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REVIEW ARTICLE

# Meningomyelocele and its management in pediatric genetics: A theme review of its biomedical and psychosocial aspects.

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**Keywords:**
Meningomyelocele, Folic acid deficiency, Congenital abnormalities, Primary prevention, Neural tube defects.

## Abstract

**Objectives:** This study aims to analyze myelomeningocele as a prevalent congenital anomaly and its general pathological aspects, while highlighting potentially protective measures and the importance of multiprofessional care. **Methods:** A theme review was conducted, encompassing studies on myelomeningocele and spina bifida. Epidemiological data, pathological aspects, and primary prevention measures such as the consumption of folic acid and vitamin B12 were analyzed, interpreted, and compiled. **Results:** Myelomeningocele is the most common manifestation of spina bifida, resulting from the incomplete closure of the neural tube. It can be influenced by genetic and environmental factors. The consumption of folic acid and vitamin B12 has been associated with a reduced risk of congenital malformations, including myelomeningocele. However, these measures do not completely eliminate cases. **Conclusion:** Primary prevention of myelomeningocele involves raising awareness about the importance of consuming folic acid and vitamin B12. Howevser, it is essential to recognize that these measures alone are not sufficient to eradicate the disease entirely. Multiprofessional care plays a crucial role in improving patients quality of life through a longitudinal and continuous approach within care networks.

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## INTRODUCTION:

Ensuring quality of life following a holistic and longitudinal view of health today has been a priority for public policies and actions that govern the private sphere of individuals in the most diverse locations. With such demand, ensuring the prevention and adequate treatment of congenital anomalies has emerged as one of the most important points and a relevant public health issue[1].

Among such health conditions, myelomeningocele (MMC) stands out for several factors, such as the possibility of presenting with high severity compared to other conditions, its considerable prevalence, the importance of attempts at prevention through prior consumption of folic acid[2], in addition to its broad field of comorbidities manifested in childhood or adulthood, with most of them being little studied or even neglected. Epidemiologically, it represents one of the main congenital neurological alterations, which, in turn, are the second most common area of congenital anomalies in newborns admitted to Intensive Care Units (ICU).[3]

Taking these arguments into consideration, it is up to health professionals to take possession of studies and precise results of the nuances of this disease and its major clinical implications, in order to provide correct gestational counseling, guide future parents and assist them in the search to avoid exposure to risk factors and ensure resolute and effective care from a therapeutic point of view, marked by assertive diagnosis and minimization of harm[4].

In summary, there must be an articulation of knowledge and professionals for correct and individualized management of each case.[5]

## METHODOLOGY:

The abstract consists of a bibliographic review with a descriptive basis carried out from the analysis of scientific articles published in the databases: PubMed, PubMed Central and Bookshelf. The following descriptors were used: "Myelomeningocele", "Folic Acid Deficiency", "Congenital Anomalies", "Primary Prevention" and "Neural Tube Defects", with the terminologies used in accordance with the Health Sciences Descriptors (DeCS). The search for articles was carried out between January 2022 and November 2023, through journals and electronic books on the internet (Figure 1).

Subsequently, the papers were selected using the following inclusion standards: theme approach, original writing in English, Portuguese or Spanish, article available in full or in abstract version, e-books and studies in humans, while the exclusion criteria were: unavailability of articles in their full reading form, articles that did not address pediatric care of the disease and that presented information that differed from the updated consensuses of the Brazilian Society of Neurosurgery or the American Society of Neurosurgery (Table 1). A total of 69 articles were analyzed, of which 41 were effectively screened by the inclusion criteria and served as the basis for this study.

### Embryology:

During the embryological process of primary neurulation, the ectodermal layer folds and begins to form a tube. At this point, there are still open spaces at the ends of the tube, known as caudal and rostral neuropores, located, respectively, at the ends of the same name, which should soon be closed by the migration of mesodermal cells[6] (Figure 2).

Independently and concomitantly with this process, a group of cells from the caudal mass forms the secondary tube called the caudal eminence, which fuses with the neural tube produced in the initial neurulation[7].

Between the 3rd and 4th weeks of embryonic development, the neural tube in formation is expected to have already closed (Figure 3). However, this process does not always occur fully, which can cause several malformations generally classified as Neural Tube Defects (NTD), especially the "open" type defects, since the "closed" defects are predominantly associated with secondary neurulation.

This broad group of problems includes spina bifida, a condition characterized by the opening of the posterior part of the bony framework that makes up the spine[8]. This opening, in turn, can lead to the protrusion of elements of the central nervous system that should be internalized and protected, such as the meninges, spinal and nervous elements, which is related to the diagnosis of myelomeningocele[9] (Figure 04).

### Causal factors:

As risk factors, there are genetic and environmental factors (Table 2). In the field of study of possible correlated genes, there are several candidates, with a considerable part of these being related to the metabolism of folic acid[10], which can undergo mutations and imply in the limited processing of folate and greater susceptibility to the disease. Furthermore, there are other genetic elements of etiologies and functions not directly associated with the vitamin component, such as GLUT3, which correlation and impact on the disease are still poorly explained in the literature.[11] Furthermore, environmental aspects include the presence of chronic maternal diseases prior to pregnancy, such as high blood pressure and diabetes, malnutrition and generalized nutritional deficiencies, and the exposure of pregnant women to alcohol and drugs such as carbamazepine, warfarin, retinoic acid, and valproic acid.[12,13,14]

### Epidemiology and related data:

In the United States of America, the prevalence of NCDs, specifically MMC and anencephaly, is approximately 0.5-1.0:1,000 individuals[8]. Compared to the results from 1990-1998, when the policy of including folic acid in foods had not yet been implemented, there was a projected drop in the number of reported cases of 26%. However, there is great variability in rates depending on the location and specificities such as local genetic distribution and access to determinants of the health-disease process, factors that contribute to a highly

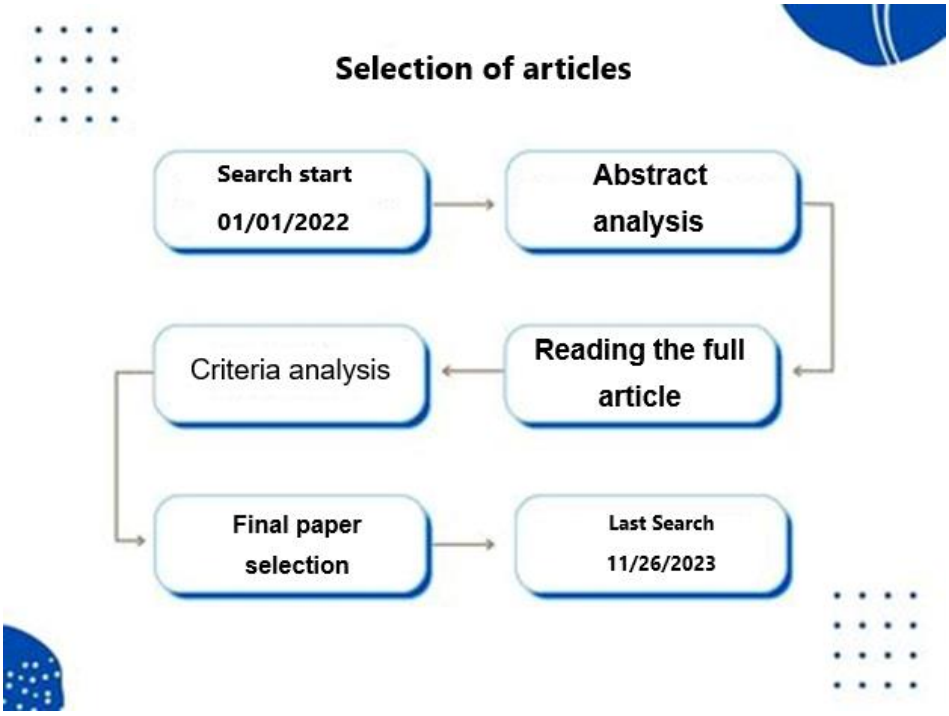



**Figure 01:** Process of selecting articles to compose the review.
Methodology for selecting articles to be included in the review

**Table 01:** Inclusion and Exclusion Criteria used in the selection, production of Authors (2023).

| Inclusion criteria: | Exclusion criteria: |
|---|---|
| Theme approach within the keywords. | Full articles not available for reading. |
| Original paper in English, Spanish or Portuguese. | Papers that did not discuss the pediatric care of the disease. |
| Paper not available in its full or abstract version, e-book and human studies. | Papers in disagreement with updated consensuses of the Brazilian and American Associations of Neurosurgery. |

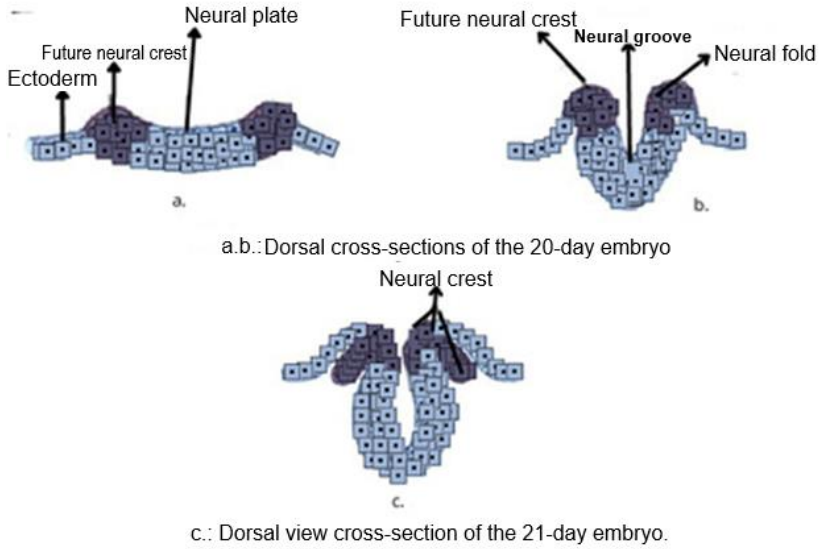



**Figure 2.** Initial development of the embryonic nervous system.
Comparison of the nervous morphology of 20- and 21-day embryos, before the closure of the neural tube.

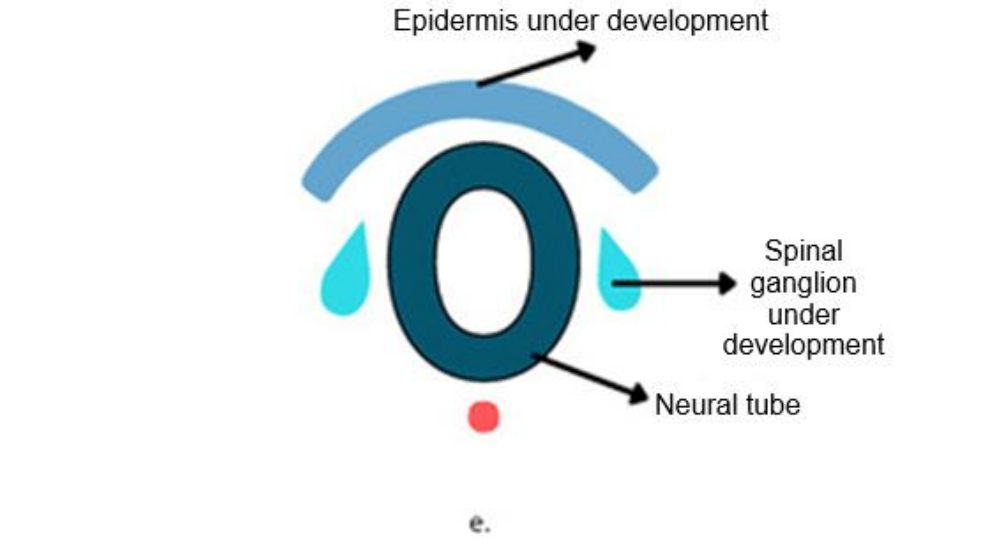



**Figure 3.** Embryonic morphology after the closure of the neural tube.
Illustration of an embryo after the neural tube has closed

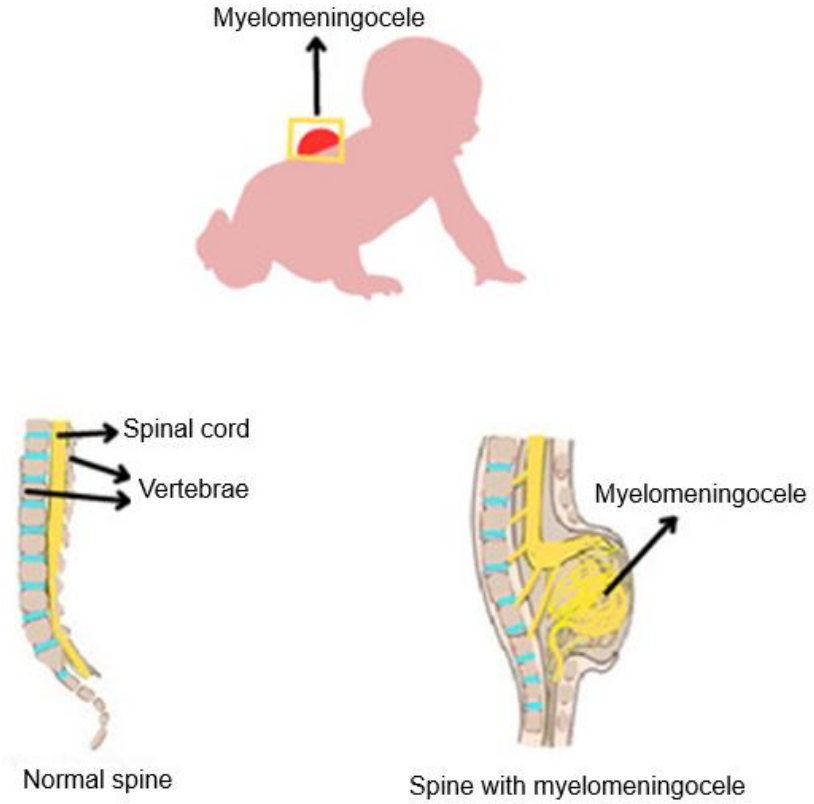



**Figure 4.** Comparative appearance of myelomeningocele.
Depiction of the deformity illustrated in a baby. Added comparison of the internal aspect of the spinal cord in contrast to a spinal column.

**Table 2.** Factors related to the cause of myelomeningocele.

| |
|---|
| Maternal comorbidities |
| Malnutrition |
| Alcohol |
| Carbamazepine |
| Retinoic acid |
| Valproic acid |
| Warfarin |
| Varfarina |

**Source:** Modified from 10,11,12,13 and 14.

heterogeneous epidemiology between different locations in the same country and even more so between different nations, which reinforces the importance of autonomy and attention in surveillance. Specifically regarding MMC, national data range from 0.83 to 1.87 per 1,000 live births.[15,16]

Although most cases are the result of multifactorial patterns, in which genetic content and socio-environmental factors coexist, approximately 2-16% of reported pathologies are related to chromosomal disorders or single-gene disorders, which is reflected in data such as that 53% of spontaneously aborted fetuses with spina bifida have balanced or unbalanced karyotype alterations. Therefore, genetic monitoring and the request for amniotic fluid karyotyping are essential when there is a previous diagnosis or clinical suspicion in the prenatal period.

Related to maternal and external factors, the use of anticonvulsant medications, anticoagulants and vitamin A derivatives during the first trimester should be considered, as there is a 1-2% increased risk. Furthermore, rates of overweight or obesity, combined with the presence of chronic comorbidities, can increase the chance of having a child with myelomeningocele to around 35%, and there may also be greater resistance to the preventive factor of folic acid, when compared to pregnant women without these same elements.[12]

## Prevention:

Due to the possibility of multiple causal factors, there are several important measures in care before and during pregnancy that must be taken to reduce the prevalence of cases[1].

Therefore, folic acid supplementation is the main preventive measure, since deficiency (whether due to total absence or reduced replacement) can alter epigenetic factors and mechanisms of synthesis, repair and development of DNA in the embryo or fetus, since there is great plasticity of genetic material in the intrauterine period, with the need to constantly perform and undo strategic methylation of genes, and this process requires the help of this compound to occur.[2]

Regarding folate dosage, studies indicate that pregnant women should consume around 600-750 mcg/day, either through foods such as green vegetables, fruits in general and nuts or through supplements resulting from government food security policies, of which the enrichment of wheat flour with the nutrient and, consequently, all its derivatives stand out.[2]

As a result, there is a growing global call for expanding food fortification and nutritional education policies, given the success already achieved and the prospects for reducing cases worldwide.[16]

Furthermore, expanding and making prenatal care accessible should also be a priority to formulate and rule out diagnostic hypotheses of MMC in an assertive manner, manage potential cases, and counsel the family. Practices involving collective education and management of the determinants of the health-disease process were also fundamental for prevention.

## Diagnosis:

Currently, given the expansion of corrective procedures before 26 weeks of gestation, diagnostic analysis in the prenatal period has become a fundamental standard for establishing a good prognosis and better consolidating a longitudinal line of care based on treatment and genetic counseling[17].

Diagnosis is commonly confirmed by ultrasound examinations, especially from the second trimester onwards. Fetal magnetic resonance imaging may be performed when surgery is necessary. Furthermore, since approximately 5-20% of cases are reflected in genetic alterations, karyotype and molecular tests of the developing fetus are also important to understand the etiology, at a secondary point in the investigation.[12]

It is important that the multidisciplinary team coordinates procedures with general monitoring, so that comorbidities, surgeries and disorders in the current pregnancy can be assessed, in addition to the existence of high-risk pregnancies and premature births.[4,5]

Despite its unquestionable importance in the study of myelomeningocele, prenatal assessment still requires more evidence that directly and precisely links the presence of impairments, especially in the cognitive area, and the malformation under discussion.

## Genetic counseling:

In Brazil, prenatal genetic counseling is growing significantly, even though cases of NTDs are decreasing due to the increase in dietary supplementation policies.[18] In general, this tool is very useful for controlling, minimizing and managing gestational risks for the mother, her baby and even future generations. From a prospective perspective, it focuses on providing guidance on folic acid intake before fertilization, as well as formatting a pedigree and family planning in the longitudinal aspect of care. From a retrospective or prenatal perspective, frequent and detailed studies of imaging tests and investigation of associated anomalies should be carried out, maintaining a communication channel between the entire family and the pregnant woman and categorizing groups and risk factors based on genetic elements for possible intrauterine surgeries to correct the congenital anomaly.[19]

The risk of recurrence depends on the cause of MMC. In isolated cases, inheritance is usually multifactorial, but in cases where there are other associated congenital anomalies, genetic testing should be performed to determine whether there is a chromosomal abnormality or monogenic disease, completely changing the risk of recurrence, which may be higher.[20]

### Corrective procedures:

This consists of a procedure that aims to correct the vertebral defect and prevent exposure of the nerve contents. Historically, intrauterine repair of MMC was the first viable and effective corrective procedure for a condition that is not intrinsically lethal, performed while the pregnancy was still ongoing in human groups. According to the results published by the MOMS (Multicenter Study of the Management of Myelomeningocele) randomized study, the open procedure during pregnancy ensures a better fetal response, greater motor capacity and greater safety of neural integrity, when compared to the same procedure in the postnatal period, but these data are changing.[21-24]

Therefore, when there is a prenatal diagnosis, the closure of the neural tube in the caudal part should be anticipated, to reduce the time of exposure of the nerve contents to the amniotic medium and, subsequently, to avoid exposure to the external environment. However, possible obstetric complications of the procedures must be considered, given the need for access via laparoscopic hysterotomy, which can generate a greater risk of ruptured membranes, prematurity and cystic formations, a relevant aspect that maintains the importance of postnatal surgical conduct for high-risk conditions.[25]

Furthermore, inherent to the surgical modality, secondary infection, in addition to mortality secondary to Chiari Malformation I and decompensation of previous hydrocephalus are considered the most robust negative outcomes.[26]

In summary, in the dichotomy between pre- or postnatal corrective methods, general aspects such as better prognosis, life expectancy and success in managing motor and nervous limitations for the fetus must be considered, without, however, ignoring the risks to delivery and the rest of the pregnancy, as well as the integrity of the mother. Therefore, there must be a clear channel of communication between the health professional and the family, to explain the main points related to the choice, respecting the deliberative power of the patients.[27,28]

### Neonatal management of groups not undergoing intrauterine surgery:

Despite the enormous importance of intrauterine management of patients with myelomeningocele, among the groups that were diagnosed only postpartum or were not eligible for the surgical modality (Table 3), intense multidisciplinary care is required to optimize survival and reduce morbidity and mortality in general. Therefore, aiming to reduce the eminent risk of infections, it should be recommended that surgical correction occur within 24 hours of the immediate postpartum period, with the central focus being the reduction of local infections and neonatal sepsis and the reconstruction of the functional anatomy of the neonate, preserving as much nervous tissue as possible.[29]

The immediate approach begins with a preoperative evaluation of patients, so that the dimensions of the malformation can be visualized and understood by both ectoscopy and imaging tests, such as Magnetic Resonance Imaging, in addition to studying the child's general condition, highlighting their weaknesses and specific needs. During the surgical procedure itself, the spinal cord tissue is repositioned, with subsequent closure of the skin. Furthermore, if hydrocephalus is present, the placement of a ventriculoperitoneal shunt to drain excess cerebrospinal fluid should also be considered. Finally, close postoperative monitoring should be performed, with subsequent referral for multidisciplinary care with varied care, which may involve orthopedic, occupational, nephrological and physical therapy management.[30,31,32]

### Symptoms and complications:

There may be several clinical manifestations, varying in severity and impairment of general development. In a comprehensive scenario, the main symptoms and symptoms associated with the condition were:

### Chiari II malformation:

A pathological condition that can accompany patients with myelomeningocele in 95% of cases. It involves the herniation of posterior neuronal contents through the dilated foramen magnum, specifically the fourth ventricle and part of the spinal cord, and is related to hydrocephalus, increased pressure and neuronal degeneration.[4,28,32,33,34]

### Cognitive impairment:

Clinical trials show that, in general cognitive tests, the score achieved by individuals with MMC is significantly lower than that obtained by healthy children/adolescents. However, this result can often be the product of other conditions common to the sample, such as hydrocephalus[35].

Despite this, the strong general correlation between the pathology itself and impairments in the cognitive area cannot be disregarded. Areas such as assessment of verbal IQ, intellectual reasoning and motor rhythm have obtained results that reinforce the idea of impairments; in studies of spontaneous verbal language there was little difference between the case group and the control group[36].

### Poor oxygenation during sleep due to respiratory problems:

Respiratory disorders and their effects on sleep are factors that greatly compromise the quality of life and health safety of the general population. Although there is still no well-

**Table 3.** Main contraindications and risks of intrauterine management of myelomeningocele.

| Contraindications | Complications |
|---|---|
| High gestational age and postdatism | Oligohydramnion and pulmonary development reduction |
| Unfixable severe fetal anomalies that are incompatible with life | Antepartum ovulary membrane rupture |
| Maternal sepsis | Premature delivery, with an increase in the incidence of prematurity retinopathy |
| Maternal metabolic decompensation | Maternal hemorrhage and adverse reactions to anesthesia |
| Pre-eclampsia | Intrauterine growth restriction |
| Eclampsia | Residual neurological deficits |

described epidemiological data, cross-sectional studies have indicated a prevalence of Apnea-Hypopnea Index (AHI) > 2.5 in 42% of cases with MMC, associated with a worse clinical picture and more severe manifestation of the disease.[37,38,39]

### Motor problems:

In the various classifications of the disease, walking problems are variable and relatively common. Mobility limitations are a cause for concern because they perpetuate social stigmas, reduce self-esteem and are potentially a cause of sedentary lifestyle, obesity and secondary health issues.

As intervention measures, physical therapy and monitoring by psychologists and physical educators, combined with medical logistics, can minimize damage and ensure better motor performance throughout life.[39]

### Fecal and urinary incontinence:

The existence of periodic bouts of constipation can cause fecal incontinence, a symptom that can be frustrating and limiting for large groups. Regarding its corrective conduct, the starting point is a conservative method, followed by trans anal irrigation, which has had its efficacy and safety proven by recent studies.

Regarding urinary flow, neurogenic bladder and deviations are common manifestations in these cases, caused by involuntary and sudden contractions of the detrusor muscle of the bladder due to damage to neural content. The use of clean intermittent catheterization and the administration of anticholinergic drugs have emerged as the gold standard for resolution.[40,41]

## CONCLUSION:

Improving quality of life and reducing morbidity and mortality should be the focus of all those who deal with patients with MMC. It is important to reinforce the role of public policies aligned with the work of a properly trained and demand-sensitive medical and multidisciplinary team, together with informed and proactive nuclear family groups. In this way, prevention can be carried out at primary, secondary, tertiary and quaternary levels in a democratic, expansive and ethical manner.

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