

Dandy-Walker Syndrome

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Tyrell Arnold

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There are several developmental anomalies that can affect the fetus during the gestational period. Among these anomalies is Dandy-Walker syndrome (DWS). Despite the extensive attention it has received in the literature, DWS remains poorly understood (Patel & Barkovich, 2002). However, this rare disorder is described as a congenital (present at birth) abnormality which specifically affects the cerebellum (major structure of the hindbrain, which consists of two halves or hemispheres) and some of its compositions; particularly the cerebellar vermis, the fourth ventricle, and an enlarged posterior fossa (e.g., Ecker, Shipp, Bromley, & Benacerraf, 2000; Engelhard & Meyer, 1995; Emerson, 2006; Obwegeser, Deutinger, & Bernaschek, 1994). In addition, most individuals with DWS are diagnosed with hydrocephalus (increased fluid in the brain).

Individuals with DWS may be difficult to identify since there are no specifically distinctive or characteristic symptoms or signs, except those seen by neuroimaging techniques and perhaps a larger than normal head due to hydrocephalus (Maria, Zinreich, Carson, Rosenbaum, & Freeman, 1987; Pascual-Castroviejo, Velez, Pascual-Pascual, Roche, & Villarejo, 1991). Ultrasound and magnetic resonance imaging (MRI), for example, have made it possible to detect cerebellar and other malformations early in the prenatal period (Donkelaar, Lammens, Wesseling, Thijssen, & Renier, 2003). However, before neuroimaging techniques, DWS was diagnosed only when hydrocephalus was suspected and/or when the posterior fossa was transilluminated (light protruding through the skull; Maria et al., 1987).

Traditionally DWS was only seen as one entity; however, through the introduction of computed tomography variations of the classic definition have been noted (Zalel, Seidman, Brandt, Lipttz, & Achiron, 2002). Now many researchers suggest that DWS is a spectrum disorder (e.g., Barkovich, Kjos, Norman, & Edwards, 1989; Long, Morgan, & Robson, 2006). Therefore, DWS is now characterized by the severity of the congenital anomalies associated with the posterior fossa, these include: Dandy-Walker malformation (DWM), Dandy-Walker variant (DWV), and mega-cisterna magna (MCM) (e.g., Akgul, Babaroglu, Bahar, Bokesoy, Birincioglu, & Cobanoglu, 2006; Boddart et al., 2003; Estroff, Scott, & Benacerraf, 1992; Planas, Peiro, Rubio, Villanueva, Seres, & Carreras, 2003); the latter two are seen as milder forms of the classic DWM (e.g., Ecker et al., 2000; Engelhard & Meyer, 1995). Furthermore, Paladini and Volpe (2006) suggest that DWM, DWV, and MCM are the most common fetal abnormalities of the posterior fossa (p. 486).

Often researchers describe Dandy-Walker malformation, Dandy-Walker variant and mega-cisterna magna as the Dandy-Walker complex (DWC; Has et al., 2004; Menon, Madkarin, Desai, & Goel, 2006). The one commonality that binds the previous three anomalies together as the DWC seems to be an anomaly of the posterior fossa (Planas et al., 2003). Furthermore, the distinction between the classic DWM and its variants can be very difficult to detect (Planas et al., 2003; Klein, Pierre-Kahn, Boddaret, Parisot, & Brunelle, 2003). Thus, many professionals suggest that a thorough screening process should be conducted on fetuses that are suspected of having DWS (e.g., Ecker et al., 2000; Engelhard & Meyer, 1995; Klein et al., 2003).

Along with the classical malformations of the posterior fossa, there are numerous other central nervous system (CNS) and non-central nervous system (non-CNS) anomalies that affect those diagnosed with DWS (e.g., Estroff et al., 1992; Limperopoulos et al., 2006). For instance, Ecker et al. (2000) found, in a sample of 50 cases of DWM patients and 49 cases of DWV patients, that 86% of those diagnosed with DWM and 80% of those diagnosed with DWV had other CNS and non-CNS anomalies. Likewise, Donkelarr, Lammens, Wessling, Thijssen, & Renier (2003) suggest that "CNS malformations are present in up to 68% of [DWM] cases," they further suggest that "the most common of which is agenesis or hypogenesis of the corpus callosum" (p. 1030). Furthermore, the more CNS and non-CNS findings there are, the poorer the prognosis is; therefore, those diagnosed with DWS without concordant anomalies have a much better prognosis (Chamberlin & Narins, 2005).

There is not a clear definition of what can be constituted as DWS (Phillips, Mahony, Siebert, Lalani, Fligner, & Kapur, 2006). Typically, definitions of the syndrome "have been modified to include findings encountered in a particular case or series of cases" (Barkovich, et al., 1989, p. 1289). Thus, Koul, Chacko, and Leven (2000), in an attempt to formalize the definition of DWS, explain that hypoplasia or aplasia of the cerebellar vermis and cystic dilatation of the fourth ventricle are the two essential features of DWS (p. 390). Furthermore, Barkovich, et al. (1989) suggested that all definitions of DWS have also included a description of a high position of the tentorium (p. 1289). Therefore, it seems logical that all definitions of DWS should include an abnormal vermis, dilatation of the fourth ventricle and anomalies of the tentorium.

Despite advances in science and in technology, the direct aetiology or cause of DWS is still unknown (e.g., Chitayat et al., 1994; Emerson, 2006; Kumar, Jain, & Chhabra, 2001; Litzman, Buckova, Ventruba, Holcikova, Mikyska, & Lokaj, 2003; Mehndiratta, Agarwal, Sharma, & Agarwal, 2000; Obwegeser et al., 2004); additionally, the aetiologies of most DWS cases have been sporadic (Lefort, et al., 2001). However, there have been reported cases of suspected aetiological origins of some individuals diagnosed with DWS, these include: chromosomal abnormalities (Akgul, et al., 2006; Has et al., 2004; Nizard, Bernard, & Ville, 2004), single gene disorders (Cavalcanti & Salomao, 1999), and environmental factors such as teratogen exposure (e.g., drugs, alcohol, rubella, etc.; Chitayat et al., 1994; Engelhard & Meyer, 1995; Estroff et al., 1992).

The incidence rate for DWS is thought to be around 1:25,000- 35,000 births (Has et al., 2004; Kolbel et al., 2003; Obwegeser et al., 1994; Ondo & DeLong, 1996), with a female to male prevalence of 1.2:1 to as high as 1.7:1 (Has et al., 2004; Kolbel et al., 2000; Pascual-Castroviejo et al., 1991). The prognosis of DWS is as variable as the anomalies that are associated with it; therefore, many researchers suggest that the prognosis of infants varies from good neurological development to motor dysfunction and severe mental retardation or even death (e.g., Boddaert et al., 2003; Chang, Russell, Callen, Filly, & Goldstein, 1994; Estroff et al., 1992; Klein et al., 2003). In other words, because of the associated complications and anomalies associated with DWS the prognosis for normal intellectual development is usually poor (Kumar et al., 2001). However, having DWS typically is not what causes individuals to have a poor prognosis; it is usually the severity of the other CNS anomalies (Obwegeser et al., 1994). In addition, infants who have DWS will usually become symptomatic within the first year of life (Obwegeser et al., 1994).

Historically, DWS has been described as early as 1887 by J. Bland Sutton (Sutton, 1887; also see Muzumdar & Goel, 2004;) Nevertheless, it was not until Blackfan and Dandy (1914) described a child with cystic dilatation of the fourth ventricle, hypoplasia of the cerebellum vermis, hydrocephalus, and separation of the cerebellar hemispheres that DWS became better known (also see Alper, 1999; Horwitz, 1997; Pearce, 2006). Actually DWS was not given its current name, "Dandy-Walker," until C. E. Benda (1954) formally gave it this name as a treatable disease (also see Caceres & Trejos, 2006; Sato, Kubota, & Nakamura, 1996). This syndrome was given the name "Dandy-Walker" to honour Walter E. Dandy (1886-1946) and later Arthur E. Walker (1907-1995) who described this anomaly in the early 1900s (Ecker et al., 2000; Chamberlin & Narins, 2005). Pascual-Castroviejo et al. (1991) suggest that since the early 1900s, more than 500 cases of DWS have need reported (p.88); however, since their report in 1991, it is quite probable that the number of reported cases of DWS is now well over 1000.

Although DWS is receiving increased attention today, as far as I am aware there has not been, to date, a comprehensive article that has considered DWS, its defining characteristics, historical context, compilation of case reports, methods of diagnosis, fetal outcome, developmental expectations, etc. Most of the information that I have found on DWS has been directly located in case reports. Therefore, the purpose of this article is to provide an overview of several of the facets of DWS. It is my intention to provide this information at an understandable level so that parents and other individuals affected directly or indirectly by this disorder can gain a better understanding.

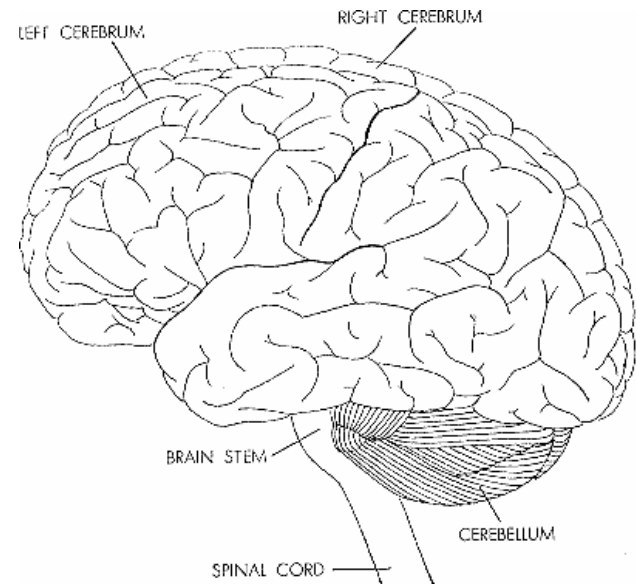
Most of all, DWS is of personal interest to me because my second child was diagnosed with this syndrome at 21 weeks gestation. During the ensuing months my wife and I experienced high levels of anxiety, partially because of the unknown and partially because nobody could tell us hard evidence regarding what it meant to have DWS. Fortunately, our daughter, Tia Lynae, was born as healthy as any child, despite minor digit anomalies. Tia is now three months old and her professional care providers suggest that she is developing and functioning normally for her age. We are so thankful that she is doing well. However, not all stories of DWS are this positive; therefore, through this article I want to help others and myself to be more informed. Thus, I hope that this article will help answer several questions that individuals may have regarding Dandy-Walker syndrome. My heart particularly goes out to those families that have been affected by DWS.

The following article will first describe the DWC: Dandy-Walker malformation, Dandy-Walker variant, and mega-cisterna magna. Second I will describe many of the associated CNS and non-CNS abnormalities that are common to DWS, as well as the etiological factors of this disorder. Third I will discuss the diagnostic methods used and their implications. Fourth I will describe what prognosis can be expected in both prenatal and postnatal DW patients. Fifth I will outline some of the treatment techniques that are currently being utilized to help individuals diagnosed with DWS. Finally I will finish this article by drawing some general conclusions about DWS and I will further suggest what can to be done in the future.

*Description of DWM, DWV, and Mega-Cisterna Magna*

The main structure of the brain that DWS directly affects is the cerebellum. Thus, it may be helpful to have a brief overview of this structure. The cerebellum (which means “little brain” in Latin) is a major structure of the hindbrain. It is found in the most posterior part of the cranium and is composed of two hemispheres which lie just above and behind the brain stem. Further the cerebellum hemispheres are situated around the cerebellar vermis—the vermis allows the two hemispheres to remain intact and to further communicate with each other.

Figure 1. The Human Brain



Much like the cerebrum (the major structure of the forebrain), the cerebellum is wrinkled because its outer surface is made up of a comparatively thin mass of tissue (Kolb, & Wishaw, 2001). The features of the cerebellum that are visible from the surface are bumps (gyri) and cracks (sulci). The cerebellum develops over a long period of time. For example, it begins embryonically as one of the first brain structures to arise and then continues through the first year of life (Limperopoulos et al., 2006). Moreover, the cerebellum is largely believed to play a role in motor control, motor learning, and even cognition such as development of language and other cognitive skills (Donkelaar et al., 2003; Niesen, 2002).

### *Dandy-Walker Malformation*

Dandy-Walker malformation (DWM), which is a congenital anomaly that directly affects the posterior fossa (i.e., areas of the brainstem and the cerebellum, Kolbel et al., 2000; see figure 2) has been classically described as a neurological triad (e.g., Estroff et al., 1992; Has et al., 2004; Kumar et al., 2001; Onto & Delong, 1996). The DWM triad consists of cystic dilation of the fourth ventricle (cavity in the hindbrain containing cerebrospinal fluid), complete or partial agenesis or absence of the cerebellar vermis (structure between the two cerebellar hemispheres), and an enlarged posterior fossa (area containing the brainstem and the cerebellum). However, DWM is further characteristic of an elevated or displaced tentorium (portion of the dura mater that separates the cerebellum from the inferior portion of the occipital lobes; Sato et al., 1996) and an enlarged cisterna magna (an open space which allows CSF between the cerebellum and the brainstem to drain; Lennon, 2002).

A displaced or absent vermis is a particularly intriguing feature of DWM. Paladini and Volpe (2006), for example, explain that “the degree of vermian hypoplasia has been demonstrated to correlate significantly with the occurrence and severity of mental retardation” (pp. 487-488). Similarly, Boddaert et al. (2003) found that in a series of 21 cases all of the individuals who were mentally retarded had either an abnormal vermis, supratentorial (forebrain) abnormalities, or seizures (p. 322). Thus, it seems the more abnormal the vermis is the more severe the prognosis may be; again this has to take into consideration the other present anomalies. For instance, Boddaert et al. (2003) hypothesized that despite the vermis being hypoplastic in DWM, a “normal lobulation of the vermis and absence of supratentorial anomalies could be associated with normal development” (p. 321). Therefore, a detection of vermian anomalies, regardless of its severity, warrants a careful search for additional abnormalities (Chang et al., 1994).

Boddaert et al. (2003) suggest that “the posterior vermis is hypoplastic in many neurogenetic syndromes with neurocognitive impairments with or without autistic behavior, such as the in fragile X, Rett and Soto Syndromes, autism, and nonspecific mental retardation” (p. 323, Original spelling).

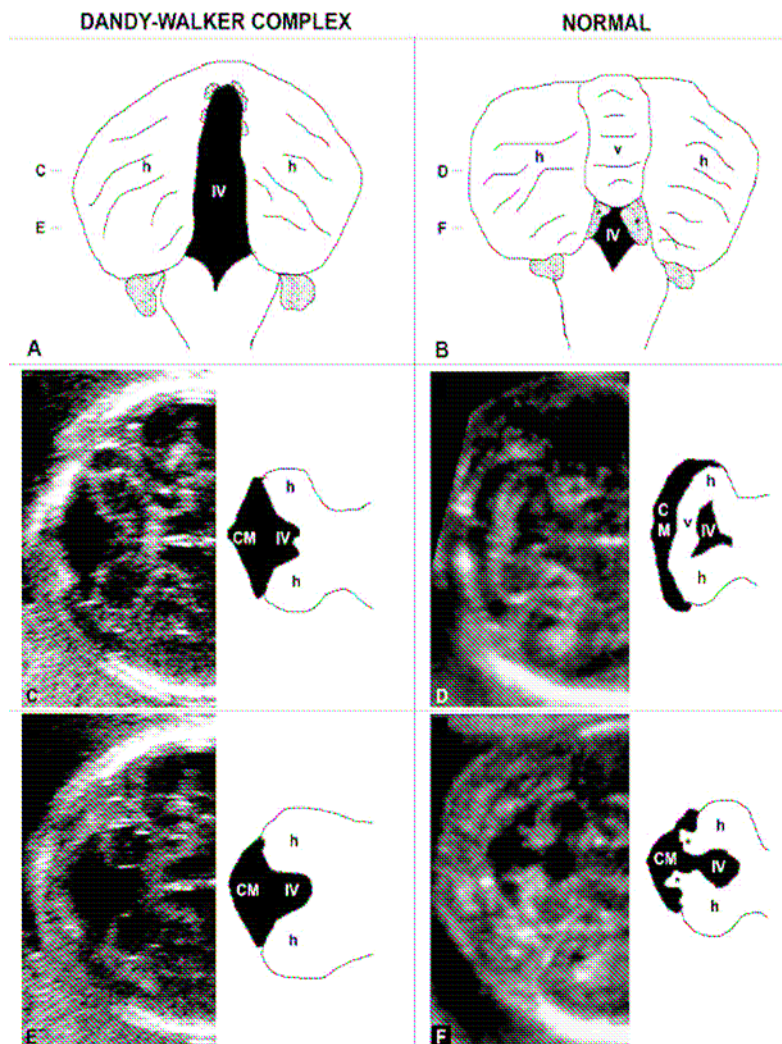


Figure 2. Normal and abnormal images of the cerebellum seen in DWS. “**A and B.** Illustrations of the dorsal cerebellum from a Dandy-Walker malformation complex (**A**) and an anatomically normal brain (**B**). The stippled zones represent collections of choroid plexus including aggregates medial to the cerebellar tonsils (asterisk in B). The approximate planes are indicated for the images in C–F. **C and D.** Ultrasound images corresponding to the superior or mid-cerebellum demonstrate a trapezoidal inter-hemispheric gap in a case with confirmed Dandy-Walker malformation complex (**C**), in contrast to the intact vermis in images from a cerebellum that was anatomically normal (**D**). **E and F.** The trapezoidal gap persists in the inferior cerebellar plane of the malformed fetus (**E**), in contrast to the keyhole-

shaped gap observed inferiorly in an anatomically normal cerebellum (**F**). v, vermis; IV, fourth ventricle; CM, cisterna magna; h, hemispheres of the cerebellum” (Phillips et al., 2006, p. 692).

Unfortunately, as mentioned previously, there has not been a firm definition describing DWM; it seems, as Barkovich et al. (1989) argue, DWM definitions have been

modified to include findings from particular cases or series of cases (p. 1289). Thus, in a recent study conducted by Klein et al. (2003), an effort was made to restrict the definition of DWM to six essential features. These features include: "1) a large posterior fossa cyst widely communicating with the fourth ventricle, 2) a small, rotated, raised cerebellar vermis, 3) an upward displaced tentorium, 4) an enlarged posterior fossa, 5) antero-lateral displaced but apparently normal cerebellar hemispheres, and 6) a normal brainstem" (p. 484). Conversely, Kumar et al. (2001) defined DWM as: "1) cystic dilation of the fourth ventricle, 2) hypoplasia of the cerebellum, 3) hydrocephalus, 4) large posterior fossa, and 5) atresia of the foramina of magendie and luschka" (p. 484). It should be noted that they suggested that all five features do not need to be present for a diagnosis. Furthermore, these two definitions demonstrate the variability seen in defining DWM; therefore, it is noted that a firm functional definition of DWM is still needed.

There are other anomalies characteristic of DWM. Of these, hydrocephalus—increased cerebrospinal fluid (CSF) in the brain—is perhaps the most common. Incidence rates vary from 70-90% of all cases (e.g., Calabro, Arcuri, & Jinkins, 2000; Litzman et al., 2003; Sonigo, Rypens, Carteret, Delezoide, & Brunelle, 1998), with 75% of individuals developing hydrocephalus within the first three months after birth (Bragg, St. George, Wynne-Jones, Hockley, & Morton, 2006; Estroff et al., 1992). In addition, many studies have reported that hydrocephalus in DWM accounts for about 4% of all cases of hydrocephalus (e.g., Cavalcanti & Salomao, 1999; Litzman et al., 2003).

It should be noted, as Maria et al. (1987) explain, "in the absence of significant lateral ventricle enlargement in utero, the presence of a posterior fossa cyst does not

necessarily assure future hydrocephalus or neurologic dysfunction" (p. 50). In other words, prenatal findings of hydrocephalus do not ensure postnatal hydrocephalus; further, hydrocephalus is not the only factor that contributes to mental retardation in infants with DWM. Additionally, aggressive and prompt treatment of hydrocephalus can decrease the mortality rate and can contribute to a good prognosis (Maria et al., 1987). Fried and Epstein (2004), for instance, explain that children treated of hydrocephalus have a predictable prognosis, with many of them developing with relatively normal intelligence (¶ 3).

Although hydrocephalus was initially described as an essential feature of DWM, current researchers suggest that hydrocephalus does not need to be present for diagnosis of DWM (Boddaert, et al., 2003; Kumar et al., 2001; Sikorski & Curry, 2005); however, hydrocephalus must be considered a complication of the disorder (Calabro et al, 2000, p. 292). Because hydrocephalus is such a common feature of DWM, it warrants further discussion.

Hydrocephalus can either be congenital—occurring during fetal development—or it can be acquired—developed after birth (Maria et al., 1987; Simpkins, 2005). On the one hand, congenital hydrocephalus is thought to arise due to a blockage of the foramina of Magendie and Luscka, the openings of the fourth ventricle of the brain through which CSF passes (Emerson, 2006; Fried & Epstein, 2004). This means that the CSF is unable to pass through the subarachnoid space, which ultimately causes the CSF to build up in the fourth ventricle causing hydrocephalus. If an infant has congenital hydrocephalus he or she will most likely be delivered by cesarean due to his or her relatively large head (Deering & Satin, 2002; Pascual-Castroviejo et al., 1991).

On the other hand, acquired hydrocephalus can occur at birth or any time thereafter and is thought to be more prevalent in DWM (Donkelaar et al., 2003). As mentioned previously, up to 75% of infants with DWM are affected with hydrocephalus within three months after birth (Bragg et al., 2006; Engelhard & Myer, 1995; Estroff et al., 1992). However, hydrocephalus can be delayed for a number of months or even years (Pascual-Castroviejo et al., 1991). For example, Sato et al. (1996) reported that a 35 year old woman began having symptoms consistent with hydrocephalus and DWM; she shortly afterwards was diagnosed with such. In another case report, Engelhard and Meyer (1995) reported that two sisters, ages 53 and 50 respectively, began having symptoms of hydrocephalus and were diagnosed at that time, in their fifties, with hydrocephalus and DWM.

There are two distinct types of hydrocephalus: communicating and non-communicating hydrocephalus. Simpkins (2005) eloquently describes the distinction between these two types of hydrocephalus in these words:

Noncommunicating hydrocephalus is basically of an obstructive nature. The CSF pathways within the ventricles become blocked and obstructed. Although this blockage can occur anywhere in the ventricular system, it usually lies either within the narrow passageways connecting the ventricles or where the CSF exits the fourth ventricle into the subarachnoid space. The small opening of the fourth ventricle fails to develop or develops immaturely, which also can lead to an obstruction in the outflow of CSF. In communicating hydrocephalus, the CSF moves freely around the ventricles, but it is blocked after it attempts to exit the ventricles. The CSF also becomes impeded as it passes over the brain. Although

the absorption sites are blocked, the CSF moves freely throughout the ventricles, and the ventricles "communicate" with each other. (p. 458)

This distinction is important to understand because individuals diagnosed with DWM and hydrocephalus are typically diagnosed with communicating hydrocephalus. This is the case because the fourth ventricle still communicates with the posterior fossa (Akgul et al., 2006; Cavalcanti & Salomao, 1999; Klein et al., 2003; Litzman et al., 2003; Smith & Levine, 2004).

There are many symptoms of hydrocephalus, which vary with age, severity, and individual tolerance to the CSF (Sikorski & Curry, 2005). Some fetuses are diagnosed with hydrocephalus during an ultrasound exam; however, in many cases infants and toddlers who have hydrocephalus are usually identified during regular child exams within the first year because of the disproportionally large head circumference for his or her age (Sikorski & Curry, 2005; Simpkins, 2005) or because of other physical symptoms (Figure 1). This may include the infant not having the ability to hold up his or her head. Simpkins (2005) explains that "infants may present with early signs such as vomiting, sleepiness, and irritability, and late signs involving failure to thrive, delay or loss of developmental milestones, seizures, and eyes that deviate downward called 'sunsetting' eyes" (p. 458; see table 1; also see Emerson, 2006; Fried & Epstein, 2004).

Although hydrocephalus often contributes to lower intellectual levels, Chang et al. (1994) argue that hydrocephalus is not the only factor responsible of mental retardation. They further suggest that early interventions to control hydrocephalus can contribute to normal intellectual development (specific treatment and management of hydrocephalus will be discussed later in the article). In addition to hydrocephalus, there

are other common anomalies of DWM; however, they too do not need to be present for diagnosis.

Table 1. Signs and symptoms of hydrocephalus in early infancy.	Signs and symptoms of hydrocephalus in late infancy and childhood.
<ul style="list-style-type: none"> <li>○ Asymptomatic</li> <li>○ Sleepiness</li> <li>○ Rapidly enlarged head</li> <li>○ Persistent vomiting</li> <li>○ Failure to thrive</li> <li>○ Irritability</li> <li>○ Delay or loss of developmental milestones</li> <li>○ Downward deviation of eyes, 'sunsetting' eyes</li> <li>○ Seizures</li> </ul>	<ul style="list-style-type: none"> <li>○ Nausea</li> <li>○ Chronic headaches</li> <li>○ Irritability</li> <li>○ Blurred vision</li> <li>○ Papilledema</li> <li>○ Diplopia</li> <li>○ Drowsiness</li> <li>○ Delays with walking or speech</li> <li>○ Urinary incontinence</li> <li>○ 'Sunsetting' eyes</li> <li>○ Changes in personality or cognition including memory loss.</li> </ul> <p style="text-align: right;">(Simpkins, 2005, p. 459).</p>

Some other common anomalies found in conjunction with DWM include, hypoplasia of the cerebellum (incomplete or underdevelopment of the cerebellum); it is often described in the literature as being "splayed" or separated (e.g., Chang et al., 1004; Smith & Levine, 2004). Nevertheless, it is very uncommon for the cerebellum to have complete agenesis (absence of the cerebellum, Donkelaar et al., 2003). Second a large posterior fossa is typically seen but is not always the case in individuals with DWM (Chang et al., 1994). This is often due to the obstruction of the fourth ventricle. For instance, in both DWM and DWV, "the cisterna magna is compressed and reduced to a virtual space between the dilated fourth ventricle and the dura mater" (Calabro et al., 2000, p. 292). Finally atresia (congenital absence or closure of a normal bodily opening) of the foramina (openings) of megendie and luschka (two channels in the fourth ventricle in which CSF normally follows) is also seen in DWM (Chamberlin & Narins, 2005).

### *Dandy-Walker Variant*

Dandy-Walker variant (DWV), which is sometimes referred to as *inferior vermian hypoplasia* (Limperopoulos et al., 2006) is often described as a milder form of DWM (e.g., Bragg et al., 2006). Also, DWV is not described as well in the literature as the classic DWM (Estroff et al., 1992), even though DWV is likely more common than the classic DWM (Sonigo et al., 1998). Additionally, as Menon et al. (2006) explain, "DWM and DWV have so many similarities that a clear cut distinction is often impossible" (p.877).

DWV "occurs when a more specific and local insult to the cerebellum takes place with little effect on the fourth ventricle" (Lennon, 2002, p. 330) as compared to the classic DWM in which the insult is more severe. DWV is further characteristic of cerebellar dysgenesis when it is not associated with a significant dilatation of the cisterna magna or an enlarged posterior fossa (Bernard, Moscoso, Renier, & Ville, 2001; Nizard et al, 2004; Sonigo et al., 1998). Also the cerebellar hemispheres, although they may be small, are usually formally and structurally normal (Has et al., 2004). In addition, there is communication between the fourth ventricle and the arachnoid space, and no hydrocephalus is present (Dokelaar et al., 2003).

Has et al. (2004) suggest that DWV may or may not be presented with an enlargement of the posterior fossa; however, Bragg et al. (2006), Estroff et al. (1992) and Lennon (2002) argue that in order for a DWV diagnosis the posterior fossa must not be enlarged. Additionally, there is often variable hypoplasia of the cerebellar vermis in cases of DWV (Estroff et al., 1992). Furthermore, DWV, like the classic DWM, commonly occurs simultaneously with other abnormalities of the CNS and non-CNS (Akgul et al.,

2006). Even though DWV is a less severe variant of the classic DWM, it still warrants a careful and cautious diagnosis. It is not uncommon for DWV to be wrongly diagnosed because over and under-estimations of the size of the vermian defect is possible (Zalel et al., 2002).

The prognosis of DWV is usually similar to that of DWM. Chang et al. (1994), for example, reported that in 37 cases of DWV and in 28 cases of DWM only 24% of those with DWV and 20% of those with DWM lived longer than a year (p. 330). Likewise, Ecker et al. (2000) reported that in 49 cases of DWV only 13 or 28% of the patients were alive at six weeks (p. 329); additionally, only 7 or 14% were reported as developmentally normal infants. In other words, like DWM, infants diagnosed with DWV can expect a spectrum of normal development to severe disability or even death (Estroff et al., 1992). However, Limperopoulos et al. (2006) found that a majority of the infants (19) in their series diagnosed with DWV were free of "major neurodevelopmental impairments and functional disabilities" (p. 1075). However, they also found that these infant's cognitive functions or IQ were about 15 points below the mean of 100, compared to infants with normal postnatal studies (p. 1075).

### *Mega-Cisterna Magna*

Of the three descriptions of the DWC, mega-cisterna magna (MCM) is perhaps the least described in the literature. MCM has also been used synonymously with Blake's pouch cyst and retrocerebellar arachnoid cyst (e.g., Calabro et al., 2000; Sonigo et al., 1998). MCM specifically affects the cisterna magna, which is a fluid filled area between the brainstem and the cerebellum (See Figure 1). MCM consists of an enlarged posterior fossa, secondary to an enlarged cisterna magna (>10mm in depth) with no

compression over the underlying cerebellum (Calabro, et al., 2000; Donkelaar et al., 2003; Paladini & Volpe, 2006; Sonigo et al., 1998). Utsunimiya, Yamashita, Takano, Ueda, & Fujii (2006) explain that a diagnosis of MCM should be made with caution as the cisterna magna in neonatal populations is comparatively larger than that of adults as the cerebellum continues to grow for several months after birth; therefore, they conclude that “because there are no definitive measurements for the size of the cisterna magna, a diagnosis of mega cisterna magna cannot be based solely on its size” (p. 475).

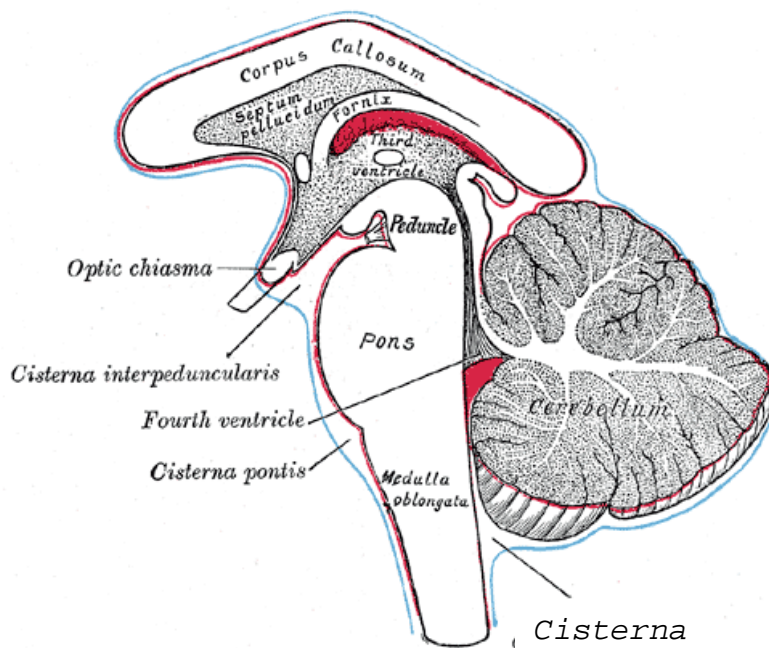


Figure 3. The Hindbrain

This figure shows many of the structures of the posterior fossa and hind brain. The cisterna magna, cerebellum, fourth ventricle and the corpus callosum are of particular interest as they are directly affected in DWS.

The vermis and the fourth ventricle is said to be normal and communicates freely in individuals diagnosed with MCM. (Donkelaar et al., 2003; Lennon, 2002). However, this classification is unclear; Planas et al. (2003) suggest vermian dysgenesis, for example, can be found in all cases of DWS (p. 373). Therefore, shunts are sometimes inserted into the cisterna magna to ensure that there is free communication of the cystic mass with

the subarachnoid space (Calabr et al., 2000). Additionally, the cerebellum yet may be hypoplastic despite the appearance of an intact vermis (Lennon, 2002).

Barkovich et al. (1989) found that it can be difficult to differentiate between DWM and MCM; Sonigo et al, (1998) explain that this may be especially hard when the cisterna magna cyst is not excessively large. The discrepancy in diagnosing MCM is cause of concern because it can lead to both over and under estimations of DWM and MCM. Typically there are, like the classic diagnosis of DWM, related CNS and non-CNS symptoms seen in conjunction with mega-cistern magna (Bargallo, Puerto, De Juan, Martinez-Crespo, & Lourdes Olondo, 2002). Long et al. (2006) reported, for example, that out of 39 cases of MCM, 24 (62%) had additional abnormalities (p. 708). However, the prognosis for this variation of the DWC is said to better than DWM or DWV, especially if it is an isolated finding (Calabro et al., 2000; Long et al., 2006). Long et al. (2006) reported that in their study, 92% of isolated MCM cases had an apparently normal outcome and that 81% of the MCM cases which were associated with other anomalies were also normal postnatally (p. 709). Nonetheless, like DWM and DWV, these individuals can expect mental capacities ranging from normal development to severe retardation (Calabro et al., 2000).

Interestingly, Sonigo et al. (1998) suggest that the MCM variant of DWS accounts for 54% of the anomalies seen in the posterior fossa (p. 220). Calabro et al. (2000) explain that "in the absence of associated supratentorial anomalies and uncontrolled or progressive hydrocephalus, patients with BPC [Blake's pouch cyst or mega-cisterna magna] have a good prognosis." They further suggest that these individuals "may have

a mild increase in head circumference, which frequently goes unobserved" (p. 294). Reassuringly the prognosis for MCM is more promising than DWM or DWV.

#### *Additional Anomalies Associated with DWS*

As was mentioned earlier, many of the individuals who are diagnosed with DWS may also have other central nervous system (CNS) and non-central nervous system (non-CNS) anomalies. Menon et al. (2006) explain that DWS "is not limited to a mere mechanical disturbance of CSF [cerebrospinal fluid] but represents a more generalized disorder of neural development" (p. 877). They further go on to advocate that DWS "warrants a search for associated extra-cranial malformations, particularly in the cardiac, skeletal, genitourinary and gastrointestinal systems (p. 877). Assessment for these anomalies is extremely important because often times the mortality rate and prognosis of the infant depends more on the associated anomalies than on the actual malformations of DWS (Has et al., 2004). Because the vast majority of these anomalies can occur in any of the three abnormalities seen in the Dandy-Walker complex, this section will describe these anomalies generally as they apply to DWM, DWV, and MCM.

Reported cases or series of cases have found a wide range of abnormalities seen in the DWC. Cedergren and Selbing (2006), for example, reported that detection rates of fetal structural anomalies vary between 22.3 and 64.7% (p. 912); additionally, Ecker et al. (2000) found that out of 99 cases of DWM and DWV, 86% of the fetuses had other anomalies (p. 329). Among these anomalies the most frequent tend to be facial and cardiovascular abnormalities (Donkelaar et al., 2003; Litzman et al., 2003). Russ, Prestorius, and Johnson (1989) suggested that in their report of 15 cases of DWS, 83% of the postnatal deaths could be attributed to associated congenital defects (401).

Of the anomalies that are commonly seen with DWS, hydrocephalus is perhaps the most common. Additionally, partial or complete agenesis of the corpus callosum is second only to hydrocephalus (e.g., Bersani & Cecchi, 2006; Gulati, Gera, Menon, Kabra, & Kalra, 2002; Kolbel et al., 2000; Lefort et al., 2001). The corpus callosum is the structure of the brain that binds the two cerebral hemispheres together and allows the two hemispheres to communicate (Kendall, 1983; Kolb & Wishaw, 2001). Partial or complete agenesis of the corpus callosum is not an uncommon neurological anomaly and interestingly, DWS accounts for about 17% of all cases of agenesis of the corpus callosum (Diagnostic Challenge, 1987). Additionally, Boddaert et al. (2003) found in a series of 20 cases that all fetuses that had an abnormal vermis also had dysgenesis of the corpus callosum.

Levine, Barnes, Madsen, Abbott, Mehta, and Edelman (1999) reported that agenesis of the corpus callosum is difficult to diagnose using ultrasound during pregnancy; therefore, they suggest that other imaging techniques should be used to achieve an accurate diagnosis of hypoplasia of the corpus callosum, especially if the corpus callosum is only partially hypoplastic. This is particularly important because partial hypoplasia of the corpus callosum typically means a good prognosis in 85% of individuals; however, hypoplasia of the corpus callosum with other associated abnormalities has a poor prognosis (Levine et al., 1999, p. 1017-1018). There are no clinical symptoms specific to hypoplasia of the corpus callosum; however, seizures, abnormal movements, developmental delay, and mental retardation are common with this anomaly (Diagnostic Challenge, 1987).

Chromosomal abnormalities are often associated with DWS. Chitayat et al. (1994) reported that upwards to half of the prenatal diagnosis of DWS are due to a

chromosome abnormality; they further explained that most of these individuals, interestingly, do not have congenital hydrocephalus (p. 412; see also Nizard et al., 2004). Russ et al. (1989) found in their series that from 12 available karyotypes (chromosome makeup) 33% were abnormal (p. 401); Has et al. (2004), likewise, found that 17.6% of their cases of DWS had abnormal chromosomes. Ecker et al. (2000), interestingly, found that in their series of cases only one of the 21 fetuses with an abnormal karyotype had ultrasound finding isolated to the posterior fossa (p. 331). It has also been reported that up to 18 different chromosomal anomalies, and 40 different genetic syndromes, have been correlated to DWS (Chen et al., 2002; also see Bernard et al., 2001).

The most common chromosomal anomalies associated with DWS include trisomy 13, trisomy 18, and Triploidy (e.g., Has et al., 2004; Kolbel et al., 2000; Nizard et al., 2004). Trisomy 18 and trisomy 13 are chromosome anomalies that occur when there are three chromosomes instead of the usual two. In other words, trisomy 18 and trisomy 13 simply means that there are three copies of the chromosome in each cell, rather than the usual pair. They are genetic disorders that are commonly associated with severe birth defects including mental retardation, and defects of many of the organ systems of the body. Unfortunately, the prognosis for infants diagnosed with either of these disorders is very poor. Twenty to 30% of babies born with trisomy 13 or 18, for example, die within three month of birth, and 90% die within the first year (Medical Genetics, 2007, par. 2).

Triploidy or triploid syndrome is a rare chromosomal anomaly characterized of there being three of every chromosome totalling 69 rather than the normal 46 chromosomes. This result in the fetus having either a combination of XXY, XXX or rarely an XYY arrangement of chromosomes (Birth Defect, 2006). This disorder, much like

trisomy 13 and 18, is lethal and most babies affected with this anomaly are lost through miscarriage. Additionally, there are also multiple birth defects seen in conjunction with triploid syndrome. Interestingly, some infants can survive for a few months after birth; this has been attributed to mosaicism, which means that some cells have the normal 46 chromosomes and the remainder of the cells have a complete extra set of chromosomes (Triploid Syndrome, 2006, par. 1).

Cardiovascular or heart anomalies are another common abnormality seen in infants diagnosed with DWS (Has et al., 2004; Nizard et al., 2004). Congenital heart defects are often associated with a poor prognosis, most commonly leading to death (Hafner, Scholler, Schuchter, Sterniste, & Philipp, 1998; Kolbel et al., 2000). Russ et al. (1989) found that out of 15 cases, 83% of infant deaths could be attributed to congenital defects (p. 401; see also Kolbel et al., 2000). Also, like the skeletal structures, the heart warrants a careful diagnosis prenatally. This is usually conducted via a fetal echocardiograph—a detailed ultrasound of the heart—which is usually conducted during an in depth ultrasound visit (Kolbel et al., 2000).

Facial abnormalities are another common anomaly associated with DWS (e.g., Bragg et al., 2006; Has et al., 2004; Nizard et al., 2004). The facial abnormalities that are most commonly seen in DWS are a cleft lip and/or a cleft plate and other minor facial dysmorphisms (Donkelaar et al., 2003; Pascual-Castroviejo et al., 1991). Facial angiomas (small growths consisting of blood vessels), a short nose, and thin lips have also been seen with DWS (Koebel et al., 2000); Pascual-Castroviejo et al. (1991) interestingly reported that there seems to be no anomalies of the ears in DWS. It should be noted that some of these anomalies are isolated cases or series of cases and cannot be

generalized to all infants diagnosed with DWS. Additionally, there are more anomalies that have been reported in cases of DWS; however, this article has only touched on a few of the more common anomalies. For a more complete list of associated anomalies see Chitayat et al. (1994, pp. 410-411).

### *Aetiology of DWS*

The aetiology or cause of DWS is unknown; however, this is not uncommon of congenital anomalies. For example, Hill and Haffner (2002) suggest that two thirds of children born with congenital malformations derive from unknown sources (p. 47). Despite this fact, it is widely known that DWS develops early in utero, during the embryonic stage (e.g., Squires, Dieffenbach, & Betz, 1998). Some suggest it occurs as early as the fifth or sixth week post-conception (Barkovich et al., 1989; Mehndiratta et al., 2000; Ondo & DeLong, 1996).

Originally Blackfan and Dandy (1914) suggested that DWS arose due to atresia (absence) of the cerebellar foramina (also see Barkovich et al., 1989); however, it has since been proven that DWS and the anomalies associated with it “develop long before the foramina of Luschka and Magendie open, and are the result of an early error in the development of the paleocerebellum” (Chitayat et al., 1994, p. 409; Kolbel et al., 2000). This means that DWS affects the phylogenetically second oldest part of the cerebellum while it is developing in the embryonic stage. Furthermore, non-neurological defects (i.e., facial anomalies, cardiac anomalies, limb anomalies, etc.) indicate that DWS develops very early in utero (Ondo & DeLong, 1996), resulting in a defect in the alar plate at an early stage of development (Kolbel et al., 2000).

There have been a number of reported etiological factors that could contribute to DWS. Planas et al. (2003), for instance, suggest in rare cases it may be inherited by an autosomal recessive pattern (see also Chamberlin & Narins, 2005); Estroff et al. (1992) explain that Meckel-Gruber syndrome, Warburg syndrome, and X-linked Aircardi syndrome could be some of the autosomal recessive disorders linked to DWS. Obwegeser et al. (1994) suggest that this recessive form probably has a recurrence risk of 25% in some families (p. 163). Planas et al. (2003) also suggest that DWS may be due to "environmental factors, including viral infections, alcohol and diabetes" (p. 373; see also Emerson, 2006). It may also be due to chromosomal defects (Obwegeser et al., 1994). Further, it has been seen in consanguineous (cousins) parents. Has et al. (2004), for instance, found that in their series of DWS, 44.8% of the parents were consanguineous.

Because of the presence of associated anomalies, Kumar et al. (2001) suggest an early embryonic developmental disturbance affecting more than just the posterior fossa structures (pp. 348-349). Although the exact timing if the insult is unknown (Bragg et al., 2006), it seems logical that DWS perhaps does not cause many of the other anomalies associated with it, but, like the other anomalies, is the result of a more severe disturbance of the fetus during the embryonic period as the neural plate differentiates (Squires et al., 1998). Furthermore, because this anomaly is associated with both chromosomal and benign pathological factors, it is likely that DWS is the result of more than one disruption during early development. This is arguably so because facial and cardiovascular malformations in DWS may arise as early as the third to fourth week of gestation (Bragg et al., 2006).

### *DWS Diagnosis and Diagnostic Techniques*

Through the use of modern diagnostic tools (e.g., ultrasound, CT, MRI, etc.), DWS is typically diagnosed in individuals before one year of age in approximately 76 to 80% of the cases (Calabro et al., 2000; Pascual-Castroviejo et al., 1991, p, 88). Historically DWS was only found incidentally (e.g., symptoms of hydrocephalus, or other neurological problems) or by autopsy (Engelhard & Meyer, 2000). Today there are a number of different neuroimaging techniques that are used to diagnose and confirm diagnoses in fetuses, infants, and all others who may be suspected of having DWS. Adult cases of DWS, for instance, are usually diagnosed incidentally by neuroimaging methods or after minor head trauma (Sato et al., 1996). However, in a majority of cases ultrasound, for example, is the most universal technique used to detect and evaluate DWS prenatally (Cedergren & Selbing, 2006; Levine et al., 1999). Therefore, today DWS is usually diagnosed during a routine fetal ultrasound (Stazzone et al., 2000).

Today it is common for pregnant mothers to receive a routine ultrasound (also known as ultrasonography or sonography) as part of prenatal care; this is typically done during the second trimester (Smith & Levine, 2004; Stazzone et al., 2000). Prenatal ultrasound is the screening technique of choice for detecting brain anomalies in utero (Stazzone et al., 2000). Additionally, ultrasound “provides real-time imaging that is safe, readily available, noninvasive, and cost-effective” (Stazzone et al., 2000, p. 835; also see Teksam et al., 2004). Because it is estimated that approximately 6000 CNS anomalies will affect neonates each year in the US alone (Levine et al., 1999), ultrasound allows practitioners and parents to more fully be aware of such anomalies. In addition, “management of the pregnancy can be modified, with optimal parental

counseling" (Boddaert et al., 2003, p. 322). Fetal ultrasound not only allows for a diagnosis of abnormalities of the posterior fossa but also allows for diagnosis of other CNS and non-CNS anomalies (Kolbel et al., 2000). For example, Ecker et al. (2000) demonstrated that 86% of DWM fetuses in their study had other identifiable anomalies seen by ultrasound.

Has et al. (2004) explain that "If [ultrasound] is incorrectly performed, it is relatively easy to create the appearance of a DWV malformation" (p. 758), which can lead to either an underestimation or overestimation of DWS (Estroff et al., 1992). Has et al. (2004) further suggest that "vermian defects may be over-under diagnosed on prenatal ultrasound examination and the distinction between DWV and other abnormalities of the posterior fossa is difficult" (p. 758). This is particularly true in late pregnancy because of shadowing from the fetal skull or when the appearances of some anomalies are difficult to detect or differentiate using ultrasound (Levine et al., 1999). Of these, agenesis of the corpus callosum is particularly difficult to diagnose, as Levine et al. (1999) argue, especially during the second trimester.

Accurately identifying DWS is extremely important because "a prenatal diagnosis of a fetal abnormality is a major parental stressor, not only because of the diagnostic uncertainty in some cases but also because the long-term outcome is often unclear" (Limperopoulos et al., 2006, p. 1075). This prenatal diagnosis gives parents the opportunity to gain information about the pregnancy and possible birth defects the infant may have, and to examine possible family planning alternatives (Schonberg & Tiffit, 2002). More importantly, an accurate diagnosis is critical as some parents may elect to discontinue with the pregnancy, even without other ultrasound or cytogenetic

abnormalities because of concerns that the child may have neurological dysfunction and disabilities (Phillips et al., 2006). Some studies suggest that up to 80% of women elect pregnancy termination in the presence of DWS (Chang et al., 1994; Limperopoulos et al., 2006). Unfortunately, not all prenatal ultrasound diagnoses of DWS are accurate. For example, Phillips et al. (2006) found, in their study, that the “concordance between ultrasound and neuropathological [autopsy] diagnosis was poor [59%]” (p. 690). They further reasoned that “this incongruity occurred despite very reasonable interobserver agreement regarding the ultrasound and autopsy interpretations” (pp. 690-691). Therefore, it has been suggested that other imaging techniques and diagnostic tools should be used to confirm DWS and its severity (Estroff et al., 1992; Phillips et al., 2006; Schonberg & Tiffet, 2002).

As neuroimaging techniques are further developed, malformations of the skeletal and nonskeletal structures are now more accurately diagnosed. Of these technological advances, 3D-ultrasound is becoming a common tool used to achieve a correct diagnosis of many fetal anomalies (e.g., facial anomalies, limb anomalies, skeletal anomalies, etc.) including DWS (Dyson et al., 2000; Obwegeser et al., 1994; Schonberg & Tiffet, 2002). 3D-ultrasound provides a powerful advantage over 2D-ultrasound as it provides a clearer picture of the fetus (Dyson et al., 2000). Paladini and Volpe (2006) suggest that 3D-ultrasound is more logical and feasible to complement traditional ultrasound, as only referral centres are able to integrate other neuroimaging techniques (e.g., fetal MRI) to confirm a diagnosis. Additionally, they argue that that 3D-ultrasound has a high correlation with MRI in its findings and measurements. However, MRI is still preferred as it shows a more comprehensive picture of the fetal brain.

Fetal magnetic resonance imaging (fetal MRI) is perhaps the most accurate non-invasive method used to diagnose DWS (Barkovich et al., 1989; Sato et al., 1996). France, for example, has been using MRI extensively to better characterize posterior fossa anomalies that have been initially diagnosed by ultrasound during the second trimester (Phillips et al., 2006). In addition, Sonigo et al. (1998) explain that "MRI is a valuable complementary tool when prenatal US [ultrasound] is incomplete, doubtful or limited" (p. 221). Additionally, Stazzone et al. (2000) suggest that examining the posterior fossa using ultrasound is often difficult because of the posterior fossa's compact anatomy (p. 835). Fetal MRI can also be helpful for assessing fetal anatomy with obese women or when hydrocephalus is present (Levine et al., 2002). Furthermore, to date, "there is no evidence that short-term exposure to electromagnetic fields harms developing fetuses" (Levine et al, 1999, p. 1017). Most of all, fetal MRI, which allows for a more reliable diagnosis, helps parents and clinicians make critical decisions and to more fully understand the severity of the malformations. This also may help parents to determine whether to continue with the pregnancy or not (Limperopoulos et al., 2006).

Fetal MRI during the mid 1980s to early 1990s was met with challenges mostly because "the random nonperiodic pattern of fetal motion does not allow gating and often causes severe image distortions" (Levine et al., 1999, pp. 1015-1016; also see Stazzone et al., 2000). Therefore, in recent years through the development of ultrafast MRI, images can now be taken in milliseconds and with higher resolution (Limperopoulos et al., 2006; Teksam, Ozyer, McKinney, Kirbas, & Cakir, 2004). This eliminates the previous problems of fetal movements (Stazzone et al., 2000), or the need of maternal or fetal sedation (Levine et al., 1999; Stazzone et al., 2000). However, fetal MRI is a relatively new technique and is not mainstream. Moreover, its diagnostic

accuracy largely depends on the expertise of the interpreter and on the quality of the images (Limperopoulos et al., 2006).

It should be noted that CNS anomalies can be more accurately diagnosed late in the pregnancy using fetal MRI, as imaging quality is typically better and as the appearance of anomalies often change over time (Limperopoulos et al., 2006). However, this is not helpful for mothers who may want to terminate the pregnancy (Teksam et al., 2004), as termination usually must be done before a certain gestational age of the fetus. Additionally, even though fetal MRI has greatly enhanced the accuracy of detection of fetal anomalies in DWS, it still lacks the diagnostic accuracy of postnatal studies (Limperopoulos et al., 2006).

Limperopoulos et al. (2006) explain that DWS, particularly DWV, can be overdiagnosed by fetal MRI; therefore, they suggest that postnatal MRI should be performed to confirm the prenatal diagnosis (also see Estroff et al., 1992). Although postnatal MRI studies may be ideal, many parents and caregivers elect not to have DWS confirmed postnatally using MRI studies (Ecker et al., 2000). There are several reasons for this. First and foremost, because the infant must be sedated, there is increased risk associated with sedation (Levine et al., 1999). Second many find it hard to justify the cost, especially since many caregivers feel that a confirmatory MRI would not change clinical management (Ecker et al., 2000). Finally ultrasound can be used to confirm DWS postnatally via the anterior fontanel ("soft spot") for several months after birth, until the cranial bones fuse and solidify.

Of the precautions that should be made when diagnosing DWS, special care must be taken to not diagnose DWS too early. Repeatedly, studies have shown that the

vermis does not completely finish developing until 17-18 weeks gestation (e.g., Ecker et al, 2000; Nizard et al., 2004; Zalel et al., 2002). For example, Ecker et al. (2000) found that two fetuses who were diagnosed with DWV, later (after 18 weeks gestation) appeared normal on ultrasound and on subsequent postnatal follow-ups. Further, there have been many reported cases of false-positives and false-negatives of DWS. This can be unsettling as many hard decisions may be made on one ultrasound diagnosis. However, DWS has been accurately found as early as 11 to 14 weeks' gestation using ultrasound (Nizard et al., 2004; Planas et al., 2003).

To more accurately assess the severity and perhaps the aetiology of DWS, there are a number of techniques used to assess such anomalies as cardiovascular defects, and chromosomal rearrangements. To assess cardiovascular anomalies prenatally, a fetal echocardiograph, as mentioned earlier, is usually preformed (Hafner et al., 1998; Kolbel et al., 2000). Echocardiography is a technique that uses ultrasound waves to assess the structure and chambers of the heart. It further can measure the hearts valves and blood flow. Additionally, echocardiographs are not limited to prenatal imaging and are commonly used postnatally (Dyson et al., 2000).

Because chromosomal anomalies are commonly associated with DWS, many professionals recommend that karyotyping be preformed on the fetus. This can either be done prenatally or postnatally. Fetal karyotyping, however, is most often preformed via amniocentesis (Chamberlin & Narins, 2005). This procedure is an invasive technique that draws amniotic fluid, which is full of the fetus' cells, from the amniotic sac. Amniocentesis is preformed by inserting a needle, under guidance of ultrasound, through the mother's abdominal and uterine wall into the amniotic sac; in which time 1-

2 ounces of amniotic fluid is taken (Schongerg & Tiff, 2002). From there the cells can then be cultured to assess the chromosomes. However, there are associated risks with this procedure. Among these risks, 0.5-1%, or 1 in 100 to 1 in 200, of these mothers will have a miscarriage due to the invasive procedure (Chromosomal Mosaicism, 2003).

### *Prognosis of DWS*

Throughout this article I have suggested what prognosis of DWS can be expected; however, at this point I would like to more explicitly discuss what prognosis can be expected of individuals diagnosed with DWS. Unfortunately and perhaps surprisingly, repeatedly studies have found that a poorer prognosis is associated with prenatal diagnosis of DWS, particularly before 21 weeks gestation (e.g., Chang et al., 1994; Ecker et al., 2000; Estroff et al., 1992; Kolbel et al., 2000; Nizard et al., 2004). This is further complicated when other associated anomalies are found (Sonigo et al., 1998). Perhaps this alarming prognosis is because more severe anomalies may be easier to detect early in utero.

Conversely, prognosis of DWS is markedly better when diagnosed postnatally (Kolbel et al., 2000; Chang et al., 1994). Kolbel et al. (2000) reported that mortality rates, for when a diagnosis of DWS is made, range from 35 to 71% prenatally and 12.5 to 24% postnatally (p. 326). This demonstrates that fetuses with more severe anomalies rarely survive into infancy. Likewise, Chitayat et al. (1994) found that up to 88% of cases with isolated DWS detected postnatally do well intellectually. The presence of other anomalies is associated with the worst prognosis (Ecker et al., 2000). Although the long-term outcome is poor in most cases, Kalidasan et al. (1995) suggest that approximately 35% of these children have a reasonable outcome. Perhaps the best determinant of

long-term prognosis of DWS is correlated best with other anomalies (e.g., Chamberlin & Narins, 2005; Long et al., 2006; Phillips et al., 2006). For instance, Estroff et al. (1992) explain that “without an abnormal karyotype and associated anomalies, the prognosis for an infant born with the prenatal diagnosis of the DWV may be favorable, resulting in a normally developing child” (p. 758). However, the extreme variability, from normal intellectual development to severe mental retardation or even death, makes counselling to parents very difficult (Estroff et al., 1992).

#### *Treatment of DWS*

To date there is no specific treatment for DWS. Once an individual is diagnosed with DWS they will most likely have the disorder their whole life. However, due to the placidity of infants, sometimes the anomalies of DWS may become minimal as the brain continues to develop postnatally. Even though DWS cannot be treated, early interventions are recommended to minimize the intellectual and physical impairments the infant may have or develop. For example, Chamberlin and Narins (2005) suggest that all DWS individuals should have a treatment team consisting of neonatologists (specialist in newborn care), developmental paediatricians, geneticist, neurologist, specialized nursing care, and occupation and physical therapists. In addition, a neurosurgeon may be required for management of hydrocephalus. Although DWS cannot be treated directly and because a majority of DWS infants will have hydrocephalus, treatment and management of hydrocephalus is usually needed.

Of the few things that can be treated in DWS, hydrocephalus usually needs to be managed as it could cause further brain damage or even death. Typically hydrocephalus cannot be treated but can be managed with high success (Chamberlin

& Narins, 2005). Hydrocephalus is most commonly managed by the surgically placement of a shunt preformed by a neurosurgeon (Fried & Epstein, 2004; Simpkins, 2005). This procedure allows the CSF to be drained from around the brain (Skiorski & Curry, 2005). This usually involves redirecting the CSF from the cranium to another site, usually the abdomen (Keating, Spence, & Lynch, 2002; Simpkins, 2005). On the one hand, depending on the severity of the hydrocephalus, an infant may need a shunt relatively soon after birth, which often can contribute to a better prognosis. On the other hand, if the hydrocephalus is not managed excessive damage to the brain could result from the built up pressure caused by the CSF (Simpkins, 2005). Most importantly, management of hydrocephalus must be guided by the needs of each specific individual case, considering both anatomic and pathophysiologic factors (Harter, 2004).

Shunting has been preformed for over 50 years and is continuing to be improved by science, by clinical innovations and biomedical products (Fried & Epstein, 2004; Simpkins, 2005). Fortunately, the prognosis of childhood hydrocephalus is predictable, with reassuring evidence that hydrocephalus, if treated properly, will have little to no effects on the child's development (Fried & Epstein, 2004). Maria et al. (1987) found, for example, a high success with shunting in their series. They suggested that "aggressive and prompt treatment of hydrocephalus with serial follow-up may have contributed to a surprisingly low mortality and good outcome in patients with DWS" (p. 50).

If an infant receives a shunt early in life, however, it may adversely affect him or her. According to Fried and Epstein (2004), early shunting comes "at the price of permanent shunt dependency in most children" (¶ 1). Additionally, there are often

complications once the shunt has been placed; the most common complications of shunts are serious infections, uncontrolled hydrocephalus, and shunt obstructions (e.g., Chamberlin & Narins, 2005; Keating et al., 2002; Pascual-Castroviejo et al., 1991). Shunt infections, for instance, will probably affect between 5 and 15% of shunted individuals. Further, of these infections, 70% of them are diagnosed within the first month and 90% of them by six months (Fried & Epstein, 2004, ¶ 43). Therefore, the infant or individual with a shunt will need frequent follow-up to ensure the shunt is working properly (Keating et al., 2002).

There are many different types of shunts that may be used to manage hydrocephalus (Kumar et al., 2001). However, the two most common shunts which are recommended are ventriculoperitoneal (VP) shunts and Cystoperitoneal (CP) shunts (e.g., Maria et al., 1987; Pascual-Castroviejo et al., 1991; Sikorski & Curry, 2005; for more detailed information on shunts see Fried & Epstein, 2004 and Simpkins, 2005). Choosing which type of shunt to use largely depends on “the presence or absence of communication between the third ventricle and posterior fossa cyst” (Sikorski & Curry, 2005, p. 267).

Although, VP and CP shunts are typically recommended, there remains no optimum method for managing DWS-related hydrocephalus (Long et al., 2006; Maria et al., 1987). For example, some professionals recommend that VP and CP shunts be used in conjunction to more effectively manage the DW cyst and hydrocephalus, and to decrease the risk of further complications (Maria et al., 1987; Sikorski & Curry, 2005). Further evidence of this is seen in a 2-to 4-year follow-up study Kumar et al. (2001) conducted; they found that out of 7 patients initially treated with only a CP shunt, 6

patients later required a VP shunt because of the reappearance or persistence of hydrocephalus (also see Sikorski & Curry, 2005).

Perhaps the most important goal "...of any DWS surgical intervention has been to reduce ventricular and cyst sizes while creating and/or maintaining pressure equilibrium between the two compartments" (Pascual-Castroviejo et al., 1991, p. 95; also see Kumar et al., 2001; Sikorski & Curry, 2005). Because shunts only drain fluid from the brain, most shunts are equipped with a programmable valve of some sort to ensure that excessive CSF is not drained, and to monitor how fast the fluid is drained (Simpkins, 2005; Fried & Epstein, 2004). This ultimately allows for a proper equilibrium between the brain and CSF.

Unfortunately, despite aggressive management of hydrocephalus, some shunts are unsuccessful and may lead to a poor prognosis and even death (Chamberlin & Narins, 2005; Naidich, Radkowski, McLone, & Leestma, 1986). For instance, Pascual-Castroviejo et al. (1991) showed that a high mortality, 12.5 to 48% still persists after DWS shunting. However, many studies are reassuringly positive, with low mortality rates and moderate to high intellectual outcome of shunted DWS. Calabro et al. (2000), for example, suggest that the cerebellar hemispheres may show some degree of re-expansion after hydrocephalus is managed by VP or CP shunting.

### *Implications*

Dandy-Walker syndrome is a congenital malformation of the posterior fossa. It is specifically characteristic of a displaced cerebellar vermis, which may have either partial or complete agenesis. Additionally, DWS is a spectrum disorder consisting of Dandy-Walker malformation, Dandy-Walker variant, and mega-cisterna magna; each

of these descriptions is based on the severity of the anomaly. Furthermore, the critical anomaly that binds these three classifications as the DWC is the associated abnormalities of the posterior fossa (Bernard et al., 2001).

DWS is not very well understood but is receiving more attention as technological advances allow for its detection earlier and more frequently. Furthermore, mice models are being used to gain further insight into the molecular and cellular mechanisms that regulate cerebellar development, which are hoped to lead to a better understanding of the nature of human cerebellar malformations (Chizhikov & Millen, 2003; Donkelaar et al., 2003; Grinberg et al., 2004). Additionally, Bragg et al. (2006) describe a study where two researchers found that they could produce DWS in mice by administering a riboflavin-deficient diet. Ultimately it is hoped that through these non-human models, we can gain a better understanding of DWS.

The prognosis and diagnosis of DWS is extremely variable, which makes parental counselling very difficult. Clinical outcome, for instance, ranges from normal development to severe motor and mental retardation or even death (Kolbel et al., 2000). This huge variability depends largely on the concurrent CNS and non-CNS anomalies related to DWS. Reassuringly, isolated cases of DWS tend to have a much better prognosis. Because DWS is so variable, it is hard for doctors to provide a sure diagnosis and prognosis of a fetus found to have DWS. Therefore, further studies, including detailed ultrasounds, fetal MRI, fetal echocardiography, and even amniocentesis should be considered to provide a surer diagnosis of DWS and associated anomalies. Furthermore, a detailed "fetal ultrasound is an important tool for assessing subsequent pregnancies following the birth of a child with DWC of unknown

etiology" (Chitayat et al., 1994, p. 406). However, the recurrence risk in siblings for DWS is very low ranging from 1-5% (Bragg et al., 2006; Obwegeser et al., 1994). Conversely, as was mentioned earlier, the recessive form of DWS has a recurrence risk of 25% (Chamberlin & Narins, 2005; Obwegeser et al., 1994).

By no means is this article completely comprehensive. The associated anomalies of the CNS and non-CNS found with DWS, for example, range extensively as no two cases of DWS are exactly the same (see Chitayat et al., 1994; Fryssira, Tsitsika, Lourida, & Manolaki, 2006). This huge variability is perhaps why a firm definition of DWS is so elusive. This article, further, did not go extensively into anomical features of DWS or developmental features of the fetal brain. Furthermore, the discussion on treatment of hydrocephalus only provided an overview of the main techniques used; however, complete articles have been dedicated to this end (e.g., Fried & Epstein, 2004; Simpkins, 2005). Conversely, this article has provided insight into the basic features of DWS, what a diagnosis of DWS is, how variable the prognosis is, associated anomalies, and general treatment practices that are currently being used.

DWS is largely an unknown disorder of the brain and is even less understood. However, as DWS receives further attention, it is hoped that this anomaly will be better understood, defined, prevented, and most of all, perhaps even cured. There are a few support groups for individuals and families affected by DWS. For example, there are six different blogs on Yahoo Health Groups that allows people to ask questions and to share their personal experiences with DWS. For instance, one of the groups explains that its purpose is "for people affected by 'Dandy-Walker Syndrome.'" Further, "this group is open to anyone interested in making friends, sharing information and support with

others affected by this disorder" (for more information visit [http://health.dir.groups.yahoo.com/dir/](http://health.dir.groups.yahoo.com/dir/Health__Wellness/Support/Diseases_and_Conditions/Dandy-Walker_Syndrome)

Health\_\_Wellness/Support/Diseases\_and\_Conditions/ Dandy-Walker\_Syndrome). I hope that this article will be of use to those affected by this rare congenital abnormality. Most of all, I am thankful everyday that my daughter is doing so well with a syndrome that ultimately could claim her life.

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