Literature Review of Long –Term Health Implications of Congenital Rubella Syndrome

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1.0 Congenital Rubella Syndrome

Rubella infection was first recorded in the mid Eighteenth Century by Henry Veale although at the time the condition was referred to by its German name of ‘Rotheln’ (Veale, 1866; Miller, 1991). Whilst rarely a serious infection in children and adults, it is now well known to have potentially devastating consequences on the developing embryo if contracted by pregnant women in the early stages of pregnancy.

Gregg (1941) an Australian Ophthalmologist, first identified the evidence of pregnant mothers with rubella transmitting congenital defects to their new born infants. Initially high incidences of cataracts were noted where mothers had contracted rubella during the first trimester of pregnancy (Forrest et al, 2002). Gregg’s early observations included the fact that low birth weight was also a common feature of affected infants (Gregg, 1941).

After Gregg, others began to observe additional defects seen as resulting from in-vitro rubella infection. South and Sever (1985) used the term ‘Congenital Rubella Syndrome’ to denote a combination of cardiac, ocular and hearing defects. Others, for example Swan et al (1946), suggested that additional defects such as deafness, low birth weight and failure to thrive, and signs of meningitis with central nervous system damage, should be added to the list of effects caused by the rubella virus (Swan et al 1946).

Duszak (2009) discusses an unusual pigmentary retinopathy, termed salt and pepper retinopathy, that was
first identified by Gregg (1941) and also reports failure to thrive as being associated with exposure. More recent descriptions of Congenital Rubella Syndrome (CRS) also list congenital anomalies such as microphthalmia, transient corneal clouding, Patent Ductus Arteriosus (PDA), mental retardation, low birth weight and feeding difficulties (Armstrong and O’Donnell 2004).

Whilst foetal infection can occur at any stage of pregnancy, Duszak (2009) describes the rubella virus as infecting and replicating in the placenta and he argues that the outcome of foetal infection is dependent on the gestational timing of the maternal rubella as the risk of foetal infection varies according to the time of onset of maternal infection. Miller (1991) reports that infection rates of infants are highest during the 1st trimester (81% overall with 100% infection rate in weeks 1 – 10) declining to a minimum of 25% at the end of the 2nd trimester, and rising back to 100% in the last month. However it is important to note that even though a mother might become infected with the rubella virus this does not automatically assume defects in the infant will occur (Frij, South & Saver 1988). The widely accepted relationship between gestational age at the time of rubella in pregnancy and clinical manifestations of CRS is shown below.

<table>
<thead>
<tr>
<th>Manifestations of CRS</th>
<th>Gestational age (weeks) at maternal infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye defects</td>
<td></td>
</tr>
<tr>
<td>Cataract</td>
<td>3-12</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>2-18</td>
</tr>
<tr>
<td>Heart defects</td>
<td>3-13</td>
</tr>
<tr>
<td>Neurological deficit</td>
<td>3-16</td>
</tr>
<tr>
<td>Deafness</td>
<td>2-18</td>
</tr>
<tr>
<td>Multiple defects</td>
<td>3-12</td>
</tr>
<tr>
<td>Minor defects</td>
<td>7-&gt;20</td>
</tr>
</tbody>
</table>
Certain neurological deficits are also widely associated with CRS. These include difficulty in shifting task, sudden shifts in mood, over reaction to minor stimuli, repetition or prolongation of a particular act (O’Donnell, 1995, Vernon 1967, O'Dea and Mayhall 1988, Munroe, 1999, Desmond et al 1978, Nicholas 2000). These types of behavioural disturbance observed in individuals with CRS are considered to be associated with frontal lobe brain damage (Gardner, 1994). Nicholas (2000) found abnormalities in cerebral blood cells, as well as retardation in the myelinisation process within the brain (Rorke & Spiro (1967) in Armstrong & O’Donnell 2004).

Autistic-like behaviour is often reported in children with CRS (Chess 1977) but according to Van Dijk (1991) there is no biologically conditioned link between rubella and autism. The ritualistic behaviours demonstrated by children with CRS are not manifestations of autism he argues, but rather a consequence of sensory deprivation (Van Dijk, 1982).

The World Health Organisation (2003) divides cases of CRS into 4 categories:

1. Suspected CRS
   a) When an infant has heart disease and deafness, and on or more of the following eye signs:
      Cataract; diminished vision; Nystagmus, squint, Microphthamos, Congenital Glaucoma;
   b) When an infant’s mother has a history of suspected or confirmed rubella during pregnancy, even if the infant shows no signs of CRS.
2. Clinically Confirmed CRS
Where a qualified physician detects two or more of the complications in section A or one from section A and one from section B below:

A: Cataracts, Congenital Glaucoma, Congenital Heart Disease, Hearing Impairment, Pigmentary Retinopathy

B: Purpura (rash), Splenomegaly, Mental retardation, Meningoencephalitis, radiolucent bone disease, jaundice with onset within 24hrs after birth.

3. Laboratory Confirmed CRS
An infant with rubella IgM antibody is considered to have clinically confirmed CRS.

4. Congenital Rubella Infection
An infant with rubella IgG antibody who does not have clinically confirmed CRS (World Health Organisation 2003, in Best 2007)

2.0 Epidemiology of CRS
The rubella virus itself was identified in 1962, by two groups of independent investigators, one in Boston, Massachusetts, and the other in Washington, DC. (Armstrong & O'Donnell, 2004, Banatvala & Brown, 2004). Since the discovery of the rubella virus epidemics have occurred at six to nine year intervals and major pandemics have occurred every ten to thirty years. The last major worldwide pandemic occurred in 1963-64, in the United States, Canada and Europe, with significant impact on the UK.

It is estimated that 30,000 babies were born in the USA with rubella damage in the 1964 epidemic (Cooper, 1985). The actual total number of affected infants born in the U.K. is unknown but before the rubella vaccine was introduced for schoolgirls in 1970, about 200-300 babies were born with congenital rubella defects annually in England and Wales, with many more in the epidemic years (Tookey, 1999).

Although the frequency of CRS reduced in the developed world after the introduction of immunization, the current study does not focus on immunization issues. Even though the incidence has reduced, individuals who were exposed to the virus before immunisation are facing ongoing health compromise. It is also important to note that as a result of the lack of total vaccination across the globe, the rubella virus is still in circulation and the World Health Organization records that there are still more than 100,000 confirmed cases each year (Banatvala & Brown, 2004). Rubella epidemics are still prevalent in the developing world and Duszak (2009) estimates that 238,000 children worldwide are born with CRS worldwide, mostly in developing countries.

Some small localised epidemics are also evidenced within specific communities. In America during the 1990’s, mini-outbreaks of rubella were documented in California, in the Amish Community, and at a meat packing plant in Iowa. These cases have occurred in populations that have not routinely received rubella vaccines (Armstrong & O'Donnell, 2004).
3.0 Pathogenesis

In the 1940’s Gregg’s work was considered revolutionary as at that time the placenta was considered an absolute barrier to infectious agents. Gregg’s observations were the first record of the teratogenic effect of a viral infection. The significance of rubella derives from its teratogenic origins. Rubella is a togavirus of the genus Rubivirus (Duszak 2009). The mechanisms by which the rubella virus causes fetal damage are not however fully understood (South & Sever, 1985; Frij, South & Sever, 1988; Cherry (ed) 1981; Reye 1974) but it is thought that the virus embeds itself in internal organs and is therefore able to colonise areas of the body for much longer than a virus that is easily shed.

Before the development of the maternal immune response, the virus spreads through the mother’s bloodstream and may affect multiple tissues, including the placenta. As a result of placental damage, the virus can then cross the placenta to the foetus. Once the placenta has been infected, the foetus undergoes cellular deficiencies that cause disturbances of organogenesis during the critical first 12 weeks of development. During the 2nd trimester onwards infection in the placenta is thought to carry a lower risk of fetal damage.

Duszak (2009) goes on to describe the manifestations of Congenital Rubella Syndrome that result from tissue destruction and scarring. This may occur from viral persistence as developing immune system mechanisms such as autoimmunity may not be sufficient to cope with rubella, resulting in defective cytotoxic cell function.
Armstrong and O'Donnell (2004) likewise offer a description of how the virus results in such ongoing damage. Firstly, the virus reduces cell division in the developing embryo or foetus, resulting in incomplete, delayed, or defective growth in major organs. An attack during the critical first trimester of development can therefore affect virtually every developing organ. Secondly, blood vessels that routinely carry oxygen are frequently obliterated causing vast hypoxic damage. Chromosomal injury and ongoing cellular destruction are also common phenomena. Rubella-specific immune complexes caused by the rubella virus may manifest as one of several immune-mediated conditions, including seizures, thyroid dysfunction, glaucoma and Type 2 diabetes mellitus. These conditions are commonly known as the ‘Late Manifestations of Congenital Rubella Syndrome’ (Armstrong & O'Donnell, 2004).

Banatvala and Brown (2004) similarly describe foetal damage as being multifactorial - a combination of virus-induced cellular damage and the effect of the virus on dividing cells.

In the UK, Best (2009) studied a cohort of 307 infants born to mothers between 1976 and 1989. Congenital defects occurred in 85% of cases infected during the first weeks of pregnancy, with multiple defects most likely to occur in those infected in the first 8 weeks. After 12 weeks gestation, the risk to the foetus declines rapidly, with only rare cases of deafness reported from exposure at 17-18 weeks gestation. Best’s findings are summarized in the following table.
Risk of congenital infection and congenital defects after maternal rubella at successive stages of pregnancy

<table>
<thead>
<tr>
<th>Gestational Age (weeks)</th>
<th>Rate of Congenital Infection</th>
<th>No. with Congenital defects/No. not infected (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-12</td>
<td>13/16 (81%)</td>
<td>11/13 (85%)</td>
</tr>
<tr>
<td>13-16</td>
<td>29/54 (54%)</td>
<td>9/26 (35%)</td>
</tr>
<tr>
<td>17-22</td>
<td>33/92 (36%)</td>
<td></td>
</tr>
<tr>
<td>23-30</td>
<td>19/63 (30%)</td>
<td></td>
</tr>
<tr>
<td>31-36</td>
<td>15/25 (60%)</td>
<td></td>
</tr>
<tr>
<td>&gt;36</td>
<td>8/8 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

Spontaneous abortion may occur in up to 20% of cases where rubella occurs in the first 8 weeks of pregnancy (Best 2009).

Accurate clinical diagnosis of CRS is based on the detection of rubella-specific immunoglobulin IgM and IgG after maternal antibodies have declined. However rubella-specific IgM is generally lost in infants with CRS by six months of age. (Vijayalakshmi et al 2007). It is likely that some of the current sample may therefore be people who do not ‘fit’ the WHO classification of CRS or who at the time of their birth were not given a laboratory tested confirmation of CRS.

4.0 Late Manifestations of Congenital Rubella Syndrome.

The concept of 'late manifestations' of congenital rubella syndrome was first used by South & Seve (1985). It was intended to denote the appearance of additional defects not
present at birth, or damage that continued after birth with the
degeneration of faculties, or the emergence of fresh
difficulties at later stages of development. 'Late emerging
difficulties' or ‘delayed manifestations’ and other similar
terms are also used by researchers.

However some caution should be attached to these terms as
there is no clear definition as to what is meant by 'late'.
Some researchers report 'late' manifestations as defects
occurring in the months immediately following birth (Merth et
al (1987) in Munroe 1999) whilst others focus on difficulties
that emerge in adolescence and adulthood (Desmond et al
1985). It is also the case that some features of the normal
development of a child would not be expected to be clinically
observed or diagnosed in a newborn so delays in such
developments would not be evident in the first few months.

Best (2009) describes congenital rubella syndrome as a
progressive disease due to persistent virus infection and
defects in the infant's immune response. Existing
manifestations, such as deafness and CNS disease, may
progress and some abnormalities may not be detected until
the second year of life or even later. These include hearing
loss, visual loss, developmental delay, diabetes mellitus,
behavioural and educational difficulties and progressive pan
encephalitis (Best 2009).

Duszak (2009) concludes that 'congenital rubella should be
viewed as a chronic disease capable of producing ongoing
vital organ damage throughout life' (p39). He cites the 'late-
onset' manifestations as being insulin-dependent diabetes
(at 50 times the rate in the general population), thyroid
dysfunction and a rare neurodegenerative disorder,
pancephalitis. It is not clear however what age range is denoted by his use of the term ‘late-onset’.

Banatvala and Brown (2004) illustrate that the impact of rubella may be seen in terms of the timing of the emergence of related conditions. They report that ocular defects, such as cataracts, glaucoma and pigmentary retinopathy, auditory defects such as sensori-neural deafness, and cardiovascular defects such as persistent ductus arteriosus and pulmonary artery stenosis are all seen in early infancy whereas other difficulties related to the functioning of the central nervous system tend to emerge at a later stage.

The Sense study (2012) concerns itself with the experiences of people with congenital rubella syndrome within the U.K. Although Brown (1989) conducted an anecdotal study of the experiences of people with CRS, no subsequent work within the U.K. has been identified. The Sense study was therefore undertaken within the context of studies completed in other Western countries. There are significant differences in these studies, and these will be noted, however they provided the Sense study with a starting point.

Research from Australia, America and Canada will be reviewed. The American and Canadian studies are particularly important in that they provide examples of the survey design which was adapted for the Sense study. Other smaller scale studies looking at the incidence of particular manifestations are also noted.

In more recent years, other European countries such as Denmark and Norway have also undertaken research and each of these countries has attempted to look at the 'late
manifestation' issue. (The Netherlands is also known to have undertaken research but no publication of the outcomes has been identified to date.)

### 4.1 Overview of Australian, American and Canadian Projects before 2000

#### Research Comparisons

<table>
<thead>
<tr>
<th>Sample Group</th>
<th>Australian</th>
<th>American</th>
<th>Canadian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who responded?</td>
<td>Deaf (some additional disabilities)</td>
<td>Deafblind</td>
<td>Deafblind/ deaf/ blind</td>
</tr>
<tr>
<td>Who responded?</td>
<td>Affected individuals</td>
<td>Parent/ Guardian</td>
<td>Parent/ Guardian</td>
</tr>
<tr>
<td></td>
<td>2000*</td>
<td>Phase 1 = 1997-1998</td>
<td></td>
</tr>
<tr>
<td>Sample Size</td>
<td>Original Group = 50</td>
<td>Phase 1 = 39 interviews</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>2000 = 32</td>
<td>Phase 2 = 88 surveys</td>
<td></td>
</tr>
<tr>
<td>(some deaths)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ages of Sample</td>
<td>1991 = 50 yrs</td>
<td>16 + yrs</td>
<td>5-62 yrs</td>
</tr>
<tr>
<td></td>
<td>2000 = 60 yrs</td>
<td>(largest % 25-26)</td>
<td></td>
</tr>
<tr>
<td>Year of Birth/ Rubella Epidemic</td>
<td>1939 – 44</td>
<td>1960’s</td>
<td>75 % in 1960’s – 70’s epidemic</td>
</tr>
</tbody>
</table>
The three studies detailed above are clearly useful, but are not comparable in terms of sampling. It should also be noted that, particularly in the case of the American and Canadian research, responses were based on anecdotal evidence rather than medical evidence. However from other independent research (cited as comparisons below) some similarities and overlaps can be identified.

4.1.2 Australian Study

Gregg’s (1941) original observations of the connection between the rubella virus, pregnancy and consequent effect of fetus development emerged from a very early group of affected infants born between 1939-1944. His sample group was reviewed in 1967 and 1991 and of the original sample of 50 participants, 32 agreed to be involved again in 2000.
The following table provides a summary of the 2000 review.

<table>
<thead>
<tr>
<th>Age of Sample</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>32</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Visual Problems</th>
<th>Cataracts/ Glaucoma</th>
<th>12 people reported either Cataracts or Glaucoma occurring within the last 10 years.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Problems</td>
<td>Cardiac Problems</td>
<td>Includes: high cholesterol, heart disease, and a variety of valve-associated problems.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(68% of the sample had heart conditions compared with 29% of general population)</td>
</tr>
<tr>
<td>Endocrine System</td>
<td>Diabetes</td>
<td>1 new case since 1967 review</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total = 5 cases</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(22% of sample group compared with 13.1% of general population)</td>
</tr>
<tr>
<td></td>
<td>Thyroid Problems</td>
<td>Mentioned in report – no statistics.</td>
</tr>
<tr>
<td></td>
<td>Early Menopause</td>
<td>8 out of 11 women.</td>
</tr>
</tbody>
</table>
The Australian study was the first research that looked at CRS and its effects on people by identifying the early manifestations and following the same group to record what happened later. Research in other countries then followed.

### 4.1.3 American Study

The American research led by O'Donnell at the Helen Keller National Centre (HKNC) was a response to concerns voiced by parents/care givers about long-term changes seen in individuals with CRS.

The research was carried out in two phases: Phase 1: 1989 – 1990 (39 interviews by phone), Phase 2: 1990 – 1991 (large scale survey mailing – 88 people). This covered a much wider range of medical conditions than the initial Australian work. The results from the sample group are reported as is wider work achieved by others, which bears a relationship to the particular disorder in question.

**Helen Keller National Centre Study Results**

**Auditory Disorders**

92% of respondents had little or no hearing at time of survey and 1 person reported acquiring hearing loss at age 10.
Other related research

“Long term follow-up of these children indicates that almost all eventually show signs of some neurological damage, the most common being sensori-neural hearing loss, which approached 93% at seven to nine years of age” Waxham & Wolinsky 1994 (p.11)

“… the hearing defect may become progressively worse after the first year of life. There have also been cases in which children with CRS, for whom audiograms and speech patterns are normal suddenly develop mild-to–profound sensor neural hearing loss. The latest age … is ten years” Sever, South and Shaver 1985 (p.8)

Ocular Damage

66% of respondents reported cataracts and more than half of these were congenital. 13% of respondents reported cases of detached retina but the age at which this occurred varied widely and it is possible that some were caused by patient behaviour rather than CRS itself. There was a high incidence of glaucoma of 30% (compared to an incidence of 0.5% in the general population).

Other research

“Glaucoma with late onset was reported by Boger in 13 patients with CRS. The diagnosis was made when the patients were between 2 and 22 years of age…” (Sever, South and Shaver 1985)
Cardiac Problems

52% of the respondents indicated the presence of a heart condition (Including Patent Ductus, Atrial or Ventral Septal Defects, Pulmonary Stenosis)

Other Research

“van Dijk, citing Menser, Dodds and Harley (1967), states that of 50 high functioning persons born with CRS in 1940, twenty-five years later – three were found with systemic arterial hypertension” (Van Dijk, 1990)

Endocrine System Difficulties

Diabetes

5 out of 88 respondents were diabetic (6%) and although this percentage is lower than that recorded by other studies, it is 20 times higher than the incidence of diabetes in the general population of the U.S.

Other Research

“The most frequent delayed manifestation of CRS is diabetes mellitus. Studies reported by Menser et al of patients from the rubella epidemic in 1941 in Sydney, Australia showed that 9 (20%) of 45 patients had overt or latent diabetes by the time they were 35 years old. An additional nine had abnormal insulin response…. The high prevalence of diabetes in this small number of patients is remarkable, since diabetes develops in the general population in only 0.1% of
individuals younger than 30 years of age.” (Sever, South and Shaver, 1985, p.166)

‘Research from the Maryland School for the Deaf (1980) and previous findings from Australia indicated that diabetes mellitus is starting to appear among rubella deaf teenagers at an alarming rate of 15 – 40%’. (Vernon, Grieve, Shaver 1980)

“Hypothyroidism, hyperthyroidism, and thyroiditis have all been reported as delayed manifestations of CRS…. Thyroid dysfunction has been identified in 5% of patients with CRS in one study” (Sever, South and Shaver 1985, p167)

Degenerative Conditions

Detailed descriptions of changes occurring in individuals with CRS were given by some of the respondents:

“Over the past four years (our son) has gradually lost his ability to walk, In the past year, he cannot stand by himself no walk at all without totally leaning on another… (He) was always very hyper…. He is also very aggressive. He still butts his head quite often and pinches if he is near us. We were recently told that (he) is on a down-hill slide and will eventually lose all control, including muscles; swallowing etc…The doctor does not know another patient with (this) condition. The doctor advised us to remodel our house to accommodate a wheelchair. Do you know how long the time between wheelchair and bed?” (O'Donnell, 1991)
Another mother reported about her 26 year old daughter:

“When (she) began her weight gain in 1982, almost overnight after being so thin since birth, I felt we had a problem. Along with this extreme weight gain, she began tantrums etc, her behaviour became so aggressive, and I could not handle her... Hirsuitism was also diagnosed. Ever since 1982, there has been one thing and then another. Diabetes was diagnosed 1988. Losing control of bowel and bladder (what appears to be faster ageing on inside than outside) Eyesight declining due to Congenital Glaucoma.... On the other side of the coin we have seen the most miraculous advancement in her mental abilities. This has been since 1988. It is almost scary sometimes because she has these conversations with you that are so adult and completely normal. (She) talks with wisdom and great reasoning” (O'Donnell, 1991)

It is also recognized that there is a degenerative condition called Progressive Rubella Panencephalitis that is very rare and does not fit the descriptions above (Sever, South & Shaver, 1985). There have been only 9 well documented cases, so far only affecting males. In this condition neurological deterioration is seen between the ages of 8 & 19 years. Behaviours and seizures become apparent. The condition can affect all limbs and causes particular problems with walking and all known cases have been fatal.
Esophageal / Gastrointestinal Difficulties

Reports of gagging and vomiting were reported:

“In the past year we have had some strange behaviours come and go with our daughter. Your late onset manifestations of CRS (document) was very insightful as (she) is definitely experiencing changes, whether physical or emotional is anyone’s guess. She has had some weight loss, a decrease in appetite with intermittent crying spells at times, and when crying she does a strange throat sound prior to this – then just sobs. During these times she gags violently as if to vomit but doesn’t. She has had most exams done – blood test, urine, complete dental checks under anesthesia and we have found no obvious physical ailment” (p.10)

“The doctors are unable to determine the cause of her recurring vomiting (every 3 – 9 weeks for the past six years)”

Behavioural difficulties

The HKNC survey includes some details about the behaviour of people with CRS and whether this had changed over the past year in question. Behaviours such as Self-stimulization, tantrums, self-injury and aggression were all reported by the respondents but the general trend suggests that these behaviours **decreased** or remained the same over the year recorded. This is interesting because the concept of ‘late manifestations’, is usually associated with things getting worse – however some caution is attached to these results as there is no information on earlier changes or other things which have influenced behaviour change e.g. an individual
may have moved house which consequently had an effect on his/her behaviour.

Summary

The American results may at first glance present a depressing picture of the long term experiences of this group of people however it is important to remember that almost a third of the sample group indicated no signs at all of any late emerging medical problems. There is also great variation in the number/ nature of late manifestations experienced. These ranged from a person who ‘only’ developed glaucoma to a person who had developed every known late manifestation on the list. Equally the probability of any one person developing a particular condition is unknown, as is the time frame in which these conditions emerge. As with each of the studies from respective countries, the CRS population will also be susceptible to the same illnesses as the general population.

It is also recognized that people with CRS may have very significant changes in their medical condition, but may be very limited in the ways they can express these changes meaningfully and this may lead to under-identification of conditions that are in fact late manifestations.
4.1.4 Canadian Study

The Canadian study was led by Stan Munroe (1999) who was based at the Canadian Deafblind and Rubella Association (CDRA).

The Canadian sample included 100 people aged 5yrs to 62yrs. 75 of the respondents contracted rubella in major epidemic periods in the 1960’s and 1970’s. The sample included people who were Deafblind, and those with a single sensory impairment of Deafness or Blindness. The study started by establishing the early manifestations of its sample group. This confirms the aspects which are commonly thought to make up CRS. The early manifestations reported included Congenital Cataracts (79%), Glaucoma (32%), Hearing Loss (94%), Heart Defect (65%), Microcephaly (Small head) (33%), Microphthalmia (Small eyes) (33%), Dual sensory impairment (80%), Dual sensory impairment and heart defect (59%), Dual sensory impairment, heart defect and microcephaly (24%).

The group also reported the identification of conditions that would generally be considered as ‘late manifestations’. These included, Glaucoma (20%), Detached Retina (11%), change in visual acuity (27%), change in hearing ability (24%), treatment for mental health (26%), at least one negative behaviour (e.g. aggression, self injury, tantrum, property destruction (23%), seizures (30%), incidence of scoliosis, kyphosis or lordosis (curvatures of the spine) (26%), deterioration in energy level, stamina and endurance (21%), persistent sleeping problems (39%), Thyroid dysfunction (10%), Diabetes (12%), Osteoporosis (7%) and motor skills difficulties. The last category included Cerebral
palsy like movements (23%), deterioration in mobility or walking during 20s (21%) and deterioration in balance during 20s (21%).

Urogenital tract difficulties such as incontinence were reported by 30% of the respondents, whilst 25% reported gastro-intestinal tract problems such as swallowing, gagging or vomiting. Sixty-five percent reported having heart defects whilst 17% had a history of pneumonia which would indicate respiratory tract weakness. Thirty seven percent reported allergy problems with 7% having symptoms of asthma.

Lifestyle Influences

The Canadian Study also looked at various social aspects of the deafblind individuals’ lives, recognizing that these too might affect an individual’s health status. The study included information on family dynamics, educational activity and placements, living situation, working situation, preferred communication, the type of intervention support received and whether other professionals’ services were used e.g. sign language interpreters.

Canadian Results Summary

The Canadian results are significant in that they confirm previously known early implications of rubella. They also report on additional deterioration of vision and hearing during youth. This supports other published information about the high incidence rate of diabetes and thyroid conditions in this group of people. The researchers also identified the deterioration of physical and mental condition in early adulthood. The Canadian study also raises questions about
cause and effect i.e. is the high rate of behavioral change reported the result of neurological changes or a reflection of physical changes?

Limitations of Canadian Survey

The Canadian study is unfortunately limited in that it does not include any real analysis of the findings and there are no comparisons with the percentages of the conditions occurring in the general population. Even though the research included questions on social factors it does not elaborate on how these may affect results for example, might changes in communication be a result of changes in family dynamics or educational placement rather than a direct result of CRS?

5.0 Other Studies

Whilst the Australian, American and Canadian Studies set the foundation for research in this area, in more recent years other countries have focused on specific aspects of the subject.

5.1 Norway

In Norway Nicholas (2000) reported on the neuropsychological functioning of an individual with CRS and its implications through a case study. His work focused on the manifestations of particular behaviour patterns that were similar to those already identified within the American and Canadian studies. Nicholas proposed the behavioral
disturbances observed in individuals with CRS may arise from impaired executive functions, particularly what has been termed rectilo-frontal disconnection syndrome. Nicholas offers this as an explanation for why certain manifestations in people with CRS are not seen at birth.

5.2 Japan

In 2004 Takasu et al. undertook research in Okinawa, Japan following the rubella epidemic in 1964-1965. A sample of 280 respondents revealed that over a fifty year period all patients had developed cataracts, deafness and/or heart disease. Three of this group had also developed diabetes.

Takasu et al (2004) note that although the prevalence of diabetes in CRS was reported to be 20% higher in Caucasian individuals, in comparison with a non CRS sample (Menser et al 1978), it is only 1.1 % higher in the Japanese sample, i.e. other studies record 22-29 cases per 100,000 in Scandinavians, Canadians and Scots but only 1.5 per 100,000 in Japanese.

5.3 Oman

Whilst extensive immunisation programmes have had a positive effect on countries in the developed world, where vaccination is not available, or where vaccination programmes have only recently been introduced, rubella outbreaks are still being recorded.
In Oman outbreaks of rubella were reported in 1992 and 1993. Khandakar et al (2004) reported on the ocular manifestations alone. Their results reported a wide variety of ophthalmic complications, however they noted that even with surgery and ‘state of the art’ ophthalmic care, the functional results for the patients were poor because of the presence of additional audiological and neurological disabilities.

Therefore surviving patients pose a burden on medical and social communities. Khandakar et al (2004) suggest that the emphasis in management ought to be prevention of CRS through effective immunization programmes, where these are available. Whilst immunization is undoubtedly important to prevent further individuals being affected, there is a risk that ongoing management of those who already have CRS may become the casualty of such an approach.

5.4 Denmark

Dammeyer (2010) reported on a Danish study aiming to test existing hypotheses of delayed manifestations in congenitally deafblind individuals with CRS using a control group of individuals whose Deafblindness is cause by aetiologies other than CRS. 127 individuals were involved in the study, 35 of whom had CRS. The prevalence of conditions recorded in other studies was noted i.e. the onset of diabetes, thyroid problems, early menopause and osteoporosis, cardiovascular effects, ocular damage, auditory damage, growth hormone deficiency, progressive rubella panencephalitis, and psychosocial problems.
The Danish study concluded that whilst not excluding the existence of delayed manifestations amongst individuals with CRS, there was no evidence to suggest that individuals with CRS have a higher risk of contracting the evaluated diseases than those with aetiologies other than CRS.

It was also proposed that the higher frequency of diabetes in different studies could be associated with the living conditions for people with multiple disabilities who often live in institutions, which may lead them to having a sedentary lifestyle and exerting little control over their diets. This may also be true for vascular, thyroid diseases and osteoporosis.

5.5 The Netherlands

A team from The Netherlands is known to have undertaken research involving people with CRS, and particularly those living in an institution. This was reported on at the 14th Deafblind International World Conference, Perth, Australia (2007). However no results have been published to date.

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