PRADER-WILLI SYNDROME

MEDICAL ALERTS

(800) 926-4797 • (941) 312-0400
www.pwsausa.org

Prader-Willi SYNDROME ASSOCIATION (USA)
SAVING AND TRANSFORMING LIVES

REVISED 2018

PRADER-WILLI SYNDROME

Prader-Willi syndrome (PWS) is a complex neurobehavioral genetic disorder resulting from abnormality on the 15th chromosome. It occurs in males and females equally and in all races. Prevalence estimates range from 1:12,000 to 1:15,000. Incidence in newborns is unknown.

PWS typically causes low muscle tone, short stature if not treated with growth hormone, cognitive deficits, incomplete sexual development, problem behaviors, and a chronic feeling of hunger that, coupled with a metabolism that utilizes drastically fewer calories than normal, can lead to excessive eating and life-threatening obesity.

It is felt to be a multistage disorder with decreased fetal movement prenatally and low birth weight. Infants have failure to thrive due to feeding problems and hypotonia. Toddlers have increased weight gain, then hyperphagia and obesity as they get older, if calories are not restricted. Most of the medical problems in Prader-Willi syndrome are related to the obesity, hypotonia, and hypothalamic dysfunction.

Some of the other factors that may cause difficulties include adverse reactions to medications, high pain tolerance, gastro-intestinal and respiratory issues, lack of vomiting, and unstable temperature. Adrenal insufficiency may also occur.

Severe medical complications can develop rapidly in individuals with PWS.

Members of the Clinical Advisory Board are available for consultation with physicians through the Prader-Willi Syndrome Association (USA).

Prader-Willi Syndrome Medical Alerts
by
Medical Specialists in Prader-Willi Syndrome

This life-saving Medical Alerts Booklet is dedicated to Janalee Heinemann in appreciation for a lifetime of service to the PWS community and the truly thousands of lives that were saved and transformed by her skill, compassion, and dedication.

Anna Loker, daughter of Jim and Carolyn Loker and Tad Tomaseski, son of Janalee and Al Heinemann

8588 Potter Park Drive, Suite 500, Sarasota, FL 34238
(800) 926-4797 (941) 312-0400 FAX: (941) 312-0142
Email: info@pwsausa.org Website: www.pwsausa.org

By
Janalee Heinemann, M.S.W.
Carolyn Loker
PWSA (USA) Clinical Advisory Board

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Revised 2015
James Loker, M.D.
Carolyn Loker
Janalee Heinemann, M.S.W.
Suzanne Cassidy, M.D.

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Kathy Clark, R.N., M.S.N. CS-BC
James Loker, M.D.

Mission

Prader-Willi Syndrome Association (USA)
is an organization of families and professionals
working together to raise awareness, offer support,
provide education and advocacy, and promote
and fund research to enhance the quality of life
of those affected by Prader-Willi syndrome.

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MEDICAL ALERT

Important Considerations for Routine or Emergency Treatment

Obesity and its related complications is the major cause of morbidity and mortality in Prader-Willi syndrome. Keeping the individual at a healthy weight will minimize these complications but there are important medical and behavior problems unique to Prader-Willi syndrome regardless of weight status.

Medical professionals can contact PWSA (USA) to obtain more information and be put in touch with a specialist as needed. Up-to-date has an excellent summary of the syndrome.

Central Adrenal Insufficiency in Individuals with Prader-Willi Syndrome

Several studies have shown CAI in individuals with PWS while others failed to show a deficiency. Stress dose of cortisol may be indicated if individual has problems after surgery or during times of stress. **http://www.pwsausa.org** and view Medical section under Adrenal Insufficiency.

Falls and Fractures

Individuals with PWS may have significant fractures from simple falls and require x-rays even if they

do not complain of pain. Persistent pain, swelling, guarding, or decreased movement of the extremity for more than a few days may warrant an x-ray.

Hyperphagia (Excessive Appetite)

Individuals with PWS must be constantly supervised in all settings to prevent access to food. In hospital settings, obtaining unguarded food can lead to rapid ingestion and fatal choking. Individuals who have normal weight have achieved this because of strict external control of their diet and food intake; these individuals are not less likely to ingest available food. There are no treatments for this relentless hunger. Insatiable appetite may lead to life-threatening weight gain, which can be very rapid and occur even on a low-calorie diet.

Medications – Adverse reactions

People with PWS may have unusual reactions to standard dosages of medications. Use extreme caution in giving medications, especially those that may cause sedation; prolonged and exaggerated responses have been reported. Metabolism of the drugs may be impaired in individuals with PWS.

Pain Insensitivity

Lack of typical pain signals is common and may mask the presence of infection or injury. Someone with PWS may not complain of pain until infection is

severe or may have difficulty localizing pain. Parent/caregiver reports of subtle changes in condition or behavior should be investigated for medical cause. Any complaint of pain by a person with PWS should be taken seriously.

Skin Lesions and Bruises

Because of a habit that is common in PWS, open sores caused by skin picking may be apparent. Individuals with PWS also tend to bruise easily. These lesions can cause serious life-threatening infections. There are approaches to help mitigate picking. **http://www.pwsausa.org** and view Medical section under Skin Picking. Appearance of such wounds and bruises may erroneously lead to suspicion of physical abuse.

Swallowing and Choking

Persons with PWS are highly likely to have an undetected swallowing problem that places them at risk for asphyxiation of a food bolus (choking), and they require a specific type of swallowing evaluation. A clinical or bedside evaluation is not sufficient to detect dysphagia in this population. They frequently cannot tell if they cleared their airway after swallowing, increasing the risk for aspiration. Choking can also occur with rapid ingestion of unguarded foods and has led to many deaths in the PWS population.

http://www.pwsausa.org and view Medical section under Choking/Swallowing.

Temperature Abnormalities

Idiopathic hyper- and hypothermia have been reported. Hyperthermia may occur during minor illness and in procedures requiring anesthesia. Fever may be absent despite serious infection. All individuals with PWS are at risk for mild hypothermia because of impaired peripheral somatosensory and central thermoregulation, poor judgment and cognitive inflexibility. Malignant hypothermia is a life-threatening problem occasionally seen in PWS. **http://www.pwsausa.org** and view Medical section under Temperature.

Vomiting – Lack of ability to vomit

Vomiting rarely occurs in those with PWS. Emetics may be ineffective, and repeated doses may cause toxicity. This characteristic is of particular concern in light of hyperphagia and the possible ingestion of uncooked, spoiled, or otherwise unhealthful food items. **The presence of vomiting may signal a life-threatening illness and may warrant immediate treatment.**

Water Intoxication

Water intoxication has occurred in relation to use

of certain medications with antidiuretic effects, as well as from excess (binging) fluid intake alone. Anti-diarrheal medications may cause severe colonic distension, necrosis and rupture and should be avoided.

http://www.pwsausa.org and view Medical section under Water Intoxication.

Respiratory Concerns

Individuals with PWS are at increased risk for respiratory difficulties. Hypotonia, weak chest muscles, swallowing abnormalities and sleep apnea are common. Anyone with significant snoring, regardless of age, should have a medical evaluation to look for obstructive sleep apnea. Infants commonly have central sleep apnea which generally improves over time but may also have obstructive sleep apnea due to hypotonia and other factors. Hypotonia can lead to diminished activity levels and low aerobic capacity. Hypoventilation may be central in origin.

In children with PWS, chronic stomach reflux and aspiration are emerging as common problems. Reflux should be considered in young children with chronic respiratory problems; videofluroscopy is the preferred test. Individuals with obstructive apnea or obesity are at more risk for reflux.

Recommendations for Evaluation of Breathing Abnormalities Associated with Sleep in Prader-Willi Syndrome

PWSA (USA) Clinical Advisory Board Consensus Statement - 12/2003

Problems with sleep and sleep disordered breathing have been long known to affect individuals with Prader-Willi syndrome (PWS). The problems have been frequently diagnosed as sleep apnea (obstructive [OSA], central or mixed) or hypoventilation with hypoxia. Disturbances in sleep architecture (delayed sleep onset, frequent arousals and increased time of wakefulness after sleep onset) are also frequently common. Although prior studies have shown that many patients with PWS have relatively mild abnormalities in ventilation during sleep, it has been known for some time that certain individuals may experience severe obstructive events that may be unpredictable.

Factors that seem to increase the risk of sleep disordered breathing include young age, severe hypotonia, narrow airway, morbid obesity and prior respiratory problems requiring intervention such as respiratory failure, reactive airway disease and hypoventilation with hypoxia. Due to a few recent fatalities reported in individuals with PWS who were on growth hormone therapy (GH), some physicians have also added this as an additional risk

factor. One possibility (that is currently unproven) is that GH could increase the growth of lymphoid tissue in the airway thus worsening already existing hypoventilation or OSA. Nonetheless, it must be emphasized that there is currently no definitive data demonstrating that GH causes or worsens sleep disordered breathing. However, to address this new concern, as well as the historically well documented increased risk of sleep-related breathing abnormalities in PWS, **the Clinical Advisory Board of the PWSA (USA) makes the following recommendations:**

1. A sleep study or a polysomnogram that includes measurement of oxygen saturation and carbon dioxide for evaluation of hypoventilation, upper airway obstruction, obstructive sleep apnea and central apnea should be contemplated for all individuals with Prader-Willi syndrome. These studies should include sleep staging and be evaluated by experts with sufficient expertise for the age of the patient being studied.

2. Risk factors that should be considered to expedite the scheduling of a sleep study should include:

- Severe obesity - weight over 200% of ideal body weight (IBW).
- History of chronic respiratory infections or reactive airway disease (asthma).

- History of snoring, sleep apnea or frequent awakenings from sleep.
- History of excessive daytime sleepiness, especially if this is getting worse.
- Before major surgery including tonsillectomy and adenoidectomy.
- Prior to sedation for procedures, imaging scans and dental work.
- Prior to starting growth hormone or if currently receiving growth hormone therapy.

Additional sleep studies should be considered if patients have the onset of one of these risk factors, especially a sudden increase in weight or change in exercise tolerance. **If a patient is being treated with growth hormone, it is not necessary to stop the growth hormone before obtaining a sleep study unless there has been a new onset of significant respiratory problems.**

Any abnormalities in sleep studies should be discussed with the ordering physician and a pulmonary specialist knowledgeable about treating sleep disturbances to ensure that a detailed plan for treatment and management is made. Referral to a pediatric or adult pulmonologist with experience in treating sleep apnea is strongly encouraged for management of the respiratory care.

In addition to a calorically restricted diet to ensure

weight loss or maintenance of an appropriate weight, a management plan may include modalities such as:

- Supplemental oxygen
- Continuous positive airway pressure (CPAP) or BiPAP
- Oxygen should be used with care as some individuals may have hypoxemia as their only ventilatory drive and oxygen therapy may actually worsen their breathing at night.
- Behavior training is sometimes needed to gain acceptance of CPAP or BiPAP.
- Medications to treat behavior may be required to ensure adherence to the treatment plan.

If sleep studies are abnormal in the morbidly obese child or adult (IBW > 200%) the primary problem of weight should be addressed with an intensive intervention - specifically, an increase in exercise and dietary restriction. Both are far preferable to surgical interventions of all kinds. Techniques for achieving this are available from clinics and centers that provide care for PWS and from the national parent support organization [PWSA (USA)]. Behavioral problems interfering with diet and exercise may need to be addressed simultaneously by persons experienced with PWS.

If airway related surgery is considered, the treating surgeon and anesthesiologist should be knowledgeable about the unique pre- and postoperative problems found in individuals affected by Prader-Willi syndrome.

Tracheostomy surgery and management present unique problems for people with PWS and should be avoided in all but the most extreme cases. Tracheostomy is typically not warranted in the compromised, morbidly obese individual because the fundamental defect is virtually always hypoventilation, not obstruction. Self-endangerment and injury to the site are common in individuals with PWS who have tracheostomies placed.

At this time there is no direct evidence of a causative link between growth hormone and the respiratory problems seen in PWS. Growth hormone has been shown to have many beneficial effects in most individuals with PWS including improvement in the respiratory system. Decisions in the management of abnormal sleep studies should include a risk/benefit ratio of growth hormone therapy. It may be reassuring for the family and the treating physician to obtain a sleep study prior to the initiation of growth hormone therapy and after 6-8 weeks of therapy to assess the difference that growth hormone therapy may make. A follow-up study after one year of treatment with growth hormone may also be indicated.

Growth Hormone Treatment and Prader-Willi Syndrome

PWSA (USA) Clinical Advisory Board Consensus Statement - 6/2009
PWSA International Consensus Statement 2013

Both statements are found at **http://www.pwsausa.org** and view Medical section under Growth Hormone.

In-Patient Considerations

Access difficulties – venous and airway

Obesity and poor muscle tone may complicate line placement. A small airway, high palate, and/or obesity may complicate ability to intubate. Saliva is often thick and sticky. Many persons with PWS will have difficult IV access due to increased fat mass and smaller than normal blood vessels. Outpatient procedures and general sedation may be especially problematic. Care must be taken during procedures done in out of hospital settings, and that proper equipment for resuscitation is immediately available and consideration for doing these procedures in an OR should be discussed. Procedures where more than light sedation is used may warrant an overnight observation.

Anesthesia

People with PWS may have unusual reactions to standard dosages of anesthetic agents. Use caution in giving anesthesia. Serious problems occur during conscious sedation, if it is not well monitored, rather than from the use of general anesthesia and airway management. Ongoing assessment of breathing and oxygen saturation is critical in all outpatient procedures including dental work.

http://www.pwsausa.org and view the Medical section for articles on Anesthesia.

- Anesthesia and Prader-Willi Syndrome: James Loker, M.D., Laurence Rosenfield, M.D.
- Anesthesia Concerns for Patients with PWS: Winthrop University

Behavior problems

Individuals are prone to emotional outbursts, obsessive-compulsive behaviors, and psychosis. Psychotropic medications may affect metabolism of anesthesia leading to shorter or longer duration of action.

Cardiac problems

Surprisingly, coronary disease is less in PWS than in individuals with similar obesity. Cardiac problems usually are due to hypoventilation right heart failure. Edema can often be seen in the obese individual

even in the absence of heart failure and is treated by weight loss and ambulation. Diuretics are usually not that beneficial in treating the edema.

Food seeking behaviors/Relentless hunger

Complete safety from access to food is essential in any health care setting. Assume individual has eaten unless verified by caregiver. Complaints of hunger should not result in access to snacks or food. Patients in the hospital should have someone with them at all times. The individual may be on a caloric restricted diet and that should be conveyed to the nutritionist and kitchen.

Hypothalamic dysfunction – Pituitary deficiencies

Hypothyroidism- Risk of central (TSH deficiency) hypothyroidism is 20-30% and may be undiagnosed prior to surgery.

Growth hormone deficiency - All individuals should be considered to be GH deficient.

Hypothalamic dysfunction is also the presumed origin of many other unique problems including temperature regulation, hunger, ventilatory effort, behavior patterns.

Hypotonia

This muscle weakness may complicate ability to cough effectively and clear airways.

Narcotics

Individuals may have an exaggerated response to narcotics. Use the lowest possible dose to achieve the desired state of anesthesia. Many individuals have delayed gastric emptying that can be compounded with narcotics.

Obesity

Consideration for obstructive apnea, pulmonary hypertension, diabetes, and right heart failure should be addressed.

Pain insensitivity

Unexplained tachypnea or tachycardia may be the only indication of pain. Behavior problems which are not typical for this person may be evidence of pain. Individuals with PWS may not respond to pain in the same manner as others and it may mask the presence of underlying problems. Since pain may not be present, other signs of underlying problems should be monitored.

Pulmonary embolism

Individuals with PWS are at risk for pulmonary embolism. DVT prophylaxis should be considered in all obese individuals. Prolonged bed rest is to be avoided.

Psychosis

There is an increased risk of psychosis in individuals with PWS, which can be triggered by significant events such as changes in routines and serious illness. Prompt attention to hallucinations or reported change in typical behavior is essential. View mental health issues **http://www.pwsausa.org/medical-issues-a-z/** under Psychiatric concerns.

Saliva abnormalities

Thick sticky saliva complicates airway management especially during conscious sedation and increases the risk of caries. Dried saliva may not be an indication of hydration status. Water drinking is minimal in the majority of individuals with PWS.

Skin picking

May complicate healing of IV sites and incisional wounds. Restraints or gloves may be necessary to protect wounds during healing.

Temperature instability

Low basal temperature is typical in healthy individuals with PWS. Hypothalamic dysregulation can lead to poor control during fever or hypothermia. There is no known predisposition to malignant hyperthermia, but depolarizing muscle relaxants should be avoided if possible.

Surgical and Orthopedic Concerns

With the increasing number of infants and children with PWS undergoing sleep assessments prior to growth hormone treatment and the potential rise in surgical procedures (e.g., tonsillectomy) requiring intubation and anesthesia, it will be important to alert the medical team about complications that may include trauma to the airway, oropharynx, or lungs due to possible anatomic and physiologic differences seen in PWS. They can include a narrow airway, underdevelopment of the larynx and trachea, hypotonia, edema, and scoliosis.

Musculoskeletal manifestations, including scoliosis, hip dysplasia, fractured bones (which may be undetected), osteoporosis and lower limb alignment abnormalities, are described in the orthopedic literature. However, care of this patient population from the orthopedic surgeon's perspective is

complicated by other clinical manifestations of PWS. **http://www.pwsausa.org** and view Medical section under Orthopedic Issues.

Postoperative Monitoring of Patients with Prader-Willi Syndrome

Patients with PWS are known to have increased morbidity after surgery due to:

- Abnormal physiological response to hypercapnia and hypoxia
- Hypotonia
- Narrow oropharyngeal space
- High incidence of central, obstructive and mixed apnea
- Thick secretions
- Obesity
- Increased incidence of scoliosis with decreased pulmonary function
- Prolonged exaggerated response to sedatives
- Increased risk for aspiration
- Decreased pain sensation
- Possible challenges with compliance to pre- and postoperative treatment procedures due to:
  - Extreme food seeking behavior and hyperphagia due to hypothalamic dysfunction
  - High incidence of gastroparesis and slow motility of the intestinal tract

– Extreme skin picking which may interfere with wound healing
– Altered temperature regulation – fever may be absent in the presence of infection. There does not seem to be a higher incidence of malignant hyperthermia
– The possibility of central adrenal insufficiency

RECOMMENDATIONS:

- Patients with PWS who undergo deep sedation and general anesthesia should be recovered overnight in a monitored unit. Infants and children may require intensive care monitoring.
- Continuous monitoring of pulse-oximetry for 24 hours postoperative with attention to airway and breathing.
- A conservative approach to pain management and use of narcotic agents.
- Full assessment of return of GI motility prior to initiation of intake by mouth because of the predisposition to ileus after surgery.
- Scheduling procedure as early in the day as possible to prevent prolonged time period where food seeking could take place.
- Direct supervision (1:1) to prevent foraging postoperatively.

- Monitor for picking at wounds and/or incisions. These may require additional dressings and other barriers including full time sitter to prevent access to surgical site and medical devices.
- Close observation of wound for signs of infection.
- Utilization of respiratory therapy interventions to prevent atelectasis and/or postoperative lung infection.
- Due to the hypotonia and obesity, individuals with PWS are at risk for deep venous thrombi (DVT) and pulmonary embolism. Patients should be under the guidelines for DVT prophylaxis.

http://www.pwsausa.org and view Medical section under Postoperative Monitoring of Patients with Prader-Willi Syndrome.

Severe Gastric Intestinal Concerns

Vomiting – Lack of ability to vomit

Vomiting rarely occurs in those with PWS. Emetics may be ineffective, and repeated doses may cause toxicity. This characteristic is of particular concern in light of hyperphagia and the possible ingestion of uncooked, spoiled, or otherwise unhealthful food items. **The presence of vomiting may signal a life-threatening illness and may warrant immediate treatment.**

Severe Gastric Illness

Gastric problems are very common in PWS due to decreased motility and gastroparesis. Abdominal distension or bloating, pain and/or vomiting may be signs of life-threatening gastric dilation, inflammation or necrosis. Rather than localized pain, there may be a general or vague feeling of being unwell. Any individual with PWS with these symptoms needs immediate medical attention. An x-ray, CT scan or ultrasound can help with the diagnosis and confirm if there is gastric necrosis and/or perforation. **If distension is noted, these individuals need close monitoring, made NPO and may need decompression with an NG tube.**

Gastric necrosis or perforation is a medical emergency requiring exploratory laparotomy or emergent surgery. Individuals with PWS may not have tenderness, rigidity or rebound normally associated with an acute abdomen.

In addition to gastric distension, colonic impaction may also be present and need to be addressed. Stomach pain can also be due to gallstones or pancreatitis. An ultrasound, chemistry analysis of the blood and CT of the abdomen will help with the diagnosis.

Constipation in Individuals with Prader-Willi Syndrome

James Loker, M.D., Pediatric Cardiologist
Ann Scheimann, M.D., M.B.A., Gastroenterologist
PWSA (USA) Clinical Advisory Board Members

Constipation is a common problem in individuals with Prader-Willi syndrome (PWS). It takes longer for food to move through the GI system in Prader-Willi syndrome*. This slower passage of food can lead to serious issues similar to the ones seen related to the stomach. Outpatient methods used to clear constipation in non-PWS patients may be ineffective due to poor fluid intake and hypotonia. Inpatient regimens frequently use large volumes of fluid which may cause problems. Reliance on these methods may lead to life-threatening conditions such as necrosis and perforation of the colon and subsequent sepsis. Due to decreased muscle tone and altered pain response, individuals with PWS may not have the same clinical exam that a non-PWS patient would have. A heavier reliance on imaging may be necessary. Individuals with PWS may be at higher risk for impaction. Rectal examination and enema may be required in addition to oral cleanout regimen. This may also be problematic in some leading to rectal picking.

Patients with PWS having constipation and receiving

repeated regimens of oral PEG (polyethylene glycol) solution for bowel cleansing should be monitored closely for abdominal distention and retention. Failure of standard constipation protocols to clear the stool in a timely manner, especially in the face of increasing abdominal distension, vomiting, decreased appetite, stoppage of food consumption and/or abdominal pain warrants surgical or GI consultation. Emergent surgical or colonoscopic intervention may be necessary.

Kuhlmann, et al. (2014) A descriptive study of colorectal function in adults with Prader-Willi syndrome: high prevalence of constipation.* ***BMC Gastroenterology*, Apr 4; Vol 14: page 63

Prader-Willi Syndrome (USA) ALERT! Risk of Stomach Necrosis and Rupture

Possibly Related to Chronic Gastroparesis

A Cause of Death from Sepsis, Gastric Necrosis or Blood Loss

Signs and symptoms of stomach necrosis and rupture:

- **Vomiting-** Any vomiting is very unusual in Prader-Willi syndrome
- **Loss of appetite-** (ominous sign)
- **Lethargy**

- **Complaints of pain, usually non-specific-** Pain sensation is abnormal in Prader-Willi syndrome due to high pain threshold; rarely complain of pain
- **Pain** is often poorly localized
- **Peritoneal signs** may be absent
- **Abdominal/stomach bloating and gastric dilation**
- **Fever may or may not be present**
- **Temperature regulation** is altered in Prader-Willi syndrome
- **Guaiac positive stools (chronic gastritis)**

An algorithm for ER evaluation of an individual with PWS and abdominal complaints is on a foldout page in the back of this publication.

These Signs should raise suspicion of STOMACH NECROSIS/RUPTURE as a possible diagnosis which can be LIFE-THREATENING!

History may include:

- **History of binge eating within the week**
- **Hyperphagia and binge eating are characteristic** of Prader-Willi syndrome, regardless of whether obese or slim

- **Frequently occurs** after holiday, or social occasion with less supervision of intake
- **History of gastroparesis-** Common in Prader-Willi syndrome, though often undiagnosed
- **Often slim or history of significant obesity followed by weight loss-** May leave the stomach wall thinned
  http://www.pwsausa.org and view Medical section under Gastric/Intestinal.

IN THE EVENT OF DEATH

In the case of a death or impending death, please call PWSA (USA) immediately **at 1-800-926-4797** for support and advice.

Reporting of Deaths

The Prader-Willi Syndrome Association (USA) has created a research database of reported deaths of individuals with PWS. Although most premature deaths are attributable to morbid obesity, cases unrelated to obesity have been noted. PWSA (USA) has a formal investigation of causes of death.

PWSA (USA) also provides bereavement support to families who have lost children with PWS. Please call PWSA (USA) to report a death and also so the family can receive support.

Organ Donation for Research

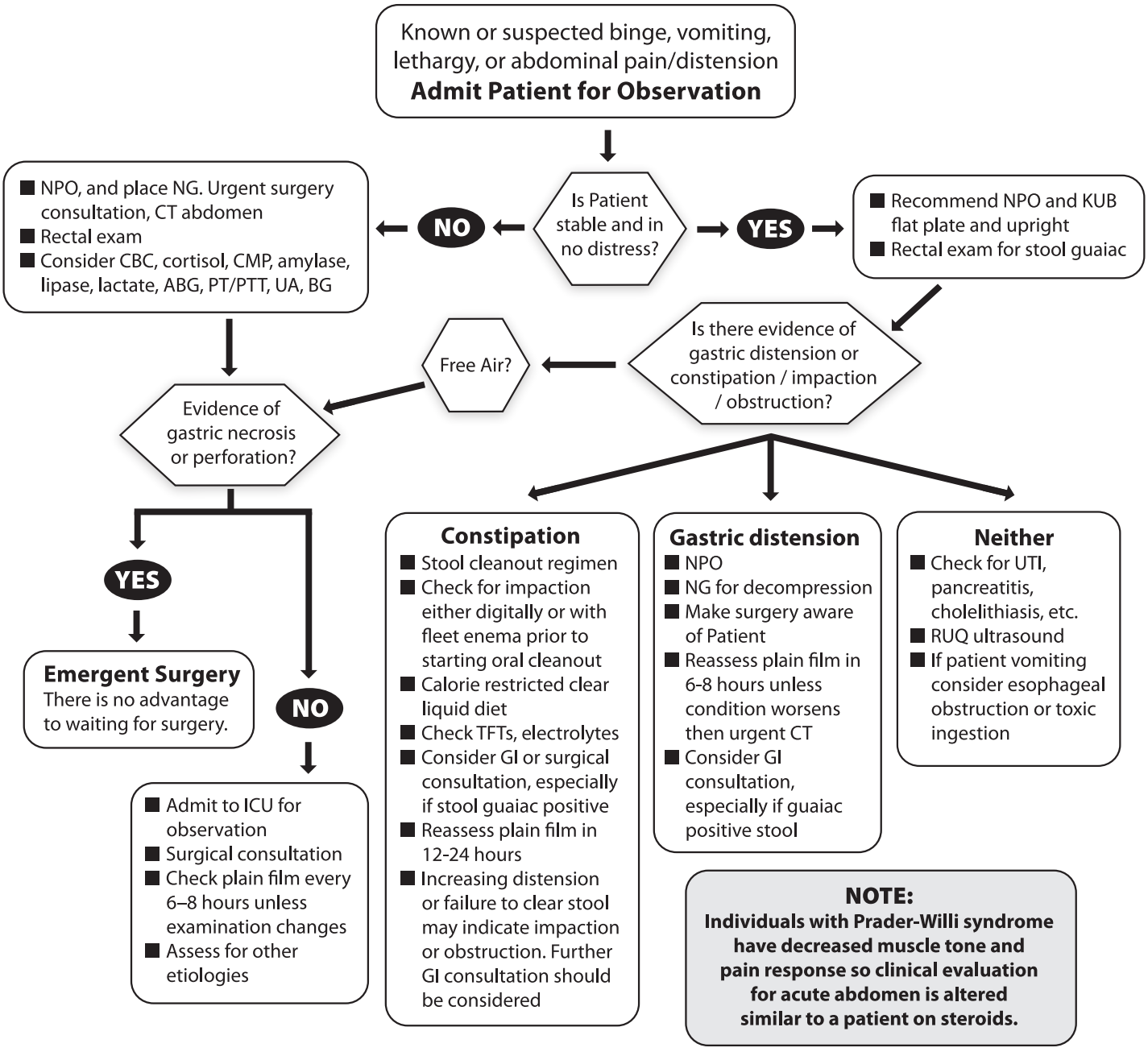
When a child or adult with PWS dies, the family may wish to consider donation of organs for research. PWSA (USA) has established a procedure for such donations.

For donating brain tissue, contact the Brain and Tissue Bank at the University of Maryland, (800) 847-1539.

http://www.pwsausa.org and view Medical section under In the Event of Death.

Important Notes

Evaluation of Individuals with Prader-Willi Syndrome with GI Complaints



Prader-Willi SYNDROME ASSOCIATION (USA)
SAVING AND TRANSFORMING LIVES

Credits: James Loker, M.D., Pediatric Cardiologist • Ann Scheimann, M.D., M.B.A., Gastroenterologist
PWSA (USA) Clinical Advisory Board Members

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Important Notes

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Prader-Willi SYNDROME ASSOCIATION (USA)
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Prader-Willi Syndrome Association (USA)
8588 Potter Park Drive, Suite 500
Sarasota, FL 34238

(800) 926-4797 • (941) 312-0400
Fax: (941) 312-0142

Email: info@pwsausa.org • Website: www.pwsausa.org