

Prenatal Diagnosis of Congenital Anomalies

What can and should be done?

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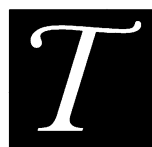
SUMMARY

Prenatal diagnosis of congenital anomalies provides an opportunity to prepare and counsel parents. It can lead to pregnancy termination; to a change in timing, mode, or location of delivery; or, in some cases, to prenatal intervention. Families with an affected fetus are best managed by a cohesive medical team. This article outlines the principles used to manage these cases.

RÉSUMÉ

Le diagnostic prénatal des malformations congénitales fournit l'occasion de préparer et de donner des conseils aux parents. Il peut s'ensuivre une décision de terminer la grossesse, de changer la date, le mode ou l'endroit de l'accouchement ou, dans certains cas, d'intervenir pendant la période prénatale. Une équipe médicale cohésive est le meilleur moyen de prendre en charge les familles affligées par un fœtus malformé. Cet article décrit les principes utilisés pour définir la ligne de conduite dans ces cas.

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TECHNOLOGICAL ADVANCES during the past 10 years have allowed us to visualize fetuses accurately. Many congenital anomalies are now diagnosed early in gestation. α -Fetoprotein monitoring has identified women who are at high risk, and techniques, such as ultrasonography, chorionic villous sampling, and cordocentesis, have permitted early diagnosis of structural and chromosomal defects.

These advances have opened a range of management options, including pregnancy termination; changes in mode (ie, cesarean or vaginal), timing (ie, preterm or term), or location (ie, community hospital or perinatal centre) of delivery; and, in highly selected cases, fetal therapy (Table 1). Optimal management of an individual case must be based on a clear understanding of the pathophysiology of the disorder, a knowledge of the natural history, and an appreciation of the ethical issues involved.

In this article current management techniques for several surgical conditions frequently diagnosed in utero are summarized. Because most of these conditions are uncommon, families should be

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referred to perinatal centres for assessment and management. Family physicians play a crucial role, however, in coordinating ongoing care and providing emotional support during what is often a highly stressful time. This review will describe principles of management, particularly from the perspective of family physicians.

Congenital hydronephrosis

Fetal hydronephrosis is frequently recognized sonographically, because the dilated bladder and renal pelvis are easily visualized and because the associated oligohydramnios is a common obstetrical indication for sonography. Fetal hydronephrosis is caused by obstruction (ureteropelvic, vesicoureteral, or urethral), neuropathy, vesicoureteral reflux, or a combination of these factors. When the process is unilateral, there is no threat to viability, but bilateral hydronephrosis has devastating consequences, including pulmonary hypoplasia from the associated oligohydramnios, chronic renal failure, and Potter's syndrome.

Most fetuses with hydronephrosis are affected unilaterally. The pregnancy should be closely monitored with repeated ultrasound examinations because the contralateral kidney sometimes becomes involved at a later date. The families of these fetuses should be referred to

Table 1. Options for management after prenatal diagnosis of a congenital anomaly

OPTION	DIAGNOSES
Elective termination	Lethal chromosomal abnormality (ie, trisomy 18) Cystic hygroma with hydrops
Change in mode of delivery (ie, cesarean section)	Massive hydrocephalus Large sacrococcygeal teratoma Conjoined twins
Change in timing of delivery (ie, preterm)	Gastroschisis with ongoing bowel damage Bowel obstruction with perforation
Change in location of delivery (ie, at perinatal centre)	Congenital diaphragmatic hernia Abdominal wall defect Intestinal obstruction Most cardiac malformations Myelomeningocele
Intervention	
• Tube decompression	Bladder outlet obstruction with oligohydramnios Fetal hydrothorax with mediastinal shift
• Open fetal surgery	Congenital diaphragmatic hernia Cystic adenomatoid malformation with hydrops

perinatal centres where they can meet with pediatric nephrologists or urologists, can be counseled about postnatal events and treatment, and can ask questions. Fetuses with isolated unilateral hydronephrosis can be delivered by obstetricians or family physicians in community hospitals and referred back to a perinatal team after birth.

Fetuses with bilateral hydronephrosis may have either ureteropelvic or bladder outlet obstruction. The most important factor in assessing prognosis is amniotic fluid volume because, in most cases, severe oligohydramnios leads to neonatal death from pulmonary hypoplasia. Most fetuses with ureteropelvic junction obstruction do not develop oligohydramnios and do not require intervention in utero.¹ But fetuses with severe long-standing oligohydramnios or marked renal dysplasia before 20 weeks' gestation usually cannot be salvaged, and pregnancy termination should be considered. Fetuses posing the greatest difficulty are those with bilateral hydronephrosis secondary to urethral obstruction, who develop oligohydramnios between 18 and 32 weeks' gestation. This small group could theoretically benefit from in utero decompression to halt ongoing damage to the developing kidneys and lungs.

Experiments have shown that prenatal decompression of fetal urinary tract obstruction arrests the adverse effects on renal development and reverses otherwise lethal pulmonary hypoplasia.^{2,3} As a result of this work, clinical bladder decompression by placement of percutaneous vesicoamniotic shunt catheters has been attempted at several centres over the past decade (*Figure 1*). Although successes have been reported, these catheters are prone to obstruction and migration and require close observation and frequent replacement.⁴ More recently, open fetal surgery has been used by Harrison's group in San Francisco.^{5,6} In pioneering work using nonhuman primates, the group developed and validated techniques for performing open fetal surgery, and established the safety of the technique for the mother and her future fertility.⁷ Although still experimental, fetal surgery could help carefully selected fetuses in the future.⁸

Congenital diaphragmatic hernia

Congenital diaphragmatic hernia (CDH) is an anatomically simple defect that is easily correctible after birth. Despite this, the mortality associated with CDH has ranged from 50% to 80%, due to bilateral pulmonary hypoplasia caused by the

presence of intrathoracic viscera during lung development. This dismal outlook has led in recent years to innovations for managing both fetuses and neonates with this disease (*Figure 2*).⁹

The most important advantage of prenatal diagnosis of CDH is the anticipation of a desperately ill newborn. The family should be referred well in advance to a perinatal centre, where the diagnosis can be confirmed by an experienced fetal sonographer, management issues can be explained and prognostic counseling done, and a relationship with the neonatologist and pediatric surgeon can be established. In every case, the child should be delivered in a tertiary care perinatal center, where neonatal, ventilatory, and surgical expertise are immediately available. This avoids the unnecessary mortality associated with transporting the sick neonate, and the delay in appropriate medical and ventilatory care that transportation entails.

Researchers have suggested that prenatal repair of CDH in poor-risk fetuses could prevent compression of the growing lungs and improve neonatal outcome. This concept is supported by considerable evidence from the fetal lamb model.¹⁰ Harrison's group has reported their preliminary¹¹ and more recent¹² experience with repair of CDH in utero – a formidable technical challenge. Despite some encouraging results, fetal surgery remains an experimental option for fetuses with CDH.

Before a management decision is made, associated abnormalities should be sought using amniocentesis and detailed ultrasound examination. If diagnosis is made in the first, or early in the second, trimester and associated lethal anomalies are found, elective termination may be offered. Fetuses without associated anomalies, who are diagnosed before 28 weeks' gestation, are candidates for open fetal surgery. If the decision is made not to intervene, or if the diagnosis is made after 28 weeks' gestation, serial ultrasound examinations should be done. In all cases an early referral should be made to a perinatal centre.

Abdominal wall defects

Abdominal wall defects, including

gastroschisis and omphalocele, can be diagnosed and differentiated prenatally by routine sonography.¹³ Omphalocele is herniation of bowel and sometimes liver into the umbilical cord. The bowel is covered by a sac, and these fetuses have a high incidence of associated structural and chromosomal anomalies. In gastroschisis, the bowel protrudes through the abdominal wall to the right of a normal umbilical cord (*Figure 3*). There is no sac, and survival mainly depends on the degree of bowel damage during development. Although these conditions differ in their natural history and pathophysiology, they should be managed similarly.

When an abdominal wall defect is diagnosed in the first or second trimester, options include elective termination of the pregnancy, early delivery before or at lung maturity, or delivery at term. The decision to terminate the pregnancy should be made only if there are associated lethal anomalies (present in approximately 30% of fetuses with omphalocele, and less than 10% of fetuses with gastroschisis).^{14,15} Most fetuses with abdominal wall defects and no associated anomalies will, with appropriate perinatal management, grow up to be normal,¹⁶ and it is crucial that prenatal counseling reflect this positive outlook.

Important management considerations include timing of delivery, mode of delivery, and transport of the patient to an appropriate centre.¹⁷ These decisions should be made by a perinatal group that includes obstetrical, neonatal, and pediatric surgical expertise. Timing of delivery is more of an issue in fetuses with gastroschisis, because early delivery prevents bowel damage in some cases.¹⁸ No evidence supports routine cesarean delivery for any of these infants, and the choice of cesarean delivery should be made on obstetrical grounds only.¹⁹ All infants with abdominal wall defects should be delivered at a tertiary care perinatal centre, where neonatal and pediatric surgical expertise are immediately available.

Neural tube defects

Hydrocephalus is commonly discovered during prenatal ultrasound examination, particularly in areas where screening for maternal serum α -fetoprotein is done.

Figure 1. **Vesicoamniotic shunt:** The shunt is placed percutaneously under ultrasound guidance. It decompresses the bladder by reconstituting amniotic fluids.

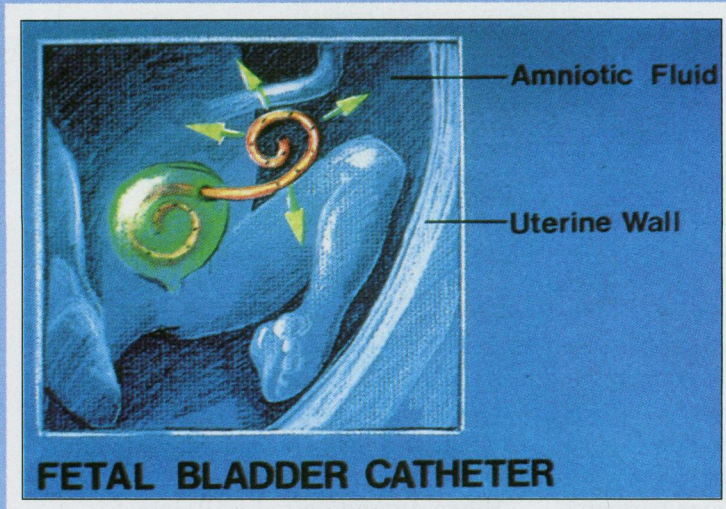


Figure 2. **Origin of pulmonary hypoplasia in fetuses with diaphragmatic hernia:** Theoretically, in utero repair of the hernia could prevent pulmonary hypoplasia and improve survival for these infants.

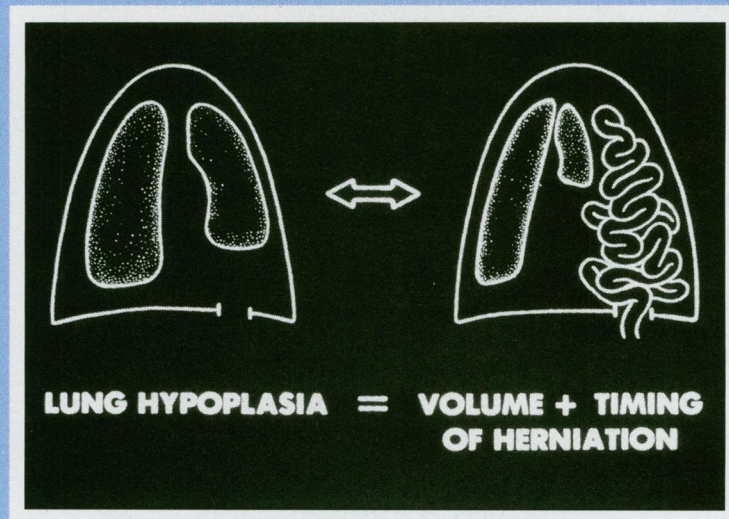
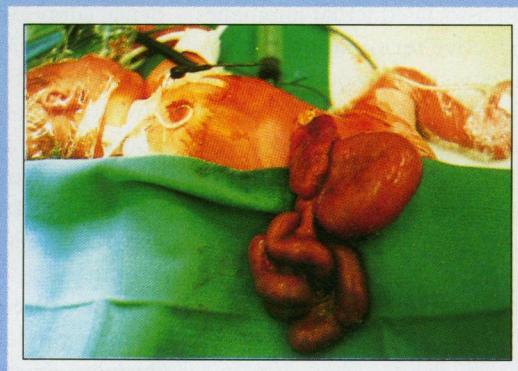


Figure 3. **Fetal gastroschisis:** A) Ultrasound image shows dilated loops of bowel floating in the amniotic fluid. B) Postnatal photograph of the infant shows dilated and thickened bowel loops.



A



B

Figure 4. Fetal gastrointestinal obstruction: A) "Double bubble" seen in duodenal atresia. The large bubble represents the dilated stomach, the smaller bubble the dilated proximal duodenum. The two bubbles are separated by the pylorus. B) Fetal abdomen has multiple fluid-filled loops of bowel, typical of a fetus with ileal atresia or meconium ileus.

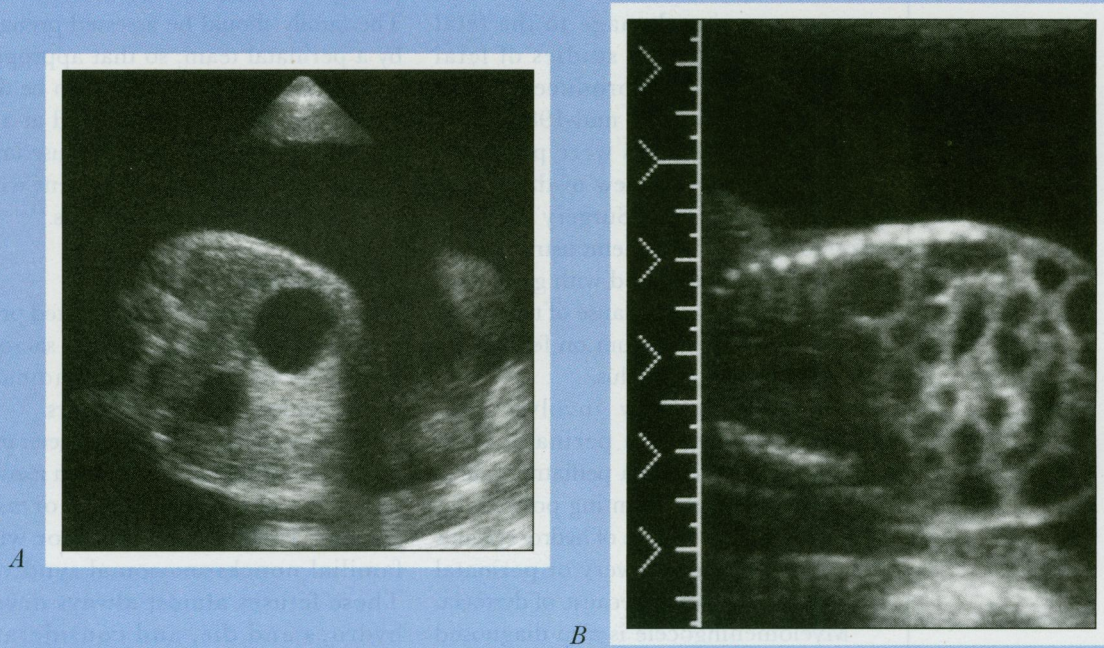
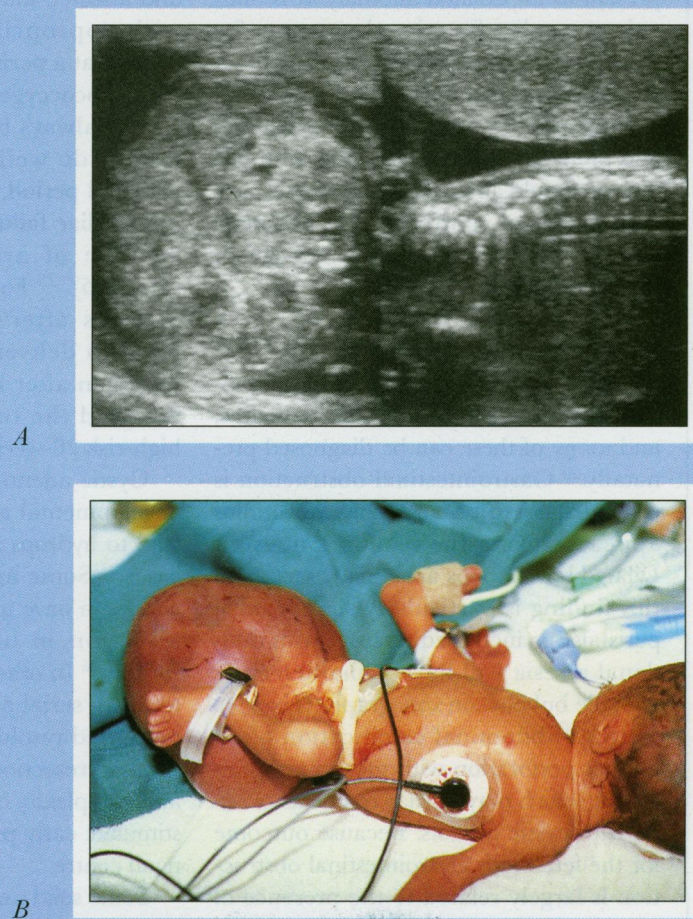


Figure 5. Fetal sacrococcygeal teratoma: A) Ultrasound image shows distal spine and a large tumour extending from the coccyx. B) Infant was delivered by cesarean section at 30 weeks' gestation because of the development of high-output cardiac failure and hydrops.



Initially researchers thought that insertion of a ventriculoamniotic shunt would decrease intraventricular pressure and prevent ongoing damage to the fetal brain. Experimental studies of fetal lambs and monkeys produced mixed results, and during the mid-1980s more than 100 such shunts were placed in human fetuses. A review of the results recorded in the Fetal Surgery Registry, centred in Winnipeg, demonstrated that very few fetuses survived with good neurological outcome.⁴ Because of this, there is currently a moratorium on fetal intervention for hydrocephalus.

Management now involves prenatal counseling by a perinatal team (which should include a pediatric neurosurgeon) and early shunting postnatally. Occasionally, the degree of hydrocephalus requires cesarean delivery or perinatal ventricular aspiration because of dystocia.

Myelomeningocele is also diagnosed frequently because of α -fetoprotein elevation. Although usually accompanied by hydrocephalus, myelomeningocele may present as an isolated anomaly. It is difficult to predict functional outcome for these fetuses, and prenatal management is, therefore, usually limited to careful investigation for associated abnormalities and prenatal counseling. Infants with this disease should all be delivered at a tertiary care perinatal centre, so that pediatric neurosurgical assessment and intervention can be expedited.

Gastrointestinal obstruction

There are multiple causes of gastrointestinal obstruction in fetuses and neonates, and many of these can be diagnosed prenatally.²⁰ Gastrointestinal obstruction is often diagnosed because polyhydramnios appears during the second trimester. Dilated bowel loops are usually seen, and this finding is particularly significant if peristalsis is increased. Fetuses with duodenal atresia will have a characteristic "double bubble" on sonographs (*Figure 4*).

Intra-abdominal calcification often implies perforation with meconium peritonitis, which may or may not be associated with cystic fibrosis. Because outcome for the fetus with gastrointestinal obstruction is largely related to the presence of associated structural and chromosomal

anomalies, careful sonographic screening, karyotype analysis, and examining family history for cystic fibrosis are imperative. The family should be assessed prenatally by a perinatal team, so that appropriate investigation and counseling can be done. The infant should be delivered at a tertiary care perinatal centre because immediate resuscitation and treatment will be needed to prevent complications.²¹

Mass lesions

Some mass lesions can be detected prenatally, including cystic hygroma, sacrococcygeal teratoma, cystic adenomatoid malformation, and solid tumours.

Fetal cystic hygroma, when seen in the first or second trimester, is often associated with a chromosomal abnormality (usually Turner's syndrome) or with a familial nonchromosomal syndrome. These fetuses almost always develop hydrops and die, and consideration should be given to elective pregnancy termination. Cystic hygromas detected late in gestation, however, are quite different, and affected infants tend to do very well with appropriate resuscitation and surgery at a perinatal centre.²²

Sacrococcygeal teratoma in fetuses is almost always benign. Although many infants do well with resection in the neonatal period, some develop high-output cardiac failure and hydrops in utero because of arteriovenous shunting (*Figure 5*).²³ For fetuses that develop hydrops after 30 weeks' gestation, preterm delivery may permit tumour resection after birth. Harrison's group resected the tumour in utero in one high-risk 26-week fetus.²⁴

Cystic adenomatoid malformation, a developmental anomaly of the lung, can lead to hydrops and fetal death in severe cases.²⁵ Some high-risk fetuses with this condition have undergone successful lung resection in utero using open fetal surgery.²⁶ In other cases, diagnosed closer to term, serial aspiration of the cyst has permitted resolution of the hydrops and surgical resection after birth. The rarity and complexity of these conditions should stimulate early prenatal referral to a perinatal centre.

Some solid tumours, such as neuroblastoma, Wilms' tumour, and hepatoblastoma,

have been diagnosed by prenatal sonography.²⁷ Prenatal diagnosis is valuable for stimulating early postnatal investigation and management.

Conclusion

Prenatal diagnosis of a congenital anomaly should be followed by early referral to a tertiary care perinatal team. Prenatal diagnosis permits the family to be counseled appropriately by experienced experts, and the delivery to be planned at a centre where neonatal and pediatric surgical expertise is immediately available. Management depends on the nature and severity of the condition and the presence or absence of associated anomalies. Prenatal diagnosis may lead to termination of the pregnancy; a change in the timing, mode, or location of delivery; or intervention in utero. Family physicians play an important role in managing these cases by providing families with ongoing support and coordination of care. ■

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For further reading

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PRESCRIBING INFORMATION

THERAPEUTIC CLASSIFICATION

Anti-inflammatory, analgesic and antipyretic agent.

INDICATION

The treatment of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis and juvenile rheumatoid arthritis.

CONTRAINDICATIONS

Naprosyn should not be given to patients with active peptic ulcer or active inflammatory disease of the gastrointestinal tract. It is also contraindicated for those who have shown a sensitivity to it and for patients in whom ASA or other NSAIDs induce the syndrome of asthma, rhinitis or urticaria. Sometimes severe and occasionally fatal anaphylactoid reactions have occurred in such individuals. Suppositories should not be given to patients under 12 years of age or those with inflammatory lesions of the rectum or anus.

WARNINGS

Peptic ulceration, perforation and gastrointestinal bleeding, sometimes severe and occasionally fatal have been reported during therapy with NSAIDs, including Naprosyn.

Naprosyn should be given under close supervision to patients prone to gastrointestinal tract irritation particularly those with a history of peptic ulcer, diverticulosis or other inflammatory disease of the gastrointestinal tract. Patients taking any NSAID should be instructed to contact a physician immediately if they experience symptoms or signs suggestive of peptic ulceration or gastrointestinal bleeding. These reactions can occur without warning at any time during the treatment. Elderly, frail and debilitated patients appear to be at higher risk from a variety of adverse reactions from NSAIDs. For such patients, consideration should be given to a starting dose lower than usual.

The safety of Naprosyn in pregnancy and lactation has not been established and its use is therefore not recommended.

PRECAUTIONS

Naprosyn (naproxen) should not be used concomitantly with the related drug Anaprox (naproxen sodium) since they both circulate in plasma as the naproxen anion.

GI system:

If peptic ulceration is suspected or confirmed, or if gastrointestinal bleeding or perforation occurs, Naprosyn should be discontinued, and appropriate treatment instituted.

Renal Effects: Patients with impaired renal function, extracellular volume depletion, sodium restrictions, heart failure, liver dysfunction, those taking diuretics, and the elderly are at greatest risk of developing overt renal decompensation. Assessment of renal function in these patients before and during therapy is recommended. Naprosyn and its metabolites are eliminated primarily by the kidneys, and therefore, a reduction in daily dosage should be anticipated to avoid the possibility of drug accumulation in patients with significantly impaired renal function.

Peripheral edema has been observed, consequently, patients with compromised cardiac function should be kept under observation when taking Naprosyn. Naprosyn Suspension contains sodium chloride (20 mg/mL). This should be considered in patients whose overall intake of sodium must be restricted.

As with other drugs used with the elderly or those with impaired liver function it is prudent to use the lowest effective dose.

Severe hepatic reactions including jaundice, and cases of fatal hepatitis have been reported with NSAIDs. The prescriber should be alert to the fact that the anti-inflammatory, analgesic and antipyretic effects of Naprosyn may mask the usual signs of infections. Periodic liver function tests and ophthalmic studies are recommended for patients on chronic therapy. Caution should be exercised by patients whose activities require alertness if they experience drowsiness, dizziness, vertigo or depression during naproxen therapy. Naprosyn may displace other albumin-bound drugs from their binding sites and may lead to drug interactions or interfere with certain laboratory tests. See Product Monograph for further details.

ADVERSE REACTIONS

(1) Denotes incidence of reported reactions between 3% and 9%. (2) Denotes incidence of reported reactions between 1% and 3%. See Product Monograph for reactions occurring in less than 1% of patients.

Gastrointestinal: Heartburn(1), constipation(1), abdominal pain(1), nausea(1), diarrhea(2), dyspepsia(2), stomatitis(2), diverticulitis(2). Rectal burning(1) has been reported occasionally with the use of naproxen suppositories.

Central Nervous System: Headache(1), dizziness(1), drowsiness(1), lightheadedness(2), vertigo(2), depression(2), and fatigue(2).

Skin: Pruritus(1), ecchymoses(1), skin eruptions(1), sweating(2), and purpura(2).

Cardiovascular: Dyspnea(1), peripheral edema(1), and palpitations(2).

Special Senses: Tinnitus(1), and hearing disturbances(2).

Others: Thirst(2).

Adverse reactions reported for SR tablets were similar to standard tablets.

DOSAGE AND ADMINISTRATION

Adult Oral: The usual total daily dosage for osteoarthritis, rheumatoid arthritis and ankylosing spondylitis is 500 mg (20 mL, 4 teaspoons) a day in divided doses. It may be increased gradually to 750 or 1000 mg or decreased depending on the patient's response. Patients with rheumatoid arthritis or osteoarthritis maintained on a dose of 750 mg/day in divided doses can be switched to a once daily dose of Naprosyn SR 750 mg. The single daily dose of Naprosyn SR should not be exceeded and can be administered in the morning or evening. Naprosyn SR tablets should be swallowed whole.

Rectal: Naprosyn Suppositories (500 mg) can replace one of the oral doses in patients receiving 1000 mg of Naprosyn daily.

Juvenile Rheumatoid Arthritis: The recommended daily dose is approximately 10 mg/kg in two divided doses.

AVAILABILITY

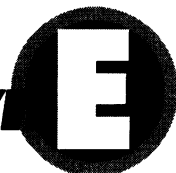
Naprosyn is available as: 125 mg, 250 mg, 375 mg, and 500 mg Tablets, as 250 mg, 375 mg and 500 mg Enteric Coated Tablets, as 750 mg Sustained-Release Tablets and 500 mg Suppositories. Suspension: Each 5 mL contains 125 mg of naproxen. Shake bottle gently before use. Pharmacists are to provide the Naprosyn Patient Information leaflet when dispensing this drug. Product Monograph available to health professionals upon request.

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