critical context for the development of children's psychosocial competence, and the mothers' welfare represents an important factor in the mother-child interaction (45-49).
The infant-parent relationship is emerging as the target of most intervention and prevention efforts in infant mental health (45; 47; 50).

1.2.2 Mental health

Infant mental health is described as the developing capacity of the child from birth to three years of age to experience, regulate, and express emotions (51). The development of this capacity makes the child capable to form close interpersonal relationships, explore the environment and acquire developmental skills (51).

The early work on infant mental health focused on the developmental changes in infants deprived of maternal contact during hospitalization (52). Even though most paediatric departments now encourage parents to stay with their infants, psychological problems, such as avoidance behaviour, lack of social responsiveness and loss of previously acquired developmental skills following hospitalization are still reported (53-56). The fact that traumatic stress may follow hospitalization and treatment procedures even though the infant is not separated from the parent may be an explanation of this. Applied newer knowledge of cerebral development and neurobiology (21) on theories of attachment and self regulation (43; 57-59) enrich this explanation. Trauma exposure may have a damaging effect on all dimensions of infant mental health and the symptoms of traumatic stress are considered to be a causal factor in the ontogenesis of psychopathology (21).

Children's responses to trauma depend on type of trauma and at which developing stage they are when exposed (60). The infant period of ages 0-2 years represents a critical stage for developing trust and mistrust toward their primary caregivers, and the oral region and its functions play a decisive role in psychosocial maturation and the development of self confidence, joy and pleasure (61). Infants explore their environment through the mouth and their senses. Invasive medical procedures in the oral region during this period may be experienced as particularly frightening for the child. The cognitive level at

this stage makes it difficult for the child to differentiate if it is the caregiver or a health care professional who is causing discomfort (17; 51; 62).

Early age of onset of mental problems may have important negative clinical prognostic implications (63).

1.3 Social outcome

Although increased survival of children with birth defects and chronic illnesses, their medical condition may have implications for how they are functioning socially when they grow up. Literature reviews of studies with a wide variety of disorders shows social problems related to school adaptation, learning, social activity and competence among surgical and chronically ill paediatric patients (9; 64; 65). In a longitudinal study of effects of major surgery and hospitalisation during first six months of life on cognitive functioning and educational attainment conducted by Ludman and colleagues, the surgery group showed significantly poorer performance than controls. Length of hospitalisation was a predictor by 12 months of age (12). By three years of age the number of operations predicted cognitive functioning, and by early adolescence mechanical ventilation beyond three days were predictor for academic attainment (12).

A powerful factor related to the adaptation of a child to serious paediatric illness is the response of the family. Exceptionally sensitive and responsive parenting could be conceptualized as a potent protective factor (3). The adaptation of children with a chronic illness is in large part a product of the relevant risk and protective factors that shape their experiences and ultimately impact the expression of their genes (3). Aspects that are important for professionals working with chronically ill children are the cognitive and emotional level of the patient, the essential role of the family, and focus on

facilitating coping and adjustment to illness to follow an optimal trajectory (9).

1.4 Oesophageal atresia and mental health and psychosocial outcome

Following initial surgery, respiratory problems and feeding problems are common and a source of considerable parental anxiety (40; 66; 67). Pharyngeal suctioning of saliva and feeding by gastrostomy may be requested in extended periods. Infants with OA may experience choking during feeding, recurrent vomiting, swallowing difficulties and acute or chronic respiratory problems. Acute dramatic episodes during feeding may appear. Uncertainties, helplessness, powerless, and afraid are words parents often used when describing their experiences caring for a child with OA (68). Parents are reported to be considerably worried by feed related symptoms (66). Repeated episodes of distress during feeding may lead to food aversions and reluctance to feed, and a combination of physical, emotional and behavioural factors may underlie problems (40).

In spite of the challenges child and parents experience in the early years, most adult patients with OA seem to have a good quality of life (69; 70). There is a paucity of studies that have examined long-term psychological outcome of children with OA. The results reporting psychosocial functioning are contradictory; ranging from comparable with those of healthy controls (40; 69; 71; 72) to added emotional and learning problems (38; 73). Because these studies have few patients in each age group and different assessment procedures have been used, it is difficult to make any firm conclusions. No assessment of mental health and psychosocial functioning has been conducted in infants and adolescents with OA.

There is a need for advanced knowledge about how oesophageal malformations and invasive treatment procedures influence mental health and psychosocial functioning in young patients with OA.

2. Aims of the study

When this study was planned in 1999/2000 there were no published studies dealing with mental health and psychosocial outcomes of infants and adolescents with OA. Little was known about the effects of serious associated anomalies, invasive treatment procedures, and complications of OA on infants' and adolescents' mental health and psychosocial functioning.

One important aim of the study was to learn more about the psychosocial aspects of OA in order to improve the foundation for assessment and treatment of the patients' overall situation, and to prevent psychosocial difficulties for the child and his/her family.

The main goal was to examine physical and mental health and psychosocial functioning in children with oesophageal atresia.
The following specific aims evolved:

1. To assess the quality of parent-infant interactions and relationships in children with oesophageal atresia by using the Parent Child Early Relational Assessment (PCERA) (paper I).

2. To assess the quality of the mother-infant interaction in children with OA compared to other hospitalized children with no feeding difficulties, and to search for possible predictors of impaired interaction (related to the medical condition) (Paper II).

3. To assess mental health in infants with OA and to find prognostic factors for mental health (related to the medical condition) (Paper III).

4. To assess mental health and psychosocial functioning among adolescents with OA compared with adolescents from the general population and to

search for prognostic predictors among individual, physical and
environmental characteristics in adolescents with OA (Paper IV).

3. Methodology

3.1 Subjects; OA groups

The sample of infants comprised all eligible infants treated at Rikshospitalet University Hospital born during 1999 through 2002 and their mothers one year after primary surgery (paper I-III). The sample of adolescents comprised all eligible children treated at Rikshospitalet University Hospital born during 1986 through 1990 in the transition from paediatric to adult service (paper IV).

3.1.1 Inclusion and exclusion criteria

Infants

The eligibility criteria excluded children who died before one year (n=2) and if the mother could not speak Norwegian (n=2). Of the remaining 40 patients, mothers of 39 children (98 %) agreed to participate. There were 27 boys and 12 girls, and median age (range) of the children was 13 (12-18) months. Socio-demographic data are presented in the papers.

Adolescents

The eligibility criteria excluded children with incomplete medical records (n=1) and children who had died (n=9). In eight cases the cause of death was serious associated anomalies with respiratory failure, or complications of extreme prematurity and major congenital heart disease. One patient died from Sudden Infant Death Syndrome (SIDS). Two patients were not invited due to present serious medical condition unrelated to OA (cancer, anorectal anomaly). Of 22 eligible patients, 21 adolescents (96 %) and one or both parents participated in the study.

3.2 Subjects; Control groups

3.2.1 Infants

As a comparison group for the assessment of mother-infant interaction comprised hospitalized infants admitted for surgery with diseases other than OA and their mothers. All eligible infants electively admitted at the surgical unit, Rikshospitalet University Hospital, during February through November 15th 2005. The sampling was done with age and gender probability proportional to size of the OA group. The eligibility criteria excluded children referred with nutritional problems; i.e. gastrostomy, or feeding related diseases; i.e. gastrooesophageal reflux disease (GORD) (co-morbid factors), or if their mother did not speak Norwegian. Because some assessment (Bayley Scales) requested external assistance, infants admitted on days when this service was not available were omitted. For practical reasons, if several eligible infants were admitted concurrently only one could be included. Mothers of 13 children were asked, and 10 (77 %) agreed to participate. The comparison group consisted of children with minor urological problems, most vesicoureteral reflux and their mothers.

3.2.2 Adolescents

Comparison group for the psychiatric and psychosocial assessments was a subsample drawn from a Norwegian epidemiological study of mental health. The study used a stratified random sampling procedure and a two stage design (74). In the first stage, screening was carried out by means of a standardized questionnaire, the Child Behavior Checklist (CBCL) (75). In the second stage, screen positive (CBCL T score ≥60 according to the American

norm) adolescents 13-15 years of age and a random sample of screen negative (CBCL T score <60) adolescents in this age group, were invited to participate in a more detailed diagnostic assessment. Thirty six adolescents (19 boys, 17 girls), mean age 14 years (range 13-15 years), and their parents participated and are referred to as the control group in paper IV. Six adolescents had been hospitalized for various medical conditions (e.g. congenital dislocation of the hip, asthma, otitis media or accidents) during their childhood. Two adolescents had chronic illness (eczema and epilepsy). Medical data were missing in three adolescents.

3.3 Refusers and missing data

Parents of one OA infant (3 %) refused to participate. Furthermore, one mother was not comfortable with videotaping but agreed to be taped in the feeding situation and one mother refused to participate in the psychiatric assessments of practical reasons but she completed the questionnaires. However, the father and child participated in the psychiatric assessments. In the infant comparison group, three of the parents (23 %) refused to participate; parents of three boys, median age 19 months (range 12-20 months) with minor urological problems (2) and umbilical hernia (1). Parents of one OA adolescent (5 %) refused to participate. All refusers in the OA groups reported practical reasons, for not participating. The higher proportion of refusals in the infant comparison group may reflect that the clinical assessment program for the infants, were tighter than the program for the OA infants. For the OA group it was the same two special nurses caring for the infants' program throughout the study. The number of refusers decreased after a meeting with the nurses, where the importance of participating in the study was emphasized.

The sample of the adolescent comparison group has previously been reported to be representative for the general Norwegian adolescent population and has

been used as comparison group for similar studies of adolescents with chronic illness (76;77). In the adolescent comparison group the frequency distribution of high and low scoring adolescents according to the CBCL in the interviewed sample, was similar to that of the general population sample.

3.4 Methods

3.4.1 Mental health

Infants were clinically assessed and psychopathology diagnosed with the Diagnostic Classification: 0-3, including the Parent-Infant Relationship Global Assessment Scale (PIR-GAS) (78). The outcome measure "infant mental health" was related to primary disorders (axis I) and relationship disorders (axis II). The validity and reliability of DC: 0-3 has been reported to be acceptable to good (79; 80). DC: 0-3 was used because it is a system of criteria which define disorders of infancy and early childhood, and is reported to be an excellent tool to document and diagnosing infant mental health in paediatric hospitals (81). The classification of mental health was based on observation of infant and infant-parent relationship during feeding and free play, a clinical child psychiatric assessment of the infant according to a standardized checklist based on "Infant and Toddler Mental Status Exam" (82;83), interview with the parents and information about the infants relations to others (paediatric nurses, surgeon, special pedagogue and child psychiatrist). The feeding and free play situation was videotaped.

In the present study the reliability of DC 0-3 axis I – II as well as PIR-GAS was measured as categorical agreement between an experienced child psychiatrist and an experienced child psychologist on ten randomized patients based on written reports from observations, all data and taped observations.

The Child Behavior Checklist (CBCL) and related instruments (ASEBA) (84-88) are the most well researched and frequently used standardized questionnaires measuring psychological aspects of paediatric surgery and allows comparisons with other population norms and between groups of children and adolescents with different health problems (11). The adolescents completed the Youth Self-Report (YSR) (89), and the mothers the CBCL for ages 4-18 (CBCL/4-18) (75). In the analyses we used scales of competences, problems and trauma related dissociative symptoms. The reliability and validity of the questionnaires have been demonstrated in clinical and non-clinical populations and across cultures (84-86;88;90) . Multi-cultural studies support the taxonomic generalisability of the CBCL/YSR-syndromes across diverse societies, including Norway (85; 86).

Psychopathology in adolescents was assessed by a semistructured diagnostic interview; Schedule of Affective Disorders and Schizophrenia for School-Age Children (K-SADS) providing DSM-IV Axis I psychiatric diagnosis (91) (OA group) and the Child Assessment Schedule (CAS) providing DSM-III-R diagnosis (92; 93) (control group). The reliability and validity of the instruments are well established (91; 94; 95). A semistructured interview based on Parental Account of Children's Symptoms (PACS) (96) with one parent was performed to obtain information on the adolescents' behaviour and emotional problems as seen by their parents (both groups). The diagnostic interviews were supplemented with questions covering the adolescents' views of the present situation regarding their oesophageal malformation (OA group).

3.4.2 Mother-infant interaction

The quality of the mother-infant interactions was assessed using the Parent Child Early Relational Assessment (PCERA) (97). The PCERA was chosen because it is a reliable and valid standardized way of evaluating the parent-

child relationship (98-104). The parent and infant are observed and videotaped in four 5-minute segments: 1) feeding, 2) structured task, 3) free play, and 4) separation-reunion. Due to practical and economic reasons, we did observation only in the feeding and the free play situation. The instrument and manual is not translated into Nordic language and the original version of the instrument and manual from 1985 (97) was used.

Two independent observers, both senior psychologists trained to use the instrument by an authorised Swedish PCERA trainer in the use of the PCERA, coded each videotape. None of the observers had participated in data collection, and they were blind to the seriousness of the medical condition of the infants.

3.4.3 Psychosocial functioning

The overall psychosocial functioning assessment of the adolescents was based on information from both adolescent and parent interviews and graded in accordance with the Children's Global Assessment Scale (CGAS) (105). Inter-rater reliability, discriminant validity and clinical usefulness of the CGAS are well documented (106; 107). A second child psychiatrist scored blind CGAS on 10 randomly selected cases based on videotaped adolescent interviews.

3.4.4 Clinical data

Infants

Medical data were recorded from the medical reports. Feeding difficulties requiring medical procedures or surgical interventions like dilatation of oesophagus, anti-reflux surgery and gastrostomy were defined as severe feeding problems. In addition, review of the medical records and interviews

with the mothers also incorporated variables associated with severity of any traumatic experiences as described elsewhere in the literature (108; 109). This included experiences of parent-child separations, number of hospitalizations, the type of traumatic medical treatment experiences, frequency and duration, relationship to the executants, and use of force. If traumatic events were reported, any trauma symptoms, such as e.g. sleeping problems, new fears and avoidance behaviour, were registered.

Adolescents

Somatic data were recorded retrospectively from the medical reports. Medical history and health problems the previous 12 months with emphasis on gastrointestinal and respiratory symptoms were obtained from the adolescents and the parents. Height (cm) and weight (kg) were recorded. A standard clinical examination was performed by a surgeon.

3.4.5 Infant development

The Bayley Scale of Infant Development (BSID-II) (110) is the most widely used measure of the development of infants and toddlers in both clinical and research settings (111). The BSID-II is applicable to children from 1 through 42 months of age. It yields a Mental Development Index (MDI) and a Psychomotor Development Index (PDI). The raw scores were converted to standard scores (mean=100, SD= 15) according to the US norms. The classification of the developmental index scores used was "accelerated performance" when scores 115 and above, "within normal limits" when scores 85-114, "mildly delayed performance" when scores 70-84, and "significantly delayed performance" when scores 69 and below (110).

3.4.6 Infant temperament

The Infant Behaviour Questionnaire (IBQ) (112) is a parental report of temperament with well established psychometric properties (111; 113; 114). The instrument is based on the definition of temperament proposed by Rothbart & Derryberry (115). According to their definition, temperament is a relatively stable, primarily biologically based individual difference in reactivity and self-regulation (115). The IBQ assesses temperamental variables by aggregating responses across a wide range of situations (116). In the present study we used the Norwegian version (unpublished translation by Anne Mari Torgersen, 1985).

3.4.7 Self-esteem

Self-esteem was assessed by the Self-Perception Profile for Adolescents (SPPA) (117). The SPPA has shown good reliability, and convergent, discriminant and factorial validity. (118). The SPPA has previously been used in similar populations (119).

3.4.8 Subjective well-being

The adolescents' experience of well-being was assessed by asking patients to indicate how well they felt on a 100-mm visual analogue scale (VAS) anchored by two extremes: "my life is extremely unpleasant" (0) and "my life feels very good" (100). VAS provides a simple technique for measuring subjective experience. It has been established as valid and reliable in a range of clinical and research applications (120).

3.4.9 Mothers' mental health

The General Health Questionnaire (GHQ) (121) is a widely used instrument to assess psychological distress. The original questionnaire consisted of 60 items, from which shorter versions of 30, 28, 20 and 12 best items were identified. We chose GHQ-30 (121) because it has a subscale for wellbeing (low self-esteem/feelings of incompetence) (122; 123). Validity and reliability of the instrument is well established (121; 124), and it has been used in similar populations (125).

Maternal anxiety was assessed by Spielberger State Trait Anxiety Inventory (STAI X-1 and 2) (126). A 12-item version was used to assess state anxiety (STAI X-1) (127). State anxiety refers to context dependent emotional reactions characterized by subjective, conscious feelings of tension, apprehension, nervousness and worry; trait anxiety refers to individual differences in anxiety proneness - that is, in the tendency to see the world as dangerous or threatening, and in the frequency that anxiety states are experienced (128). STAI X-1 and 2 are valid and reliable instruments and widely used self evaluation questionnaires which have been used in several studies in similar populations (129;130).

3.4.10 Family strain

A clinical global assessment of Chronic Family Difficulties (CFD) (131; 132) was based on all parental information available from an interview about the previous and present family situation, strain or difficulties such as economy, housing, employment, network support, practical care for the children, possible marital and family discord, and the physical and mental health of all family members.

3.5 Statistics

The study has a cross-sectional design which is efficient to identify associations between outcome and possible risk factors, but this require caution about deciding cause and effect and interference of risk for development of disease (133). Due to economic and practical reasons the samples in this study are small. However, all eligible OA patients in the respective age groups treated at Rikshospitalet University Hospital were included and the percentage of responses was satisfactory in all groups (93 %, 98 %, and 96 % in paper II, III and IV respectively).

To calculate the sample size needed to estimate the proportion of mental health disorder in the OA population (power-study), we used the confidence interval (CI) associated to the proportion. We assumed a proportion of mental health disorders in the general OA child population equal to 30 %. Next, we decided to base our sample size such that the width of the associated 90 % confidence interval was 2*15 % or less; (30% ± 15%). This gave us a sample size equal to 26. This estimate means that with a sample size of N=26, a true proportion of 30 % psychopathology would be accompanied a 90 % confidence interval ranging from 15% to 45%.

The relevant precautions, possible problems related to sample size and design, and the rationale underlying the statistical analyses are presented in the papers and in section 5.2.

3.6 Ethical aspects of the study

The study was approved by the Regional Ethics Committee for Medical Research and the Norwegian social science data services. Informed written

consent was obtained from the parents and the adolescents. A likert's score 2-3 on GHQ-30 item 29 may indicate severe depression and suicidal ideation needing immediate medical attention. According to the study protocol, parents reporting such scores were urgently contacted in order to clarify need for referral to acute psychiatric treatment. Non-responders were followed up once by a written reminder. When clinical problems were identified in patients or in mother-child interaction, referrals for further treatment were discussed with adolescents and parents.

4. Results

4.1 Summary of paper I

ASSESSMENT OF EARLY MOTHER-CHILD RELATION IN INFANTS WITH OESOPHAGEAL ATRESIA

Fifteen one year old infants with OA and their parents were used to demonstrate how the Parent-Child Early Relational Assessment (PCERA) can be used to explore the mother-child interaction in a clinical sample of children. The infants and their mothers were videotaped for five minutes episodes during feeding and free play, and the quality of the mother-infant interactions was assessed by PCERA.

The results showed areas of strength regarding most of the maternal, infant and dyadic components. There was concern about maternal positive physical contact, maternal quality of verbalizations to or about the child, maternal social initiative, infant's communicative competence and infant's visual contact with mother. This concern of social proximity between infants and their mothers was most prominent in the feeding situation.

The study indicates that OA in infants may constitute stressors impinging on the parent-infant relationship. PCERA was found to be an adequate assessment tool with acceptable reliability to evaluate the mother-infant interaction.

4.2 Summary of paper II

DOES OESOPHAGEAL ATRESIA INFLUENCE MOTHER-INFANT INTERACTION?

The study enrolled 37 one-year-old infants with OA born in 1999 to 2002 and their mothers. A comparison group comprised 10 infants with urological problems without feeding difficulties and their mothers. Parent Child Early Relational Assessment (PCERA) was used to assess mother-child interaction in feeding and play situation. General Health Questionnaire and State Trait Anxiety Inventory were used to assess maternal psychological distress and anxiety.

Many aspects of mother-OA infant interaction showed strength. However, mothers of OA children were compared to control-mothers significantly influenced in their ability to interact and the OA-mothers' "positive affective involvement, sensitivity and responsiveness" during feeding was in range of concern. Small, but significant effect of the mother's feeling of incompetence on their interaction was found.

Conclusion: Mothers' attitude during feeding was negatively influenced in interaction between mother and OA infant. The results suggest possibility for improvement in mother infant interaction by enhancing mothers' welfare when caring for infants with EA in medical services.

4.3 Summary of paper III

MENTAL HEALTH IN INFANTS WITH OESOPHAGEAL ATRESIA

This study enrolled thirty nine infants with OA treated consecutively during 2000-2003 and their mothers. Infant mental health was assessed by Diagnostic Classification: 0-3. Medical and environmental data were collected from medical records and semi structured interview with the mothers. Child development was assessed with Bayley scales (BSID-II). Maternal psychological distress, anxiety, and child temperament were assessed by self report questionnaires (GHQ-30, STAI, and IBQ).

Thirty one percent of the infants with OA showed mental health disorders by one year of age. Prognostic factors predicting mental health were posttraumatic symptoms reported by mother, more than one operation, mechanical ventilation beyond one day and moderate/severe chronic family strain. Relational trauma, vulnerable attachment and impaired self-development are highlighted as possible pathways for psychopathology.

Conclusion: Children with OA are vulnerable to mental health disorders, and this study may help clinicians to identify children at risk.

4.4 Summary of paper IV

MENTAL HEALTH AND PSYCHOSOCIAL FUNCTIONING IN ADOLESCENTS WITH OESOPHAGEAL ATRESIA.

The study group enrolled 21 adolescents with OA and one or both parents. A comparison group comprised 36 adolescents from the general population. Questionnaires (Child Behavior Checklist; CBCL and Youth Self Report; YSR), and interview (Schedule for Affective Disorders and Schizophrenia for School-Age Children; K- SADS) were used to assess OA adolescents' mental health. Parental Account of Children's Symptoms interview (PACS) yielded supplemental parental information. Psychosocial functioning was assessed by Children's Global Assessment Scale (CGAS). Harter Self Perception Profile questionnaire (SPPA) was used to assess self-esteem, and Visual Analog Scale (VAS) to evaluate well-being. Maternal psychological distress was assessed by General Health Questionnaire (GHQ-30). Chronic family strain was assessed by Chronic Family Difficulties (CFD). Physical health was assessed by growth and clinical symptoms.

Mental health and psychosocial functioning did not differ from the comparison group. 7/21 OA adolescents had special education. Dilatations of oesophagus, birth weight, well-being, and maternal psychological distress were prognostic factors predicting mental health. Height SDS, birth weight, well-being, dissociative symptoms and family strain were prognostic factors predicting psychosocial functioning.

Conclusion: OA adolescents adjusted well and mental health and psychosocial functioning did not differ from controls. Some complications to OA (dilatations and declined height) may have negative influence on mental health and psychosocial functioning.

5. Discussion

The major findings in the present study were that about 1/3 of the OA infants showed mental health disturbances; mainly trauma related (paper III). Prognostic factors predicting infant mental health were posttraumatic symptoms reported by mother, more than one operation, mechanical ventilation beyond one day and moderate/severe chronic family strain. Furthermore, the mother-child interaction showed overall strength, however, the OA mothers' attitude in the mother-infant interaction were impaired (paper II). Significant effect of the mother's feeling of incompetence on their interaction was found. Finally, the OA adolescents adjusted well and their mental health and psychosocial functioning was comparable with adolescents in the general population (paper IV). Dilatations of oesophagus, birth weight, well-being, and maternal psychological distress were prognostic factors predicting OA adolescents' mental health. Height SDS, birth weight, well-being, dissociative symptoms and family strain were prognostic factors predicting their psychosocial functioning.

The main focus in the present discussion will cover some links between major findings, with special reference to the latest literature, and a discussion of methodological limitations and clinical implications and implications for further research.

5.1 Discussion of major findings

5.1.1 Mental health, mother-infant interaction and psychosocial functioning

Mental health disorders were identified in about one third (31 %) of the OA infants by one year of age (paper III). This is the first study where emotional and psychosocial behaviours in a group of chronically ill infants' have been systematically categorized according to a mental health diagnostic classification system. Nevertheless, the result is consistent with previous reports on the impact of hospitalization, surgery and other interventional procedures during infancy on children's short and long- term mental health and psychosocial functioning (8; 11; 17; 54; 55; 64; 134-139).

Most of the primary mental disorders (60 %; DC: 0-3 axis I) were related to long-term effects of traumatic experiences connected to clinical symptoms or to treatment procedures. Severe trauma against mouth and throat and choking with feeding were examples of trauma reported by the mothers, and phenomena like distress to reminders of the trauma, dissociation, restricted range of affect, and food refusal were examples of symptoms observed at follow up.

The study indicates that OA in infants may constitute stressors impinging on the mother-infant relationship. Interestingly, it was the maternal interactive behaviour during feeding that was affected (paper II). In contrast, by one year of age Ludman et al (140) did not reveal any adverse effects of neonatal surgery or hospitalization on the relationship between the mother and child.

Goldberg and colleagues reported impaired infant-mother attachment in infants with congenital heart disease and suggested disease specific impact on the mother-infant relationship (141). The results in our study (paper II) may reflect the specific challenges the nature of OA brings into the mother's part of the mother-infant interaction. Surprisingly, this finding were not related to analyzed characteristics of the mother, severity of child's feeding difficulties,

or any other analyzed characteristics of the child's illness or treatment procedures.

The identification of strain in the mother-infant interaction (paper II and III) combined with the discovery that several OA infants' exposed to traumatic experiences (paper III) may suggest interaction between several relational factors comprising the development of mental health disorder in infants with OA making their attachment vulnerable (43; 57; 59).

Based on the assessments of the infants in the study (paper III), we hypothesize that relational trauma, vulnerable attachment and impaired self development may represent possible pathways for psychopathology for OA children. Relational factors implicit in non-optimal caregiving, represented by more than one operation, mechanical ventilation beyond one day, moderate/severe chronic family strain and posttraumatic symptoms (paper III), may impinge the child's working model of self and parent, and thus make their attachment vulnerable.

However, how may we understand that the OA adolescents in the study adjusted so well (paper IV) considering psychopathology observed in about one third of the OA infants (paper III)? First, this is not a longitudinal study and infants and adolescents comprise different individuals. Next, the trajectory of development of a person is not determined during infancy, although development always builds on what was previously present (142). There is an ongoing transactional process between the individual, and genetics and environment, which forms the trajectory from infancy to adolescence. In this transactional process, the quality of the child-caregiver relationship is crucial. The results from the study showed overall strength in the mother-OA infant interaction (paper I-II). Thus, despite a possibility for vulnerable attachment in early childhood, the trajectory may develop well if they are not exposed to new trauma or chronic strain.

Compared with studies of adolescents with other chronic diseases the results

of the present study (paper IV) are in accordance with studies of mental health and psychosocial functioning in adolescents with Hirschprung's disease (76), and juvenile chronic arthritis (143), but contradictory to studies of adolescents with anorectal anomalies (16), bladder exstrophy and epispadia (144), and congenital heart disease (145). We may speculate that specific challenges related to the different diseases in various ages, may contribute to the diverse outcomes. For example, the most challenging period for the children with OA and their parents was during infancy and early childhood, while the majority of parents of the OA adolescents had no concerns about the future of their child (paper IV). The majority of the OA adolescents experienced minor symptoms from airways and upper gastrointestinal tract and they had developed strategies to improve swallowing (paper IV). This is different from the findings of a study with adolescents with anorectal anomalies, where the majority experienced persistent fecal dysfunction involving problems with constipation and soiling (16). Effective management of the illness may enhance self-esteem through coping well and the result will be optimal adaptation (146). It seems that this is the case for OA adolescents.

Furthermore, children with a chronic illness or paediatric patients experiencing medical treatment related trauma, may do well developmentally if the child-raring environment is supportive and the functioning of significant others is satisfactory (147; 148). On group level, the mothers of OA infants (paper III) and OA adolescents (paper IV) in the present study were functioning well psychologically and the mother-OA infant interaction showed overall strength (paper I-II). These results may reflect that well functioning mothers and good mother-infant relationship among children with OA may provide a context promoting the development of psychosocial competence despite the challenges mother and child experience.

Possible developmental pathways to mental disorders will be more thoroughly explored in section 5.1.3.

5.1.2 Predictors

Operations and mechanical prolonged ventilation were predictors for mental health disorder in infants with OA (paper III), whereas oesophageal dilatations predicted more emotional and behavioural problems in the OA adolescents (paper IV). These results may reflect that it is the degree of life threat and acuity of illness rather than the chronic characteristics of the illness that is essential in mental health outcome in medically ill children (149).

None of the OA adolescents had symptoms qualifying PTSD (paper IV). However, trauma related symptoms predicted psychological/ psychosocial outcome in both OA infants (paper III) and OA adolescents (paper IV). These results may add further support to research on the impact of traumatic events on mental health in medically ill patients (149).

Height was a predictor for psychosocial functioning in OA adolescents (paper IV). Short stature commonly is perceived to be associated with social and psychologic disadvantage (9). Based on the results in the present study (paper II) we may speculate that the mothers' feelings of competence and the mothers' attitude in the mother-child interaction during feeding could be a potent mediator for growth. Understanding this more thoroughly is likely to be important in facilitating the target of therapeutic interventions. Prospective studies are needed to explore this further.

Chronic family stress had negative impact on OA infants' mental health (paper III) as well as on OA adolescents' psychosocial functioning (paper IV). These results may reflect that family stress is a powerful factor related to the adaptation of children with serious paediatric illnesses. The fact that family support is a potential protector throughout childhood and adolescence highlight the importance of early identification of strain in families with a child with OA.

5.1.3 Possible developmental pathways to mental disorders

The context of our understanding of early development of child mental health implies theories of attachment and self development, as well as cerebral development and neurobiology. Based on the results of this study we may suggest some possible pathways of the developmental trajectory in children with OA.

OA infants needing prolonged mechanical ventilation and repeated surgical interventions experienced a less optimal caring situation than the other OA infants since they had to be nurtured by health care professionals for extended periods. According to clinical experience, we hypothesize that the mothers of these children are traumatized by experiencing prolonged period of life-threatening illness in the child, compromising the care they should like to provide for their child. Traumatized mothers are emotionally and functionally unavailable for their children (51; 150; 151). When infants are ill and symptomatic they are especially dependent upon their caregivers' responsiveness (150). Thus the infants in this study showing posttraumatic symptoms are supposed to be more vulnerable to insensitivity in the caregiver than those without such symptoms. Based on the results in this study (paper III) we hypothesize an interaction between several relational factors comprising the development of mental health disorders in infants with OA.

According to attachment theory (57; 59), the primary function of early object relationship is to provide the infant with a sense of security in environments that include pain, stress and fear. The child seeks to get closer to the primary caregiver on the assumption that she or he will be able to reduce discomfort (43); working models begin to be formed in the middle of the first year of life. Relational factors implicit in non-optimal caregiving; more than one operation, mechanical ventilation beyond one day, moderate/severe chronic family strain and posttraumatic stress symptoms (paper III), may impinge the child's working model of the self and parent, and thus make their attachment vulnerable. This vulnerable attachment may represent a possible mechanism

for the posttraumatic disorders as well as other psychopathology exhibited by the OA infants.

A child's understanding of a traumatic experience is influenced by its degree of dependence of the parent. The complicated role the parent plays when allowing and not protecting them from stressful or painful events hinge on the child's cognitive level (151). At the developmental level 0-18 moths an infant may not be able to differentiate who the protector versus perpetrator is or if he/she is truly helping the child or deliberately causing harm and pain (17; 51; 62).

Emerging data suggest that children often experience medical treatment (e.g. invasive, frightening, and/or painful treatment procedures) as traumatic (152). Such kind of trauma may be viewed as "inflicted" by caregivers or medical professionals rather than perceived as a disease entity that is not under human control (149). Neurobiological mechanism that influence psychological responses to extreme stress such as altered functioning and reactivity of noradrenergic neurons may be particularly involved in hyperarousal and re-experiencing symptoms of Post Traumatic Stress Disorder (DSM-IV) (148). We may hypothesize that similar mechanisms may be involved in Traumatic Stress Disorder-symptoms (DC: 0-3) (78).

The children's adaptation or negative outcome associated with serious paediatric illnesses depends in large on the product of relevant risk and protective factors that shape the children's' experiences and ultimately impact the expression of their genes (3). Traumatic experiences related to symptoms and treatment of OA may create enduring alterations in the neurotransmitter and endocrine systems that mediate stress response (21; 22) and may be a pathway of impaired psychosocial functioning in adolescents with OA. However, despite their vulnerability during the first year of life symptomatic infants with OA may develop well if sufficient protective factors are present;

good maternal psychological health, low family strain, good functioning mother-child relationship.

The findings in this study highlight the importance of knowledge of child development when treating medically ill infants and young children. The results may indicate support to theories and previous reports that highlight relational trauma, vulnerable attachment and impaired self development as possible pathways to mental health disorders following hospitalization of infants and young children (43; 62; 153; 154).

5.2 Discussion of design and methods

Some additional comments to aspects of design and methods described earlier and in the papers are added below.

5.2.1 Small samples and sample representativity

The focus in the study sampling was more on similar age than a large number of participants. Thus the sample sizes are inevitable small. However, statistical analyses of differences between the cases and controls can be performed using Fisher's exact test (155). When we calculated sample sizes, we chose a 90% CI. Using the same calculation method in our sample of 39 infants with OA with 31 % psychopathology, the true proportion of psychopathology will with 90 % certainty lie within the range of 19 % to 43 %.

We have no reason to doubt that the selection of subjects in the OA and comparison groups in the study are random, and missing values are few and random.

5.2.2 Validity and reliability

The validity and reliability of the assessment instruments used in the study are documented by others and references are reported in section 3 and in the papers. The sample sizes in this study are too small to do psychometric analyses of the instruments. However, inter-rater agreement between two raters' scorings of the PCERA, DC: 0-3, K-SADS (percentage categorical agreement/Kappa) was moderate to good. The internal consistence (Cronbach's alpha) of PCERA scales and the intraclass correlation for PCERA scales and CGAS were acceptable for the actual population. In paper I, all PCERA items were rated by two raters, and their mean score on single items were used in the analyses, which make the result more robust.

When this study was planned, the diagnostic classification criteria of DSM III-R were revised and DSM IV was published. K-SADS was the new diagnostic interview providing DSM-IV diagnosis replacing CAS which provided DSM-III-R diagnosis. K-SADS has some positive qualities compared with CAS, e.g. criteria for PTSD. However, it may be speculated if the instrument is sensitive enough to differentiate mild psychiatric disturbances.

The DC: 0-3 system is a diagnostic classification system in its early development and the criteria for different types of disorders are not yet precise enough (discriminative validity is not yet established) and the manual does not specify standard ways of assessing the parent-infant relationship. Cut off points for diagnoses are not well established and sensitivity and specificity problems of the diagnostic system may be a bias. More studies of links between symptoms, diagnostic categories, and interactive patterns are needed. The present study shows that advanced knowledge about psychopathology in infancy is very important.

5.3 Clinical implications

Children with OA are vulnerable to mental health disorders, and this study may help clinicians to identify children at risk (paper III). Some complications to OA (oesophageal stricture dilatations, declined stature) may have negative influence on long term mental health and psychosocial functioning (paper IV).

The results suggest possibility for improvement in mother infant interaction by enhancing mothers' welfare when caring for infants with OA in medical services (paper II). Increased consciousness about early intervention methods is required in health care services for medically ill infants. On the basis of the results in this study, waiting for the results of future research with larger OA and control samples, we will consider extra attention to mother's feelings of competence. Teaching programs should include techniques of assessments of infants, of parents, and of interactions (156). Increased knowledge of early intervention methods, such as PCERA video replay (97; 157), and Marte Meo (158; 159), may create a basis for individual treatment plans and follow-up consultations.

PCERA was found to be an adequate assessment tool with acceptable reliability to evaluate the mother-infant interaction. Translation of the PCERA manual into the Nordic languages is requested (paper I).

5.4 Future research

There is a need for multicentre studies for replication of the results in this study with large OA sample and controls. There is need for prospective studies. The infant sample in this study makes it possible to conduct a prospective follow-up study. Furthermore, there is a need for research on the psychometric properties of the instruments assessing infant mental health and parent-child interaction.

There is a need for future research of specific treatment approaches for traumatic stress in medically ill patients.

6. Summary in Norwegian

Kronisk sykdom i spedbarnsperioden kan påvirke foreldre-barn samspillet og den mentale helsen til barnet. I denne undersøkelsen ønsket vi å undersøke kvaliteten på mor-barn samspillet, psykisk helse og psykososial fungering hos pasienter med øsofagus atresi.

Vi undersøkte 39 spedbarn med øsofagus atresi ved ett års alder og deres mødre, og 21 ungdommer med øsofagus atresi og deres mødre. Vi brukte kontroll grupper som hadde tilsvarende alders- og kjønns fordeling.

Vi samlet medisinske data fra journalene. Mor-barn samspill ble målt ved hjelp av en videobasert observasjonsmetode (Parent Child Early Relational Assessment) (PCERA) skåret av to uavhengige observatører. Barnet ble undersøkt av barnepsykiater og psykisk helse ble klassifisert etter Diagnostic Classification 0-3 (DC: 0-3). Ungdommenes mentale helse og psykososial fungering ble målt ved hjelp av intervju (K-SADS) og spørreskjemaer (YSR/CBCL) og et globalt mål på psykososial fungering (CGAS). Ungdommenes selvfølelse ble målt ved hjelp av spørreskjema (SPPA). Mødrenes psykiske stress og velvære ble målt ved hjelp av spørreskjemaer (GHQ-30, STAI).

Resultatene viste at mødrenes bidrag i mor-barn-samspillet var negativt påvirket i spisesituasjonen i forhold til kontrollgruppen. Vi fant psykiske forstyrrelser hos 1/3 av spedbarna, hovedsakelig relatert til opplevd traume i forbindelse med symptomer og behandling av sykdommen. Flere operasjoner og utvidet behandling på respirator var prognostiske faktorer som predikerte psykiske forstyrrelser, i tillegg til kronisk stress i familien.

Ungdommene med øsofagus atresi hadde tilpasset seg sykdommen godt og skilte seg ikke ut fra kontrollene i forhold til psykisk helse og psykososial

fungering. Langtids komplikasjoner av sykdommen (blokkinger av spiserøret og lav høyde) var prognostiske faktorer som predikerte psykisk helse og psykososial fungering, ved siden av kronisk familie stress.

Konklusjon: Mødrene til spedbarn med øsofagus atresi var negativt påvirket i samspillet i spisesituasjonen. En tredjedel av spedbarna hadde psykiske forstyrrelser. Blant ungdommene viste det seg at ungdommer med øsofagus atresi ikke skilte seg ut fra kontrollene i forhold til psykisk helse eller psykososial fungering.

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PAPERS I-IV

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IV