



THOMSON REUTERS™

# IODINE

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## DRUGDEX® Evaluations

### IODINE

#### 0.0 Overview

##### 1) Class

a) This drug is a member of the following class(es):

- Antibacterial
- Antibacterial Cleansing Agent
- Antithyroid Agent
- Expectorant
- Iodide Supplement
- Iodine** Supplement
- Mineral/Nutriceutical Combination
- Parenteral Mineral-Trace Mineral
- Radiation Emergency, Thyroid Blocking Agent

##### 2) Dosing Information

###### a) Iodine

###### 1) Adult

###### a) Disinfection

- 1) 2% aqueous solution TOPICALLY for minor wounds
- 2) 2% tincture TOPICALLY on intact skin
- 3) 2% in glycerin TOPICALLY on mucous membranes

###### b) Thyroid storm

- 1) 5 to 10 drops of Lugol's solution (8 mg iodide/drop) or 1 to 2 drops of saturated solution of potassium iodide (50 mg of iodide/drop) 3 times a day mixed in water or juice

###### 2) Pediatric

###### a) Disinfection

- 1) 2% aqueous solution TOPICALLY for minor wounds
- 2) 2% tincture TOPICALLY on intact skin
- 3) 2% in glycerin TOPICALLY on mucous membranes

###### b) Potassium Iodide

###### 1) Adult

###### a) Cutaneous sporotrichosis

- 1) initial, 5 drops (using a standard eye-dropper) saturated solution ORALLY 3 times daily; increase as tolerated to 40 to 50 drops ORALLY 3 times daily; continue for 2 to 4 weeks after all lesions have healed (Kauffman et al, 2007)

###### b) Implementation of protective measures to prevent injury due to radiation sources, Thyroid gland; Prophylaxis

- 1) 130 mg ORALLY daily (Prod Info IOSTAT(TM) oral tablets, 2005; Prod Info THYROSHIELD(TM) oral solution, 2005)

###### c) Induction of involution of thyroid

- 1) 60-250 mg ORALLY 3 times a day for 10 days before surgery

###### d) Lymphocutaneous sporotrichosis

- 1) initial, 5 drops (using a standard eye-dropper) saturated solution ORALLY 3 times daily; increase as tolerated to 40 to 50 drops ORALLY 3 times daily; continue for 2 to 4 weeks after all lesions have healed (Kauffman et al, 2007)

###### 2) Pediatric

###### a) Cutaneous sporotrichosis

- 1) initial, 1 drop (using a standard eye-dropper) saturated solution ORALLY 3 times daily; increase as tolerated up to MAX of 1 drop/kg or 40 to 50 drops ORALLY 3 times daily (whichever is lowest); continue for 2 to 4 weeks after all lesions have healed (Kauffman et al, 2007)

###### b) Implementation of protective measures to prevent injury due to radiation sources, Thyroid gland; Prophylaxis

- 1) over 12 y and weigh 150 lbs or greater, 130 mg ORALLY daily (Prod Info IOSTAT(TM) oral

- tablets, 2005; Prod Info THYROSHIELD(TM) oral solution, 2005)
  - 2) over 12 y and weigh 150 lbs or less, 65 mg ORALLY daily (Prod Info IOSTAT(TM) oral tablets, 2005; Prod Info THYROSHIELD(TM) oral solution, 2005)
  - 3) 3 to 12 y, 65 mg ORALLY daily (Prod Info IOSTAT(TM) oral tablets, 2005; Prod Info THYROSHIELD(TM) oral solution, 2005)
  - 4) 1 mo to 3 y, 32.5 mg ORALLY daily (Prod Info IOSTAT(TM) oral tablets, 2005; Prod Info THYROSHIELD(TM) oral solution, 2005)
  - 5) birth to 1 mo, 16.25 mg ORALLY daily (Prod Info IOSTAT(TM) oral tablets, 2005; Prod Info THYROSHIELD(TM) oral solution, 2005)
  - c) Lymphocutaneous sporotrichosis
    - 1) initial, 1 drop (using a standard eye-dropper) saturated solution ORALLY 3 times daily; increase as tolerated up to MAX of 1 drop/kg or 40 to 50 drops ORALLY 3 times daily (whichever is lowest); continue for 2 to 4 weeks after all lesions have healed (Kauffman et al, 2007)
- 3) Contraindications
- a) **Iodine**
    - 1) hypersensitivity to **iodine**
    - 2) burn patients
  - b) Potassium Iodide
    - 1) hypersensitivity to iodide products
    - 2) renal disorders
    - 3) **iodine**-induced goiter
- 4) Serious Adverse Effects
- a) Potassium Iodide
    - 1) Goiter, Prolonged or excessive use
    - 2) Hypothyroidism, Prolonged or excessive use
    - 3) Immune hypersensitivity reaction
    - 4) Thyroid adenoma, Prolonged or excessive use
- 5) Clinical Applications
- a) **Iodine**
    - 1) FDA Approved Indications
      - a) Disinfection
      - b) Thyroid storm
  - b) Potassium Iodide
    - 1) FDA Approved Indications
      - a) Implementation of protective measures to prevent injury due to radiation sources, Thyroid gland; Prophylaxis
    - 2) Non-FDA Approved Indications
      - a) Cutaneous sporotrichosis
      - b) Induction of involution of thyroid
      - c) Lymphocutaneous sporotrichosis

## 1.0 Dosing Information

Drug Properties

Adult Dosage

Pediatric Dosage

### 1.1 Drug Properties

- A)** Information on specific products and dosage forms can be obtained by referring to the Tradename List (Product Index)
- B)** Synonyms
  - Ca Iodide
  - Calcium Iodide
  - Iodine**
  - KI

K Iodide  
Na Iodide  
Potassium Iodide  
Sodium Iodide  
Zinc Iodide  
Zn Iodide

**C) Physicochemical Properties**

**1) Iodine**

**a) Molecular Weight**

**1) 126.9 (Dollery, 1991) (Fleeger, 1992)**

**2) Potassium Iodide**

**a) Molecular Weight**

**1) 166.00**

**3) Sodium Iodide**

**a) Molecular Weight**

**1) Elemental iodine: 126.9 (Nichoalds, 1983); Sodium iodide: 149.89 (Fleeger, 1994)**

**1.3 Adult Dosage**

**1.3.1 Normal Dosage**

Iodine

Potassium Iodide

**1.3.1.A Iodine**

Oral route

Topical application route

**1.3.1.A.1 Oral route**

**1.3.1.A.1.a Endemic goiter**

**1) A 400-microgram daily dose of iodine, as di-iodotyrosine, has been successfully used to treat patients with ENDEMIC GOITER due to iodine deficiency. The iodine caused a significant reduction in the size of diffuse goiters (Hintze et al, 1989).**

**1.3.1.A.2 Topical application route**

**1.3.1.A.2.a Disinfection**

**1) For DECONTAMINATION OF MINOR WOUNDS, a 2% aqueous solution applied to the affected area is recommended (AMA Department of Drugs, 1986b). For DISINFECTION OF INTACT SKIN, a 2% tincture in an alcoholic vehicle is used (Goodman & Gilman, 1970; AMA Department of Drugs, 1986b; Osol, 1980a). For DISINFECTION OF MUCOUS MEMBRANES, a 2% solution of iodine in glycerin is the preparation of choice (Goodman & Gilman, 1970; Osol, 1980a).**

**1.3.1.B Potassium Iodide**

**1.3.1.B.1 Oral route**

Cutaneous sporotrichosis

Erythematous condition

Implementation of protective measures to prevent injury due to radiation sources, Thyroid gland;  
Prophylaxis

Lymphocutaneous sporotrichosis

#### **1.3.1.B.1.a Cutaneous sporotrichosis**

1) As an alternative treatment to itraconazole for cutaneous sporotrichosis, the recommended dose of saturated solution of potassium iodide (SSKI) is an initial dose of 5 drops (using a standard eye-dropper) orally 3 times daily, increasing as tolerated to 40 to 50 drops orally 3 times daily. The treatment should be continued for 2 to 4 weeks after all lesions have healed, usually a total of 3 to 6 months (Kauffman et al, 2007).

#### **1.3.1.B.1.b Erythematous condition**

1) The usual dose of potassium iodide for the treatment of erythematous dermatoses, including erythema nodosum, nodular vasculitis, and erythema multiforme, is 300 milligrams orally three times a day (Horio et al, 1981; Horio et al, 1983; Schulz & Whiting, 1976a).

#### **1.3.1.B.1.c Implementation of protective measures to prevent injury due to radiation sources, Thyroid gland; Prophylaxis**

1) The recommended dose of potassium iodide (KI) as a thyroid-blocking agent following exposure to radioisotopes of **iodine** in adults over 18 through 40 years with predicted radioactive exposures greater than or equal to 10 centigray (cGy) (eg, from a nuclear reactor accident) is 130 milligrams/day (mg) orally. Adults over 40 years of age need KI only when a large internal radiation dose (greater than or equal to 500 cGy) to the thyroid is projected. Pregnant and lactating women should receive 130 mg/day if predicted thyroid exposure is expected to be 5 cGy or greater. Repeat dosing should be avoided in these women if possible to reduce the risk of blocking fetal thyroid function and hypothyroidism in the nursing neonate (FDA, 2001).

2) Therapy should be started as soon as possible prior to or after possible radiation exposure, preferably within 3 to 4 hours, and continue until the risk for significant exposure to radioiodines no longer exists. The thyroid-blocking effect of a single 130-milligram dose persists for 24 hours; daily therapy beyond 7 to 14 days appears unnecessary in the absence of continued exposure (FDA, 2001; Becker, 1987a; Becker et al, 1984); (Schleien, 1983).

#### **1.3.1.B.1.d Lymphocutaneous sporotrichosis**

1) As an alternative treatment to itraconazole for lymphocutaneous sporotrichosis, the recommended dose of saturated solution of potassium iodide (SSKI) is an initial dose of 5 drops (using a standard eye-dropper) orally 3 times daily, increasing as tolerated to 40 to 50 drops orally 3 times daily. The treatment should be continued for 2 to 4 weeks after all lesions have healed, usually a total of 3 to 6 months (Kauffman et al, 2007).

#### **1.3.1.B.1.e Important Note**

1) Administer enteric coated potassium iodide only when indicated; discontinue immediately if nausea, vomiting, abdominal pain, distention, or GI bleeding occurs.

## **1.4 Pediatric Dosage**

### 1.4.1 Normal Dosage

Iodine

Potassium Iodide

#### 1.4.1.A Iodine

Oral route

Topical application route

##### 1.4.1.A.1 Oral route

###### a) EUTHYROID GOITER

1) JUVENILE GOITERS, in children 13 to 15 years of age, respond rapidly to daily treatment with either 150 micrograms of iodide, 100 micrograms of levothyroxine, or 50 micrograms of levothyroxine plus 100 micrograms of iodide (Einenkel et al, 1992a). However, treatment with levothyroxine alone only temporarily blocked the thyroid's tendency to enlarge and withholding or reducing the dose resulted in relapse.

##### 1.4.1.A.2 Topical application route

###### 1.4.1.A.2.a Disinfection

1) For DECONTAMINATION OF MINOR WOUNDS, a 2% aqueous solution applied to the affected area is recommended (AMA Department of Drugs, 1986b). For DISINFECTION OF INTACT SKIN, a 2% tincture in an alcoholic vehicle is used (Goodman & Gilman, 1970; AMA Department of Drugs, 1986b; Osol, 1980a). For DISINFECTION OF MUCOUS MEMBRANES, a 2% solution of **iodine** in glycerin is the preparation of choice (Goodman & Gilman, 1970; Osol, 1980a).

#### 1.4.1.B Potassium Iodide

##### 1.4.1.B.1 Oral route

Cutaneous sporotrichosis

Implementation of protective measures to prevent injury due to radiation sources, Thyroid gland; Prophylaxis

Lymphocutaneous sporotrichosis

###### 1.4.1.B.1.a Cutaneous sporotrichosis

1) As an alternative treatment to itraconazole for cutaneous sporotrichosis, the recommended dose of saturated solution of potassium iodide (SSKI) in children is an initial dose of 1 drop (using a standard eye-dropper) orally 3 times daily, increasing as tolerated to a maximum of 1 drop/kilogram or 40 to 50 drops orally 3 times daily (whichever is lowest). The treatment should be continued for 2 to 4 weeks after all lesions have healed, usually a total of 3 to 6 months (Kauffman et al, 2007).

###### 1.4.1.B.1.b Implementation of protective measures to prevent injury due to radiation sources, Thyroid gland; Prophylaxis

The recommended dose of potassium iodide as a thyroid-blocking agent following exposure to

radioisotopes of **iodine** with predicted radioactive exposures greater than or equal to 5 centigray (eg, from a nuclear reactor accident) is:

Children and adolescents over 3 through 18 years: 65 milligrams/day (adolescents approaching adult size (70 kilograms or greater) should receive 130 milligrams/day)

Infants 1 month through 3 years: 32 milligrams/day

Neonates birth through 1 month: 16 milligrams/day

**1)** In neonates, repeat dosing should be avoided to minimize the risk of hypothyroidism during the critical phase of brain development. Treated infants should be monitored for hypothyroidism. Saturated potassium iodide solution can be diluted in milk, formula, or water (FDA, 2001).

**2)** Therapy should be started as soon as possible prior to or after possible radiation exposure, preferably within 3 to 4 hours, and should continue until the risk for significant exposure to radioiodines no longer exists (FDA, 2001). The thyroid-blocking effect of a single 130-milligram dose persists for 24 hours; daily therapy beyond 7 to 14 days appears unnecessary in the absence of continued exposure (FDA, 2001; Becker, 1987a; Becker et al, 1984); (Schleien, 1983).

#### 1.4.1.B.1.c Lymphocutaneous sporotrichosis

**1)** As an alternative treatment to itraconazole for lymphocutaneous sporotrichosis, the recommended dose of saturated solution of potassium iodide (SSKI) in children is an initial dose of 1 drop (using a standard eye-dropper) orally 3 times daily, increasing as tolerated to a maximum of 1 drop/kilogram or 40 to 50 drops orally 3 times daily (whichever is lowest). The treatment should be continued for 2 to 4 weeks after all lesions have healed, usually a total of 3 to 6 months (Kauffman et al, 2007).

#### 1.4.1.B.1.d Important Note

**1)** Administer enteric coated potassium iodide only when indicated; discontinue immediately if nausea, vomiting, abdominal pain, distention, or GI bleeding occurs.

## 2.0 Pharmacokinetics

Onset and Duration

ADME

### 2.1 Onset and Duration

#### A) Onset

##### 1) Initial Response

**a)** Water purification, solution: approximately 15 minutes (Osol, 1980; Kahn & Visscher, 1975; Goodman & Gilman, 1970a).

**1) IODINE** is rapidly microbicidal; when added to drinking water for emergency decontamination, amebicidal and bactericidal activity is seen within about 15 minutes (Osol, 1980; Kahn & Visscher, 1975; Goodman & Gilman, 1970a).

### 2.3 ADME

Absorption

Distribution

Metabolism

Excretion

## Extracorporeal Elimination

**2.3.1 Absorption****A) Iodine****1) Bioavailability****a) TOPICAL:** Slight (Reynolds, 1990).

**1) IODINE** is only slightly absorbed when applied topically in the usual amounts (Reynolds, 1990).

**B) Potassium Iodide****1) Bioavailability**

**a) ORAL:** Potassium iodide is readily absorbed in the intestinal tract (Sterling & Heymann, 2000).

**2.3.2 Distribution****A) Distribution Sites****1) Potassium Iodide****a) OTHER DISTRIBUTION SITES**

**1) Iodide** concentrates in the thyroid gland, salivary glands, gastric mucosa, choroid plexus, placenta, and mammary glands (Sterling & Heymann, 2000).

**2.3.3 Metabolism****A) Metabolism Sites and Kinetics**

**1) IODINE** which is absorbed systemically is rapidly converted to iodide (AMA Department of Drugs, 1986), which is taken up into the thyroid (Reynolds, 1990). With a 100-microgram iodide dose, about 20% is taken up by the thyroid (Hurrell, 1997).

**2.3.4 Excretion****A) Kidney****1) Iodine****a) Renal Excretion (%)**

**1) 85% to 90%** (Hurrell, 1997).

**a) IODINE** is excreted mainly in the urine in the form of iodides (Reynolds, 1990). With normal intake, 85% to 90% of absorbed iodide is excreted directly in the urine (Hurrell, 1997).

**2) Potassium Iodide****a) Renal Excretion (%)**

**1) 90%** (Sterling & Heymann, 2002).

**a) Ninety percent** of orally administered potassium iodide is excreted in the urine (Sterling & Heymann, 2000).

**B) Other****1) Potassium Iodide****a) OTHER EXCRETION**

**1) approximately 10%** (Sterling & Heymann, 2000).

**a) Approximately 10%** of an oral dose of potassium iodide is excreted in the sweat, feces, and breast milk (Sterling & Heymann, 2000).

**2.3.6 Extracorporeal Elimination****A) Hemodialysis****1) Dialyzable:** Yes

**a) Clearance of iodine** 120 mL/minute with standard hemodialysis (high flux F80 dialyzer without ultrafiltration; dialysate flow rate 550 mL/minute) (Kanakiriya et al, 2003).

**B) Hemofiltration****1) Dialyzable:** Yes

**a) Clearance of iodine** 37 mL/minute on day 1 and 44 mL/minute on day 2 during continuous



venovenous hemodiafiltration (CVVHDF) (high flux F80 dialyzer without ultrafiltration; dialysate and HF flow rate 2 L/hour) (Kanakiriya et al, 2003).

### 3.0 Cautions

Contraindications

Precautions

Adverse Reactions

Teratogenicity/Effects in Pregnancy/Breastfeeding

Drug Interactions

#### 3.0.A Black Box WARNING

##### 1) Potassium Iodide

###### a) Oral (Solution)

###### Consumer packaging

Take potassium iodide (KI) only when public officials tell you. In a nuclear radiation emergency, radioactive **iodine** could be released into the air. KI protects only the thyroid gland from uptake of radioactive **iodine**. Therefore, KI should be used along with other emergency measures that will be recommended to you by public officials.

If you are told to take this medicine, take it one time every 24 hours. Do not take it more often. More KI will not help you. Too much KI may increase the chances of side effects. Do not take this medicine if you know you are allergic to **iodine** (Prod Info THYROSHIELD(TM) oral solution, 2005).

### 3.1 Contraindications

#### A) Iodine

- 1) hypersensitivity to **iodine**
- 2) burn patients

#### B) Potassium Iodide

- 1) hypersensitivity to iodide products
- 2) renal disorders
- 3) **iodine**-induced goiter

### 3.2 Precautions

#### A) Potassium Iodide

- 1) acute bronchitis
- 2) Addison's disease
- 3) dehydration
- 4) goiter, autoimmune thyroid disease
- 5) hyperthyroidism
- 6) pregnancy, lactation (can cause fetal goiter, infant thyroid suppression)
- 7) tuberculosis

### 3.3 Adverse Reactions

Cardiovascular Effects

Dermatologic Effects

Endocrine/Metabolic Effects

Gastrointestinal Effects

Hematologic Effects

Immunologic Effects

Neurologic Effects

Respiratory Effects

Other

### 3.3.1 Cardiovascular Effects

#### 3.3.1.A Potassium Iodide

Cardiac dysrhythmia

Vasculitis

##### 3.3.1.A.1 Cardiac dysrhythmia

a) Irregular heart beat may occur with potassium iodide (Olin, 1990a).

##### 3.3.1.A.2 Vasculitis

a) Vasculitis has been associated with the use of potassium iodide (Sterling & Heymann, 2000a). Leckhout et al (1987) reported a case of systemic vasculitis attributed to a 12-day course of potassium iodide therapy (300 milligrams 3 times daily). Systemic vasculitis was diagnosed on the basis of significant impairment of renal function, eye involvement (papillitis), and a skin biopsy which showed a leukocytoclastic vasculitis.

### 3.3.2 Dermatologic Effects

#### 3.3.2.A Potassium Iodide

Acne

Iododerma

Rash

##### 3.3.2.A.1 Acne

a) Iodides may cause a flare-up of adolescent acne (Olin, 1990a).

##### 3.3.2.A.2 Iododerma

a) Ioderma is a severe skin eruption associated with the use of iodides. It has been reported more frequently in patients with underlying diseases such as rheumatoid arthritis, multiple myeloma, lymphoma, polyarteritis nodosa, or subacute glomerulonephritis. Skin eruptions exhibit various appearances such as bullous, vesicular, petechial, erythematous, or vegetating and can occur anywhere on the body (Sterling & Heymann, 2000a).

##### 3.3.2.A.3 Rash

a) DERMATITIS secondary to iodism may occur with prolonged therapy with inorganic iodides (Olin, 1990a).

b) Use of potassium iodide by nursing mothers may cause a rash in the infant (Olin, 1990a).

### 3.3.3 Endocrine/Metabolic Effects

Iodine

Potassium Iodide

#### 3.3.3.A Iodine

##### 3.3.3.A.1 Thyroid dysfunction

**a)** Although **iodine** supplementation has been reported to aggravate postpartum thyroid dysfunction (PPTD) in women with thyroid peroxidase antibody (TPO-Ab) (Kampe et al, 1990), supplementation during pregnancy and the postpartum period at a level typical of vitamin-mineral supplements (150 micrograms per day) did NOT induce or worsen PPTD in moderately deficient, TPO-Ab-positive women (Nohr et al, 2000).

**b)** A high rate of occurrence of thyroid dysfunction and goiter among Peace Corps volunteers in Niger was attributed to **iodine** excess from issued water purification systems containing based antimicrobial filters. Daily intake of **iodine** from filtered water was at least 50 milligrams (330 times the recommended dietary allowance of 0.15 milligrams). By August, 1998, water filtration systems in Niger were replaced by boiling or microfiltration and chlorine purification (Khan et al, 1998).

**c)** Administration of pharmacological doses of iodide to euthyroid patients with a previous episode of thyroid dysfunction during recombinant interferon-alpha (rIFN-alpha) treatment for hepatitis induced another episode of thyroid dysfunction (hypothyroidism or hyperthyroidism) in 5 of 8 patients. Patients who did not manifest thyroid dysfunction during rIFN-alpha treatment (n=8) did not develop thyroid dysfunction with excess **iodine** (Minelli et al, 1997).

#### 3.3.3.B Potassium Iodide

Hyperthyroidism

Hypothyroidism

Thyroid adenoma

##### 3.3.3.B.1 Hyperthyroidism

**a)** In a study of 8 female patients ranging in age from 34 and 66 years, 4 patients with goiter developed THYROTOXICOSIS after daily administration of 5 drops of potassium iodide (180 mg of iodide) for periods ranging from 10 to 18 weeks. Two of the patients became overtly thyrotoxic within 7 to 10 weeks of initiation of potassium iodide therapy. Serum thyroxine levels rose into toxic range. The patients developed weight loss, tachycardia, atrial fibrillation, sweating, and tremor. These signs and symptoms of hyperthyroidism increased when iodide therapy was withdrawn. This was presumably because hormonal synthesis was increased by iodides while secretion of hormone was partially inhibited. The authors suggested that, except when **iodine** deficiency is present or when **iodine** is given for control of pre-existing thyrotoxicosis, large doses of **iodine** patients with goiter or to patients with any underlying thyroid disease (Vagenakis et al, 1972a).

##### 3.3.3.B.2 Hypothyroidism

**a)** Prolonged use of iodides may lead to hypothyroidism, including MYXEDEMA, in patients sensitive to iodides. **Iodine**-induced GOITER may occur. Concurrent use of antithyroid agents may potentiate the hypothyroid effect of iodides (Olin, 1990a). Children with cystic fibrosis appear to have an exaggerated susceptibility to the goitrogenic effect of iodides (Olin, 1990a); (Rosenstein, 1978).

**b)** In certain instances, **iodine** administration for months or years can result in HYPOTHYROIDISM called the Wolff-Chaikoff effect. However, most persons receiving long-term iodides are prevented from the development of hypothyroidism by an autoregulatory mechanism. Excess inhibition of **iodine** organification, but this is usually short-lived and does not lead to hypothyroidism despite continued administration of **iodine**. By autoregulatory mechanisms, thyroidal transport declines in the presence of excess **iodine**, allowing the intrathyroidal to fall below the level necessary to inhibit organification (Shopsin et al, 1973). The hypothyroid state may resolve after withdrawal of iodide therapy and may be remedied faster by administration of thyroid hormone.

**c)** Goiter formation occurs frequently among children given high doses of iodides for respiratory tract problems. Hypothyroidism may occur early or may be delayed for as long as several years. Although goiter formation is usually the first manifestation of thyroid disease, hypothyroidism may occur without palpable thyroid enlargement. Because the symptoms are non-specific and develop gradually, hypothyroidism may go undetected for a prolonged period of time. Patients with Grave's disease and Hashimoto's thyroiditis are especially sensitive to the effects of iodides (Barnes et al, 1975).

### 3.3.3.B.3 Thyroid adenoma

**a)** Thyroid ADENOMA may occur from prolonged doses or excessive doses of potassium iodide (Olin, 1990a).

## 3.3.4 Gastrointestinal Effects

### 3.3.4.A Potassium Iodide

Gastrointestinal tract finding

Parotitis

Sialoadenitis

#### 3.3.4.A.1 Gastrointestinal tract finding

**a)** Gastrointestinal distress was reported in individuals receiving potassium iodide as a thyroid blocking agent during the Chernobyl reactor accident. Gastrointestinal distress occurred more frequently in children than adults (FDA, 2001).

**b)** Nonspecific small bowel lesions (STENOSIS with or without ULCERATIONS) associated with use of enteric-coated potassium iodide tablets has been reported. The lesions may cause HEMORRHAGE, OBSTRUCTION, and PERFORATION, often requiring surgery; DEATH has occurred (Olin, 1990a).

#### 3.3.4.A.2 Parotitis

**a)** Rarely, parotitis may occur with potassium iodide (Olin, 1990a).

#### 3.3.4.A.3 Sialoadenitis

**a)** Inflammation of the salivary gland can occur with potassium iodide administration (FDA, 2001).

## 3.3.5 Hematologic Effects

Iodine

Potassium Iodide

### 3.3.5.A Iodine

#### 3.3.5.A.1 Drug-induced eosinophilia

- a) Eosinophilia may occur as a manifestation of hypersensitivity (Reynolds, 1990).

### 3.3.5.B Potassium Iodide

#### 3.3.5.B.1 Drug-induced eosinophilia

- a) Eosinophilia has been associated with potassium iodide use (Sterling & Heymann, 2000a).

## 3.3.7 Immunologic Effects

Iodine

Potassium Iodide

### 3.3.7.A Iodine

Immune hypersensitivity reaction

Immune system finding

#### 3.3.7.A.1 Immune hypersensitivity reaction

- a) Hypersensitivity reactions may occur after topical application of any (AMA Department of Drugs, 1986a); ANGIOEDEMA, ARTHRALGIAS, CUTANEOUS HEMORRHAGE, eosinophilia, FEVER, LYMPHADENOPATHY, PURPURA, and URTICARIA may occur (Reynolds, 1990).

#### 3.3.7.A.2 Immune system finding

- a) Thyroid microsomal autoantibodies appeared in 10% of a group of euthyroid patients receiving iodide 0.2 milligrams/day for endemic goiter. Antibody titers decreased markedly after termination of iodide supplementation (Kahaly et al, 1997).

### 3.3.7.B Potassium Iodide

#### 3.3.7.B.1 Immune hypersensitivity reaction

- a) Patients may be markedly sensitive to iodides; hypersensitivity reactions may occur immediately or hours after administration. Manifestations may include ANGIOEDEMA, cutaneous and MUCOSAL HEMORRHAGES, and symptoms resembling SERUM SICKNESS (FEVER, ARTHRALGIA, LYMPHADENOPATHY, EOSINOPHILIA) (Olin, 1990a). URTICARIA, THROMBOTIC THROMBOCYTOPENIC PURPURA, and fatal PERIARTERITIS have been reported.
- b) Potassium iodide may precipitate severe systemic illness in patients with hypocomplementemic vasculitis. Patients with chronic urticaria or systemic lupus erythematosus are at particularly high risk (Curd, 1979).

### 3.3.9 Neurologic Effects

#### 3.3.9.A Potassium Iodide

##### 3.3.9.A.1 Central nervous system finding

- a) Central nervous system effects may include CONFUSION, NUMBNESS, TINGLING, pain, or WEAKNESS in the hands or feet, and weakness or heaviness of the legs (Olin, 1990a).

### 3.3.15 Respiratory Effects

#### 3.3.15.A Potassium Iodide

##### 3.3.15.A.1 Pulmonary edema

- a) Pulmonary edema has been associated with potassium iodide use (Sterling & Heymann, 2000a).

### 3.3.16 Other

#### 3.3.16.A Potassium Iodide

Iodine poisoning

Poisoning, chronic

##### 3.3.16.A.1 Iodine poisoning

- a) IODISM may develop, particularly with administration of large doses over prolonged periods. Manifestations include skin eruptions, oral burning, CORYZA, EYE IRRITATION, EYELID EDEMA, FRONTAL HEADACHE, PULMONARY EDEMA, gastric disturbances, and inflammation of the tonsils, pharynx, larynx, and submaxillary and parotid glands. Signs and symptoms generally resolve spontaneously within a few days of discontinuing therapy (Olin, 1990a).

##### 3.3.16.A.2 Poisoning, chronic

- a) (Kurtz & Aber, 1982) reported the case of a 73-year-old male with a 15-year history of ingestion of 10 drops a day of potassium iodide for a 15-year history of paroxysmal nocturnal fevers, shaking, chills, night sweats, coughing and vomiting. He was hospitalized for fever and was found to be anemic. The potassium iodide was discontinued and after 14 days the patient reported a decrease in severity of night sweats, an absence of fever, an improvement in appetite and a general sense of well being. In addition, the anemia had resolved. The patient was diagnosed with potassium iodide-induced fever. Although the pathogenesis of iodide fever is not fully understood, it may be due to a hypersensitivity mechanism in which activated **iodine** combines with a protein moiety to produce an immunogenic molecule.

## 3.4 Teratogenicity/Effects in Pregnancy/Breastfeeding

### A) Teratogenicity/Effects in Pregnancy

#### 1) Iodine

- a) Thomson Pregnancy Rating: Fetal risk has been demonstrated.

- 1) Evidence has demonstrated fetal abnormalities or risks when used during pregnancy or in women

of childbearing potential. An alternative to this drug should be prescribed during pregnancy or in women of childbearing potential.

See Drug Consult reference: PREGNANCY RISK CATEGORIES

**b) Crosses Placenta:** Yes

**c) Clinical Management**

**1) Excess iodine** is harmful to the unborn fetus; use of potassium iodide, ammonium iodide or sodium iodide during pregnancy has been associated with goiter, hypothyroidism, respiratory problems, enlarged heart, compression of the trachea, and death in infants (Pennington, 1990). Iodides, including topical applications and douches, are best avoided during pregnancy and lactation. However, nutritional supplement doses of vitamins and minerals are generally considered safe during pregnancy. Dietary **iodine** requirements are increased during pregnancy to a recommended dietary reference intake of 220 micrograms daily, an amount 47% over nonreproducing adult women (Picciano, 2003).

**d) Literature Reports**

**1) Iodide** readily crosses the placenta. Fetal thyroid begins to concentrate gestation, and can be affected by exposure to potassium iodide during this period and thereafter. Rare cases of fetal goiter, with or without hypothyroidism, and potential airway obstruction, have been reported (Arena & Drew, 1986). A literature review of iodide-induced fetal goiter reported over a 17-year period revealed 14 of 49 cases in which tracheal compression resulted in death (Mehta et al, 1983). In the majority of the cases, maternal asthma was the indication for iodide therapy.

**2) Use of fensol powders**, historically an **iodine**-containing antitussive, was associated with fetal goiter in eight infants when used by women during various times in pregnancy (Schardein, 1985). Fetal goiter can cause choking in the newborn (Parmalee et al, 1940) and neurological disorders (Crepin, 1978). Fetal goiter appears to be caused by a rebound effect from excess goiter has been reviewed (Klevit, 1969).

**3) Chronic topical maternal use of povidone-iodine** during pregnancy has been associated with clinical and biochemical hypothyroidism in the infant (Danziger et al, 1987). Vaginal douching with povidone-iodine solution during early pregnancy increased the and fetal thyroid (Mahillon et al, 1989).

**4) Iodine** supplementation during pregnancy (150 micrograms per day) in a geographical region of mild to moderate **iodine** deficiency decreased maternal TSH (thyroid stimulating hormone) and increased neonatal TSH in comparison to values when mothers were not supplemented with The unexpected finding of reduced TSH in the neonates was thought not to be of clinical significance, as all had normal thyroid hormone values (Nohr & Laurberg, 2000).

**2) Potassium Iodide**

**a) Thomson Pregnancy Rating:** Fetal risk has been demonstrated.

**1) Evidence** has demonstrated fetal abnormalities or risks when used during pregnancy or in women of childbearing potential. An alternative to this drug should be prescribed during pregnancy or in women of childbearing potential.

See Drug Consult reference: PREGNANCY RISK CATEGORIES

**b) Crosses Placenta:** Yes

**c) Clinical Management**

**1) Due to reports of fetal goiter**, tracheal compression, and death with extended use, potassium iodide should not be used during pregnancy (except for short-term use prior to surgery).

**d) Literature Reports**

**1) Potassium iodide** readily crosses the placenta. Fetal thyroid begins to concentrate 14 weeks gestation, and can be affected by exposure to potassium iodide during this period and thereafter. Rare cases of fetal goiter, with or without hypothyroidism, and potential airway obstruction, have been reported. A literature review of iodide-induced fetal goiter reported over a 17-year period revealed 14 of 49 cases in which tracheal compression resulted in death (Mehta et al, 1983a). In the majority of the cases, maternal asthma was the indication for iodide therapy.

**2) Neonatal hyperthyroidism** was reported in an infant following prenatal exposure to carbimazole and potassium iodide for the treatment of maternal Graves' disease (Domenech et al, 1985). The infant also had anomalies such as gynecomastia, bone age advancement, elevated FSH and estradiol, and irregular skin pigment on the neck and trunk, which led investigators to suspect McCune-Albright syndrome.

**B) Breastfeeding**

**1) Iodine**

- a) American Academy of Pediatrics Rating: Maternal medication usually compatible with breastfeeding. (Anon, 2001)
  - b) World Health Organization Rating: Compatible with breastfeeding. Monitor infant for side effects. (Anon, 2002)
  - c) Thomson Lactation Rating: Infant risk is minimal.
    - 1) The weight of an adequate body of evidence and/or expert consensus suggests this drug poses minimal risk to the infant when used during breastfeeding.
  - d) Clinical Management
    - 1) The American Academy of Pediatrics has rated **iodine** as compatible with breastfeeding (Anon: Committee on Drugs & American Academy of Pediatrics, 1994). However, significant infant exposure has been reported (Postellon & Aronow, 1982) and some experts continue to advise against use of **iodine** preparations which can result in significant systemic levels (Lawrence & Lawrence, 1999). **Iodine** applied to intact skin is minimally absorbed. However, systemic or excessive use of vaginal preparations containing **iodine**, should be avoided in lactating women. **Iodine** (iodide) concentrates in breast milk, achieving much higher concentrations than in maternal plasma, which could result in significant infant exposure and possible thyroid dysfunction or goiter (Atkinson et al, 1982).
  - e) Literature Reports
    - 1) Chronic topical maternal use of povidone-**iodine** during pregnancy and breast feeding has been associated with clinical and biochemical hypothyroidism in the infant (Danziger et al, 1987). In a single case, excessive maternal use of povidone **iodine** vaginal gel resulted in high milk/plasma ratios and high infant serum levels of **iodine**. An **iodine**-like odor was also noted on the infant (Postellon & Aronow, 1982).
    - 2) One case of severe transient congenital hypothyroidism has been reported in a breastfed infant whose mother performed vaginal douching with povidone-**iodine** (20 days). Douching was discontinued and maternal milk and urine levels were normal seven days later. The infant was treated with 25 micrograms L-T4 per day for seven days and thyroid function remained normal two months later. Simple routine urine **iodine** transient hypothyroidism early, decreasing length of treatment and stress on the infant (Delange & Chanoine, 1988).
- 2) Potassium Iodide
- a) American Academy of Pediatrics Rating: Maternal medication usually compatible with breastfeeding. (Anon, 2001)
  - b) World Health Organization Rating: Avoid breastfeeding if possible. Monitor infant for side effects. (Anon, 2002)
  - c) Thomson Lactation Rating: Infant risk cannot be ruled out.
    - 1) Available evidence and/or expert consensus is inconclusive or is inadequate for determining infant risk when used during breastfeeding. Weigh the potential benefits of drug treatment against potential risks before prescribing this drug during breastfeeding.
  - d) Clinical Management
    - 1) **Iodine** (iodide) concentrates in breast milk, achieving much higher concentrations than in maternal plasma, which could result in significant infant exposure and possible thyroid dysfunction or goiter (Anderson, 1991). Administration of potassium iodide to lactating women in the event of a radiation emergency may pose a risk of hypothyroidism in the nursing infant; however, these women should receive the drug for their own protection. Repeat dosing should be avoided if possible (Anon, 2004).
  - e) Literature Reports
    - 1) No human studies regarding the use potassium iodide during lactation have been published.
- 3) Drug Levels in Breastmilk
- a) Parent Drug
    - 1) Milk to Maternal Plasma Ratio
      - a) 6.3 (Atkinson et al, 1988)

### 3.5 Drug Interactions

#### Drug-Drug Combinations



## Intravenous Admixtures

**3.5.1 Drug-Drug Combinations**

Acenocoumarol

Anisindione

Bugleweed

Bugleweed

Dicumarol

Lithium

Phenindione

Phenprocoumon

Warfarin

**3.5.1.A Acenocoumarol**

- 1) Interaction Effect: decreased anticoagulant effectiveness
- 2) Summary: In hyperthyroid patients, the metabolism of vitamin K clotting factors is increased, resulting in increased sensitivity to oral anticoagulants (Prod Info Tapazole(R), 2000; Chute et al, 1994). Antithyroid drugs, by reducing the extent of hyperthyroidism, decrease the metabolism of clotting factors and thus reduce the effects of oral anticoagulants (Hansten, 1980). On the other hand, patients on anticoagulant therapy who are euthyroid due to antithyroid agents may develop marked hypoprothrombinemia if the antithyroid medications are ceased and they become thyrotoxic again (Vagenakis et al, 1972). In one case report, treating patients with both methimazole and warfarin necessitates intensive and frequent monitoring, since alterations in thyroid function affect the response to anticoagulation (Busenbark & Cushnie, 2006).
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: probable
- 6) Clinical Management: In patients receiving oral anticoagulant therapy, the prothrombin time ratio or international normalized ratio (INR) should be closely monitored with the addition and withdrawal of treatment with antithyroid drugs, and should be reassessed periodically during concurrent therapy. Increased anticoagulant doses may be required to maintain the desired level of anticoagulation.
- 7) Probable Mechanism: decreased metabolism of clotting factors
- 8) Literature Reports
  - a) One case report describes changes in thyroid hormone concentrations that significantly affected warfarin-induced anticoagulation in a patient with Graves' disease. A 54-year old man was treated with methimazole 30 mg/day for hyperthyroidism and enoxaparin then warfarin for atrial fibrillation. In the following 3 months after discharge, the patient's warfarin was repeatedly increased to 85 mg/week to achieve and maintain a therapeutic INR (range 2 - 3). The patient remained adequately anticoagulated for 12 weeks, when the methimazole dose was decreased to 10 mg/day. Continued hypothyroidism necessitated a stop of methimazole for 5 days, then resumed at a dose of 5 mg/day. This resulted in a suprathreshold INR, and the warfarin was decreased to 60 mg/week. What followed was a pattern of methimazole dosage adjustments leading to significant changes in thyroid function, and subsequent changes in INR. After approximately 14 months of warfarin therapy, Two ECGs confirmed sustained normal sinus rhythm and anticoagulation was discontinued (Busenbark & Cushnie, 2006).

**3.5.1.B Anisindione**

- 1) Interaction Effect: decreased anticoagulant effectiveness

- 2) Summary: In hyperthyroid patients, the metabolism of vitamin K clotting factors is increased, resulting in increased sensitivity to oral anticoagulants (Prod Info Tapazole(R), 2000; Chute et al, 1994). Antithyroid drugs, by reducing the extent of hyperthyroidism, decrease the metabolism of clotting factors and thus reduce the effects of oral anticoagulants (Hansten, 1980). On the other hand, patients on anticoagulant therapy who are euthyroid due to antithyroid agents may develop marked hypoprothrombinemia if the antithyroid medications are ceased and they become thyrotoxic again (Vagenakis et al, 1972). In one case report, treating patients with both methimazole and warfarin necessitates intensive and frequent monitoring, since alterations in thyroid function affect the response to anticoagulation (Busenbark & Cushnie, 2006).
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: probable
- 6) Clinical Management: In patients receiving oral anticoagulant therapy, the prothrombin time ratio or international normalized ratio (INR) should be closely monitored with the addition and withdrawal of treatment with antithyroid drugs, and should be reassessed periodically during concurrent therapy. Increased anticoagulant doses may be required to maintain the desired level of anticoagulation.
- 7) Probable Mechanism: decreased metabolism of clotting factors
- 8) Literature Reports
  - a) One case report describes changes in thyroid hormone concentrations that significantly affected warfarin-induced anticoagulation in a patient with Graves' disease. A 54-year old man was treated with methimazole 30 mg/day for hyperthyroidism and enoxaparin then warfarin for atrial fibrillation. In the following 3 months after discharge, the patient's warfarin was repeatedly increased to 85 mg/week to achieve and maintain a therapeutic INR (range 2 - 3). The patient remained adequately anticoagulated for 12 weeks, when the methimazole dose was decreased to 10 mg/day. Continued hypothyroidism necessitated a stop of methimazole for 5 days, then resumed at a dose of 5 mg/day. This resulted in a suprathreshold INR, and the warfarin was decreased to 60 mg/week. What followed was a pattern of methimazole dosage adjustments leading to significant changes in thyroid function, and subsequent changes in INR. After approximately 14 months of warfarin therapy, Two ECGs confirmed sustained normal sinus rhythm and anticoagulation was discontinued (Busenbark & Cushnie, 2006).

### 3.5.1.C Bugleweed

- 1) Interaction Effect: reduced uptake of iodine
- 2) Summary: Bugleweed interfered with uptake of radioactive reports and should not be used in conjunction with it for either treatment or diagnostic purposes (Keller et al, 1993a).
- 3) Severity: moderate
- 4) Onset: rapid
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of bugleweed with
- 7) Probable Mechanism: not specified
- 8) Literature Reports
  - a) At least 14 uncontrolled clinical trials or case series have been reported in the German medical literature supporting the efficacy of various extracts of *Lycopus europaeus* or *Lycopus virginicus* (bugleweed), sometimes with *Leonurus cardiaca* (motherwort) herb added, in relieving symptoms of hyperthyroidism (Keller et al, 1993).

### 3.5.1.D Bugleweed

- 1) Interaction Effect: additive antithyroid effects
- 2) Summary: *Lycopus europaeus* and *Lycopus virginicus* (bugleweed) have antithyroid activity and should not be taken with drugs that are intended to alter thyroid function (Sourgens et al, 1982; Sourgens et al, 1980). Some practitioners of natural medicine have used bugleweed to decrease the required dose of these drugs but expert supervision is required (Keller et al, 1993c).
- 3) Severity: moderate
- 4) Onset: rapid
- 5) Substantiation: theoretical

- 6) Clinical Management: Avoid concomitant use of bugleweed with antithyroid agents.
- 7) Probable Mechanism: bugleweed may decreased T3 levels, possibly the result of peripheral T4 deiodination, bugleweed may change the conformation of TSH, and inhibit cAMP
- 8) Literature Reports
  - a) Oral administration of an ethanol extract of *Lycopus europaeus* 1000 milligrams/kilogram (mg/kg) resulted in significant reductions (p less than 0.05) in T3 levels beginning at 6 hours and lasting for more than 24 hours compared to controls. T4 levels were significantly decreased compared to controls only after 24 hours. A reduction in thyroid-stimulating hormone (TSH) occurred after 24 hours compared to controls in a study using male Wistar rats. Significant increases in TSH compared to controls were reported at 9 and 12 hours (p values not reported). Oral administration of 200 mg/kg resulted in increases in TSH to 129+/-25 nanogram/milliliter (ng/mL) compared to 26+/-10 ng/mL in control animals. Intraperitoneal (IP) injection of *Lycopus europaeus* 50 milligrams resulted in significant decreases in T3 (p less than 0.05) and TSH levels at 3 hours (p less than 0.01). At 6 hours the effect was less although TSH remained significantly reduced compared to controls (p less than 0.05). At 9 hours T3, T4 (p less than 0.05 compared to controls), and TSH levels were all increased compared to controls. T4 levels were not significantly different compared to controls at 3 and 6 hours. Male Wistar rats received ethanol preparations of *Lycopus europaeus* orally by gavage or by IP injections. Rats were sacrificed and thyroid and pituitary glands were examined 3 to 24 hours after treatment. Rats were also sacrificed at 10, 30, 60, and 180 minutes after treatment for evaluation of absorption and metabolism of plant constituents (Winterhoff et al, 1988).
  - b) At least 14 uncontrolled clinical trials or case series have been reported in the German medical literature supporting the efficacy of various extracts of *Lycopus europaeus* or *Lycopus virginicus* (bugleweed), sometimes with *Leonurus cardiaca* (motherwort) herb added, in relieving symptoms of hyperthyroidism (Keller et al, 1993b).

### 3.5.1.E Dicumarol

- 1) Interaction Effect: decreased anticoagulant effectiveness
- 2) Summary: In hyperthyroid patients, the metabolism of vitamin K clotting factors is increased, resulting in increased sensitivity to oral anticoagulants (Prod Info Tapazole(R), 2000; Chute et al, 1994). Antithyroid drugs, by reducing the extent of hyperthyroidism, decrease the metabolism of clotting factors and thus reduce the effects of oral anticoagulants (Hansten, 1980). On the other hand, patients on anticoagulant therapy who are euthyroid due to antithyroid agents may develop marked hypoprothrombinemia if the antithyroid medications are ceased and they become thyrotoxic again (Vagenakis et al, 1972). In one case report, treating patients with both methimazole and warfarin necessitates intensive and frequent monitoring, since alterations in thyroid function affect the response to anticoagulation (Busenbark & Cushnie, 2006).
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: probable
- 6) Clinical Management: In patients receiving oral anticoagulant therapy, the prothrombin time ratio or international normalized ratio (INR) should be closely monitored with the addition and withdrawal of treatment with antithyroid drugs, and should be reassessed periodically during concurrent therapy. Increased anticoagulant doses may be required to maintain the desired level of anticoagulation.
- 7) Probable Mechanism: decreased metabolism of clotting factors
- 8) Literature Reports
  - a) One case report describes changes in thyroid hormone concentrations that significantly affected warfarin-induced anticoagulation in a patient with Graves' disease. A 54-year old man was treated with methimazole 30 mg/day for hyperthyroidism and enoxaparin then warfarin for atrial fibrillation. In the following 3 months after discharge, the patient's warfarin was repeatedly increased to 85 mg/week to achieve and maintain a therapeutic INR (range 2 - 3). The patient remained adequately anticoagulated for 12 weeks, when the methimazole dose was decreased to 10 mg/day. Continued hypothyroidism necessitated a stop of methimazole for 5 days, then resumed at a dose of 5 mg/day. This resulted in a suprathreshold INR, and the warfarin was decreased to 60 mg/week. What followed was a pattern of methimazole dosage adjustments leading to significant changes in thyroid function, and subsequent changes in INR. After approximately 14 months of warfarin therapy, Two ECGs confirmed sustained normal sinus rhythm and anticoagulation was discontinued (Busenbark & Cushnie, 2006).

**3.5.1.F Lithium**

- 1) Interaction Effect: increased hypothyroid effect
- 2) Summary: Concomitant potassium iodide and lithium therapy may result in hypothyroidism. This effect is related to a synergistic hypothyroid effect of both lithium and iodide (Jorgensen et al, 1973).
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Concurrent therapy with lithium and potassium iodide should be avoided if possible. If deemed clinically appropriate, consider monitoring thyroid function tests periodically during therapy.
- 7) Probable Mechanism: additive hypothyroid effects

**3.5.1.G Phenindione**

- 1) Interaction Effect: decreased anticoagulant effectiveness
- 2) Summary: In hyperthyroid patients, the metabolism of vitamin K clotting factors is increased, resulting in increased sensitivity to oral anticoagulants (Prod Info Tapazole(R), 2000; Chute et al, 1994). Antithyroid drugs, by reducing the extent of hyperthyroidism, decrease the metabolism of clotting factors and thus reduce the effects of oral anticoagulants (Hansten, 1980). On the other hand, patients on anticoagulant therapy who are euthyroid due to antithyroid agents may develop marked hypoprothrombinemia if the antithyroid medications are ceased and they become thyrotoxic again (Vagenakis et al, 1972). In one case report, treating patients with both methimazole and warfarin necessitates intensive and frequent monitoring, since alterations in thyroid function affect the response to anticoagulation (Busenbark & Cushnie, 2006).
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: probable
- 6) Clinical Management: In patients receiving oral anticoagulant therapy, the prothrombin time ratio or international normalized ratio (INR) should be closely monitored with the addition and withdrawal of treatment with antithyroid drugs, and should be reassessed periodically during concurrent therapy. Increased anticoagulant doses may be required to maintain the desired level of anticoagulation.
- 7) Probable Mechanism: decreased metabolism of clotting factors
- 8) Literature Reports
  - a) One case report describes changes in thyroid hormone concentrations that significantly affected warfarin-induced anticoagulation in a patient with Graves' disease. A 54-year old man was treated with methimazole 30 mg/day for hyperthyroidism and enoxaparin then warfarin for atrial fibrillation. In the following 3 months after discharge, the patient's warfarin was repeatedly increased to 85 mg/week to achieve and maintain a therapeutic INR (range 2 - 3). The patient remained adequately anticoagulated for 12 weeks, when the methimazole dose was decreased to 10 mg/day. Continued hypothyroidism necessitated a stop of methimazole for 5 days, then resumed at a dose of 5 mg/day. This resulted in a suprathreshold INR, and the warfarin was decreased to 60 mg/week. What followed was a pattern of methimazole dosage adjustments leading to significant changes in thyroid function, and subsequent changes in INR. After approximately 14 months of warfarin therapy, Two ECGs confirmed sustained normal sinus rhythm and anticoagulation was discontinued (Busenbark & Cushnie, 2006).

**3.5.1.H Phenprocoumon**

- 1) Interaction Effect: decreased anticoagulant effectiveness
- 2) Summary: In hyperthyroid patients, the metabolism of vitamin K clotting factors is increased, resulting in increased sensitivity to oral anticoagulants (Prod Info Tapazole(R), 2000; Chute et al, 1994). Antithyroid drugs, by reducing the extent of hyperthyroidism, decrease the metabolism of clotting factors and thus reduce the effects of oral anticoagulants (Hansten, 1980). On the other hand, patients on anticoagulant therapy who are euthyroid due to antithyroid agents may develop marked hypoprothrombinemia if the antithyroid medications are ceased and they become thyrotoxic again (Vagenakis et al, 1972). In one case report, treating patients with both methimazole and warfarin necessitates intensive and frequent

monitoring, since alterations in thyroid function affect the response to anticoagulation (Busenbark & Cushnie, 2006).

3) Severity: moderate

4) Onset: delayed

5) Substantiation: probable

6) Clinical Management: In patients receiving oral anticoagulant therapy, the prothrombin time ratio or international normalized ratio (INR) should be closely monitored with the addition and withdrawal of treatment with antithyroid drugs, and should be reassessed periodically during concurrent therapy. Increased anticoagulant doses may be required to maintain the desired level of anticoagulation.

7) Probable Mechanism: decreased metabolism of clotting factors

8) Literature Reports

a) One case report describes changes in thyroid hormone concentrations that significantly affected warfarin-induced anticoagulation in a patient with Graves' disease. A 54-year old man was treated with methimazole 30 mg/day for hyperthyroidism and enoxaparin then warfarin for atrial fibrillation. In the following 3 months after discharge, the patient's warfarin was repeatedly increased to 85 mg/week to achieve and maintain a therapeutic INR (range 2 - 3). The patient remained adequately anticoagulated for 12 weeks, when the methimazole dose was decreased to 10 mg/day. Continued hypothyroidism necessitated a stop of methimazole for 5 days, then resumed at a dose of 5 mg/day. This resulted in a supratherapeutic INR, and the warfarin was decreased to 60 mg/week. What followed was a pattern of methimazole dosage adjustments leading to significant changes in thyroid function, and subsequent changes in INR. After approximately 14 months of warfarin therapy, Two ECGs confirmed sustained normal sinus rhythm and anticoagulation was discontinued (Busenbark & Cushnie, 2006).

#### 3.5.1.1 Warfarin

1) Interaction Effect: decreased anticoagulant effectiveness

2) Summary: In hyperthyroid patients, the metabolism of vitamin K clotting factors is increased, resulting in increased sensitivity to oral anticoagulants (Prod Info Tapazole(R), 2000; Chute et al, 1994). Antithyroid drugs, by reducing the extent of hyperthyroidism, decrease the metabolism of clotting factors and thus reduce the effects of oral anticoagulants (Hansten, 1980). On the other hand, patients on anticoagulant therapy who are euthyroid due to antithyroid agents may develop marked hypoprothrombinemia if the antithyroid medications are ceased and they become thyrotoxic again (Vagenakis et al, 1972). In one case report, treating patients with both methimazole and warfarin necessitates intensive and frequent monitoring, since alterations in thyroid function affect the response to anticoagulation (Busenbark & Cushnie, 2006).

3) Severity: moderate

4) Onset: delayed

5) Substantiation: probable

6) Clinical Management: In patients receiving oral anticoagulant therapy, the prothrombin time ratio or international normalized ratio (INR) should be closely monitored with the addition and withdrawal of treatment with antithyroid drugs, and should be reassessed periodically during concurrent therapy. Increased anticoagulant doses may be required to maintain the desired level of anticoagulation.

7) Probable Mechanism: decreased metabolism of clotting factors

8) Literature Reports

a) One case report describes changes in thyroid hormone concentrations that significantly affected warfarin-induced anticoagulation in a patient with Graves' disease. A 54-year old man was treated with methimazole 30 mg/day for hyperthyroidism and enoxaparin then warfarin for atrial fibrillation. In the following 3 months after discharge, the patient's warfarin was repeatedly increased to 85 mg/week to achieve and maintain a therapeutic INR (range 2 - 3). The patient remained adequately anticoagulated for 12 weeks, when the methimazole dose was decreased to 10 mg/day. Continued hypothyroidism necessitated a stop of methimazole for 5 days, then resumed at a dose of 5 mg/day. This resulted in a supratherapeutic INR, and the warfarin was decreased to 60 mg/week. What followed was a pattern of methimazole dosage adjustments leading to significant changes in thyroid function, and subsequent changes in INR. After approximately 14 months of warfarin therapy, Two ECGs confirmed sustained normal sinus rhythm and anticoagulation was discontinued (Busenbark & Cushnie, 2006).

### 3.5.5 Intravenous Admixtures

Drugs

Solutions

#### 3.5.5.1 Drugs

Iodine

Sodium Iodide

##### 3.5.5.1.A Iodine

Alprostadil

Ampicillin

Chloramphenicol

Chloramphenicol Sodium Succinate

Cimetidine

Diatrizoate Meglumine

Diatrizoate Meglumine/Diatrizoate Sodium

Diatrizoate Sodium

Diatrizoate Sodium/Diatrizoate Meglumine

Diazepam

Diphenhydramine

Epinephrine

Erythromycin Gluceptate

Gentamicin

Heparin

Heparin Sodium

Hydrocortisone Sodium Succinate

Iohexol

Iopamidol

Iothalamate

Iothalamate Meglumine

Ioxaglate

Ioxaglate Meglumine

loxaglate Meglumine/loxaglate Sodium  
 loxaglate Sodium  
 Lidocaine  
 Meperidine  
 Methylprednisolone Sodium Succinate  
 Metrizamide  
 Nitroglycerin  
 Papaverine  
 Papaverine Hydrochloride  
 Phentolamine  
 Protamine  
 Tolazoline  
 Urokinase  
 Vasopressin

#### 3.5.5.1.A.1 Alprostadil

##### a) Compatible

- 1) Alprostadil 4 U/mL with iopamidol 5 mL of a solution containing change after mixing (Kim et al, 1992at)
- 2) Alprostadil 4 U/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing **iodine** 282 mg/mL, no change after mixing (Kim et al, 1992au)
- 3) Alprostadil 4 U/mL with DIATRIZOATE SODIUM 5 mL of a solution containing 300 mg/mL, no change after mixing (Kim et al, 1992au)
- 4) Alprostadil 4 U/mL with iothalamate 5 mL of a solution containing change after mixing (Kim et al, 1992bq)
- 5) Alprostadil 4 U/mL with iohexol 5 mL of solution containing change after mixing (Kim et al, 1992br)
- 6) Alprostadil 4 U/mL with ioxaglate 5 mL of a solution containing change after mixing (Kim et al, 1992bs)

#### 3.5.5.1.A.2 Ampicillin

##### a) Compatible

- 1) Ampicillin 100 mg/mL with ioxaglate 5 mL of a solution containing change after mixing (Kim et al, 1992k)
- 2) Ampicillin 100 mg/mL with iothalamate 5 mL of a solution containing no change after mixing (Kim et al, 1992t)
- 3) Ampicillin 30 mg/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing **iodine** 283 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989g)
- 4) Ampicillin 100 mg/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing **iodine** 282 mg/mL, no change after mixing (Kim et al, 1992w)
- 5) Ampicillin 30 mg/mL with iopamidol 5 mL of a solution containing visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989k)
- 6) Ampicillin 100 mg/mL with iopamidol 5 mL of a solution containing change after mixing (Kim et al, 1992ab)
- 7) Ampicillin 30 mg/mL with iohexol 5 mL of a solution containing

visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ai)

**8)** Ampicillin 100 mg/mL with iohexol 5 mL of solution containing change after mixing (Kim et al, 1992bi)

**9)** Ampicillin 30 mg/mL with DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing **iodine** temperature (Irving & Burbridge, 1989g)

**10)** Ampicillin 30 mg/mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing **iodine** 320 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989bf).

**11)** Ampicillin 100 mg/mL with DIATRIZOATE SODIUM 5 mL of a solution containing 300 mg/mL, no change after mixing (Kim et al, 1992w)

**12)** Ampicillin 30 mg/mL with iothalamate meglumine 5 mL of an solution containing 282 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989bh)

#### 3.5.5.1.A.3 Chloramphenicol

##### a) Compatible

**1)** Chloramphenicol 33 mg/mL with IOTHALAMATE MEGLUMINE 5 mL of a solution containing 282 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ab)

**2)** Chloramphenicol 33 mg/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989aj)

**3)** Chloramphenicol 33 mg/mL with iohexol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989aq)

**4)** Chloramphenicol 33 mg/mL with iopamidol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989aw)

**5)** Chloramphenicol 33 mg/mL with DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg at room temperature (Irving & Burbridge, 1989aj)

**6)** Chloramphenicol 33 mg/mL with 5 mL of an ioxaglate meglumine and ioxaglate sodium solution containing 320 mg **iodine** (Irving & Burbridge, 1989bc)

#### 3.5.5.1.A.4 Chloramphenicol Sodium Succinate

##### a) Compatible

**1)** Chloramphenicol sodium succinate 200 mg/mL with ioxaglate 5 mL of a solution containing **iodine** 320 mg/mL, no change after mixing (Kim et al, 1992h)

**2)** Chloramphenicol sodium succinate 200 mg/mL with iothalamate 5 mL of a solution containing **iodine** 282 mg/mL, no change after mixing (Kim et al, 1992an)

**3)** Chloramphenicol sodium succinate 200 mg/mL with DIATRIZOATE SODIUM 5 mL of a solution containing **iodine** 300 mg/mL, no change after mixing (Kim et al, 1992ay)

**4)** Chloramphenicol sodium succinate 200 mg/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing **iodine** 282 mg/mL, no change after mixing (Kim et al, 1992ay)

**5)** Chloramphenicol sodium succinate 200 mg/mL with iopamidol 5 mL of a solution containing **iodine** 300 mg/mL, no change after mixing (Kim et al, 1992bu)

**6)** Chloramphenicol sodium succinate 200 mg/mL with iohexol 5 mL of solution containing **iodine** 300 mg/mL, no change after mixing (Kim et al, 1992ci)

#### 3.5.5.1.A.5 Cimetidine

##### a) Conflicting Data

##### 1) Incompatible

**a)** Cimetidine 100 mg/mL with ioxaglate 5 mL of a solution containing



mg/mL, precipitate persisting after centrifugation (Kim et al, 1992ax)

**b)** Cimetidine 100 mg/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing **iodine** 282 mg/mL, resulted a white suspension that persisted longer than 1 minute (Kim et al, 1992bw)

**c)** Cimetidine 150 mg/1 mL with ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL, formation of a thread-like precipitate was reported (Shah & Gerlock, 1987c)

**d)** Cimetidine 150 mg/mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989au)

## 2) Compatible

**a)** Cimetidine 150 mg/mL with iohexol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989c)

**b)** Cimetidine 100 mg/mL with iohexol 5 mL of solution containing no change after mixing (Kim et al, 1992f)

**c)** Cimetidine 150 mg/mL with iopamidol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989j)

**d)** Cimetidine 100 mg/mL with iopamidol 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992aa)

**e)** Cimetidine 100 mg/mL with DIATRIZOATE SODIUM 5 mL of a solution containing **iodine** 300 mg/mL, no change after mixing (Kim et al, 1992bv)

**f)** Cimetidine 150 mg/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989as)

**g)** Cimetidine 150 mg/mL with iothalamate meglumine 5 mL of a solution containing 282 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989av)

**h)** Cimetidine 150 mg/mL with DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg hours at room temperature (Irving & Burbridge, 1989as)

**i)** Cimetidine 100 mg/mL with iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992cp)

### 3.5.5.1.A.6 Diatrizoate Meglumine

#### a) Conflicting Data

##### 1) Incompatible

**a)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing meperidine 25 mg/mL, precipitate persisting after centrifugation (Kim et al, 1992u)

**b)** DIATRIZOATE SODIUM AND DIATRIZOATE MEGLUMINE 5 mL of a solution containing 292.5 mg **iodine**

precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 1 hour at room temperature (Irving & Burbridge, 1989r)

**c)** DIATRIZOATE SODIUM 8% and DIATRIZOATE MEGLUMINE 52% - Renografin(R) - 1 or 2 mL with diphenhydramine 1 mL, concentration not specified, physically compatible for 1 hour but a precipitate was detected after 48 hours in direct admixture in syringe; temperature not specified (Marshall et al, 1965; Trissel, 1988)

**d)** Diatrizoate sodium and diatrizoate meglumine 5 mL of a solution containing 292.5 mg **iodine**/mL with papaverine 32 mg/mL, a transient precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 2 hours at room temperature (Irving & Burbridge, 1989z)

**e)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing papaverine 30 mg/mL, precipitate persisting after centrifugation (Kim et al, 1992ba)

**f)** Diatrizoate meglumine 5 mL of a solution containing 283 mg papaverine 32 mg/mL, a transient precipitate formed which cleared within 5 minutes at room temperature (Irving & Burbridge, 1989z)

- g)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing protamine 10 mg/mL, precipitate persisting after centrifugation (Kim et al, 1992bk).
  - h)** DIATRIZOATE MEGLUMINE (Renografin(R) - 76), reported to form a thick, gelatinous precipitate when prepared in a 1 to 1 admixture in serum (Martin & Taylor, 1976); precipitate formation reported if the dye is not flushed out of the catheter prior to administration of the protamine (Iannone, 1975)
  - i)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg protamine 10 mg/mL, immediate formation of a precipitate was reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989b)
  - j)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing diphenhydramine 50 mg/mL , precipitate persisting after centrifugation (Kim et al, 1992bj)
  - k)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg diphenhydramine 12.5 mg/0.25 mL, a transient precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 1 hour at room temperature (Irving & Burbridge, 1989r)
  - l)** Cimetidine 100 mg/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing **iodine** 282 mg/mL , resulted a white suspension that persisted longer than 1 minute (Kim et al, 1992bw)
  - m)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing diazepam 5 mg/mL, resulted a white suspension that persisted longer than 1 minute (Kim et al, 1992cf)
  - n)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing phentolamine 10 mg/mL, resulted a white suspension that disappeared within 1 minute (Kim et al, 1992cm)
- 2) Compatible**
- a)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing urokinase 1200 U/mL, no change after mixing (Kim et al, 1992)
  - b)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg gentamicin 800 mcg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989d)
  - c)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing gentamicin 40 mg/mL, no change after mixing (Kim et al, 1992o)
  - d)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing tolazoline 25 mg/mL, no change after mixing (Kim et al, 1992p)
  - e)** DIATRIZOATE SODIUM 5 mL of a solution containing tolazoline 25 mg/mL, no change after mixing (Kim et al, 1992p)
  - f)** Ampicillin 30 mg/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing **iodine** 283 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989g)
  - g)** Ampicillin 100 mg/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing **iodine** 282 mg/mL , no change after mixing (Kim et al, 1992w)
  - h)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing nitroglycerin 120 mcg/mL, no change after mixing (Kim et al, 1992z)
  - i)** DIATRIZOATE MEGLUMINE (Hypaque 60%(R)) 5 mL of a solution containing **iodine** 283 mg/mL with methylprednisolone sodium succinate (Solu-Medrol(R)) 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989m)
  - j)** DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg **iodine** hours at room temperature (Irving & Burbridge, 1989d)
  - k)** Erythromycin gluceptate (10 mg/mL with 5 mL of a diatrizoate meglumine solution containing **iodine** 283 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989p)
  - l)** DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg **iodine** visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989s)
  - m)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing

- vasopressin 20 U/mL, no change after mixing (Kim et al, 1992ae)
- n)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg epinephrine 1 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989v)
- o)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing epinephrine 1 mg/mL, no change after mixing (Kim et al, 1992al)
- p)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg heparin sodium 5,000 U/0.5 mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989y)
- q)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing heparin 1000 U/mL, no change after mixing (Kim et al, 1992aq)
- r)** Alprostadil 4 U/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing **iodine** 282 mg/mL, no change after mixing (Kim et al, 1992au)
- s)** Diatrizoate sodium and diatrizoate meglumine 5 mL of a solution containing 292.5 mg **iodine**/mL with papaverine 32 mg/mL, a transient precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 2 hours at room temperature (Irving & Burbridge, 1989ac)
- t)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg hydrocortisone sodium succinate 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989s)
- u)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing hydrocortisone sodium succinate 167.09 mg/mL, no change after mixing (Kim et al, 1992bc)
- v)** Diatrizoate meglumine 5 mL of a solution containing 283 mg papaverine 32 mg/mL, a transient precipitate formed which cleared within 5 minutes at room temperature (Irving & Burbridge, 1989ac) DIATRIZOATE SODIUM AND DIATRIZOATE MEGLUMINE
- w)** Diatrizoate sodium and diatrizoate meglumine 5 mL of a solution containing 292.5 mg **iodine**/mL with papaverine 32 mg/mL, a transient precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 2 hours at room temperature (Irving & Burbridge, 1989ac)
- x)** Chloramphenicol 33 mg/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989aj)
- y)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing lidocaine 5 mg/mL, no change after mixing (Kim et al, 1992bf)
- z)** Chloramphenicol sodium succinate 200 mg/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing 1992ay)
- aa)** DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg **iodine** hours at room temperature (Irving & Burbridge, 1989v)
- ab)** Cimetidine 150 mg/mL with DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989as)
- ac)** Cimetidine 150 mg/mL with DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg hours at room temperature (Irving & Burbridge, 1989as)
- ad)** DIATRIZOATE MEGLUMINE (5 mL of a solution containing 283 mg erythromycin gluceptate 10 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989)
- ae)** Chloramphenicol 33 mg/mL with DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg hours at room temperature (Irving & Burbridge, 1989aj)
- af)** Ampicillin 30 mg/mL with DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing hours at room temperature (Irving & Burbridge, 1989g)
- ag)** DIATRIZOATE MEGLUMINE and DIATRIZOATE SODIUM (MD-60(R)) 5 mL of a

solution containing **iodine** 292.5 mg/mL with methylprednisolone sodium succinate (Solu-Medrol(R)) 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989m)

### 3.5.5.1.A.7 Diatrizoate Meglumine/Diatrizoate Sodium

#### a) Compatible

- 1) Erythromycin gluceptate (10 mg/mL with 5 mL of a diatrizoate meglumine and diatrizoate sodium solution containing **iodine** temperature) (Irving & Burbridge, 1989p)

### 3.5.5.1.A.8 Diatrizoate Sodium

#### a) Conflicting Data

##### 1) Incompatible

**a)** DIATRIZOATE SODIUM AND DIATRIZOATE MEGLUMINE 5 mL of a solution containing 292.5 mg **iodine**

precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 1 hour at room temperature (Irving & Burbridge, 1989r)

**b)** DIATRIZOATE SODIUM 8% and DIATRIZOATE MEGLUMINE 52% - Renografin(R) - 1 or 2 mL with diphenhydramine 1 mL, concentration not specified, physically compatible for 1 hour but a precipitate was detected after 48 hours in direct admixture in syringe; temperature not specified (Marshall et al, 1965; Trissel, 1988)

**c)** Diatrizoate sodium and diatrizoate meglumine 5 mL of a solution containing 292.5 mg **iodine**/mL with papaverine 32 mg/mL, a transient precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 2 hours at room temperature (Irving & Burbridge, 1989z)

**d)** DIATRIZOATE SODIUM 5 mL of a solution containing papaverine 30 mg/mL, resulted a white suspension that disappeared within 1 minute (Kim et al, 1992ba)

**e)** DIATRIZOATE SODIUM 5 mL of a solution containing diphenhydramine 50 mg/mL , precipitate persisting after centrifugation (Kim et al, 1992bj)

**f)** DIATRIZOATE SODIUM 5 mL of a solution containing protamine 10 mg/mL , precipitate persisting after centrifugation (Kim et al, 1992bk)

**g)** DIATRIZOATE SODIUM 5 mL of a solution containing meperidine 25 mg/mL, precipitate persisting after centrifugation (Kim et al, 1992u)

**h)** DIATRIZOATE SODIUM 5 mL of a solution containing phentolamine 10 mg/mL, resulted a white suspension that disappeared within 1 minute (Kim et al, 1992cm)

##### 2) Compatible

**a)** DIATRIZOATE SODIUM 5 mL of a solution containing urokinase 1200 U/mL, no change after mixing (Kim et al, 1992)

**b)** DIATRIZOATE SODIUM 5 mL of a solution containing gentamicin 40 mg/mL, no change after mixing (Kim et al, 1992o)

**c)** DIATRIZOATE SODIUM 5 mL of a solution containing nitroglycerin 120 mcg/mL, no change after mixing (Kim et al, 1992z)

**d)** DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg **iodine** hours at room temperature (Irving & Burbridge, 1989d)

**e)** DIATRIZOATE SODIUM 5 mL of a solution containing vasopressin 20 U/mL, no change after mixing (Kim et al, 1992ae)

**f)** DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg **iodine** visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989s)

**g)** DIATRIZOATE SODIUM 5 mL of a solution containing heparin 1000 U/mL, no change after mixing (Kim et al, 1992aq)

**h)** Alprostadil 4 U/mL with DIATRIZOATE SODIUM 5 mL of a solution containing

**iodine** 300 mg/mL, no change after mixing (Kim et al, 1992au)

- i)** Diatrizoate sodium and diatrizoate meglumine 5 mL of a solution containing 292.5 mg **iodine**/mL with papaverine 32 mg/mL, a transient precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 2 hours at room temperature (Irving & Burbridge, 1989ac)
- j)** Chloramphenicol sodium succinate 200 mg/mL with DIATRIZOATE SODIUM 5 mL of a solution containing **iodine**
- k)** DIATRIZOATE SODIUM 5 mL of a solution containing hydrocortisone sodium succinate 167.09 mg/mL, no change after mixing (Kim et al, 1992bc)
- l)** DIATRIZOATE SODIUM 5 mL of a solution containing lidocaine 5 mg/mL, no change after mixing (Kim et al, 1992bf)
- m)** DIATRIZOATE SODIUM 5 mL of a solution containing epinephrine 1 mg/mL, no change after mixing (Kim et al, 1992al)
- n)** DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg **iodine** hours at room temperature (Irving & Burbridge, 1989v)
- o)** Cimetidine 100 mg/mL with DIATRIZOATE SODIUM 5 mL of a solution containing **iodine** 300 mg/mL, no change after mixing (Kim et al, 1992bv)
- p)** Cimetidine 150 mg/mL with DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg hours at room temperature (Irving & Burbridge, 1989as)
- q)** DIATRIZOATE SODIUM 5 mL of a solution containing diazepam 5 mg/mL, no change after mixing (Kim et al, 1992cb)
- r)** Chloramphenicol 33 mg/mL with DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg hours at room temperature (Irving & Burbridge, 1989aj)
- s)** Ampicillin 30 mg/mL with DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing hours at room temperature (Irving & Burbridge, 1989g)
- t)** DIATRIZOATE MEGLUMINE and DIATRIZOATE SODIUM (MD-60(R)) 5 mL of a solution containing **iodine** 292.5 mg/mL with methylprednisolone sodium succinate (Solu-Medrol(R)) 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989m)
- u)** Ampicillin 100 mg/mL with DIATRIZOATE SODIUM 5 mL of a solution containing **iodine** 300 mg/mL, no change after mixing (Kim et al, 1992w)

#### 3.5.5.1.A.9 Diatrizoate Sodium/Diatrizoate Meglumine

##### a) Conflicting Data

##### 1) Incompatible

**a)** DIATRIZOATE SODIUM AND DIATRIZOATE MEGLUMINE 5 mL of a solution containing 292.5 mg **iodine** precipitate was reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989b)

##### 2) Compatible

**a)** DIATRIZOATE SODIUM AND DIATRIZOATE MEGLUMINE (5 mL of a solution containing 292.5 mg **iodine** compatible for 2 hours at room temperature) (Irving & Burbridge, 1989)

#### 3.5.5.1.A.10 Diazepam

##### a) Conflicting Data

##### 1) Incompatible

**a)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing diazepam 5 mg/mL, resulted a white suspension that persisted longer than 1 minute (Kim et al, 1992cf)

##### 2) Compatible

- a) Diazepam 5 mg/mL with ioxaglate 5 mL of a solution containing no change after mixing (Kim et al, 1992d)
- b) Diazepam 5 mg/mL with iohexol 5 mL of solution containing change after mixing (Kim et al, 1992bt)
- c) DIATRIZOATE SODIUM 5 mL of a solution containing diazepam 5 mg/mL, no change after mixing (Kim et al, 1992cb)
- d) Diazepam 5 mg/mL with iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992ce)
- e) Diazepam 5 mg/mL with iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992cj)

### 3.5.5.1.A.11 Diphenhydramine

#### a) Conflicting Data

##### 1) Incompatible

- a) DIATRIZOATE SODIUM AND DIATRIZOATE MEGLUMINE 5 mL of a solution containing 292.5 mg **iodine** precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 1 hour at room temperature (Irving & Burbridge, 1989r)
- b) DIATRIZOATE SODIUM 8% and DIATRIZOATE MEGLUMINE 52% - Renografin(R) - 1 or 2 mL with diphenhydramine 1 mL, concentration not specified, physically compatible for 1 hour but a precipitate was detected after 48 hours in direct admixture in syringe; temperature not specified (Marshall et al, 1965; Trissel, 1988)
- c) Diphenhydramine 12.5 mg/0.25 mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg was reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989u)
- d) Diphenhydramine 50 mg/1 mL with ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL, formation of a dense, cloudy precipitate was reported (Shah & Gerlock, 1987a)
- e) DIATRIZOATE SODIUM 5 mL of a solution containing diphenhydramine 50 mg/mL , precipitate persisting after centrifugation (Kim et al, 1992bj)
- f) DIATRIZOATE MEGLUMINE 5 mL of a solution containing diphenhydramine 50 mg/mL , precipitate persisting after centrifugation (Kim et al, 1992bj)
- g) DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg diphenhydramine 12.5 mg/0.25 mL, a transient precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 1 hour at room temperature (Irving & Burbridge, 1989r)
- h) Diphenhydramine 50 mg/mL with ioxaglate 5 mL of a solution containing mg/mL, precipitate persisting after centrifugation (Kim et al, 1992cg)

##### 2) Compatible

- a) Diphenhydramine 50 mg/mL with iohexol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989a)
- b) Diphenhydramine 50 mg/mL with iohexol 5 mL of solution containing mg/mL, no change after mixing (Kim et al, 1992e)
- c) Diphenhydramine 50 mg/mL with iopamidol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989e)
- d) Diphenhydramine 50 mg/mL with iopamidol 5 mL of a solution containing 300 mg/mL, no change after mixing (Kim et al, 1992r)
- e) Diphenhydramine 50 mg/mL with iothalamate 5 mL of a solution containing 282 mg/mL, no change after mixing (Kim et al, 1992bh)
- f) Diphenhydramine 1 mL with IOTHALAMATE MEGLUMINE (60%) - Conray(R) - 1, 2, 5, 10, 20 or 40 mL, concentration not specified, no precipitate detected within 48 hours in direct admixture in syringe; temperature not specified (Marshall et al, 1965a; Trissel,

1988a)

**g)** Diphenhydramine 12.5 mg/0.25 mL with iothalamate meglumine (60%) - Conray(R) 5 mL of a solution containing 282 mg room temperature (Irving & Burbridge, 1989a)

**h)** Diphenhydramine 1 mL with iothalamate meglumine (80%) - Angio-Conray(R) - 1, 2, 5, 10, 20 or 40 mL, concentration not specified, no precipitate detected within 48 hours in direct admixture in syringe; temperature not specified (Marshall et al, 1965a; Trissel, 1988a)

**i)** Diphenhydramine, concentration not specified, with iothalamate meglumine, % unspecified, 5 mL, no precipitate formation was detected in direct admixture in syringe; duration not specified (Stevens, 1975; Trissel, 1988a)

### 3.5.5.1.A.12 Epinephrine

#### a) Compatible

- 1) Epinephrine 1 mg/mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989i)
- 2) Epinephrine 1 mg/1 mL with ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL, clear solution reported; conditions not specified (Shah & Gerlock, 1987)
- 3) Epinephrine 1 mg/mL with iohexol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989o)
- 4) Epinephrine 1 mg/mL with iohexol 5 mL of solution containing change after mixing (Kim et al, 1992ac)
- 5) Epinephrine 1 mg/mL with iothalamate 5 mL of a solution containing no change after mixing (Kim et al, 1992ah)
- 6) Epinephrine 1 mg/mL with ioxaglate 5 mL of a solution containing change after mixing (Kim et al, 1992ai)
- 7) DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg epinephrine 1 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989v)
- 8) DIATRIZOATE MEGLUMINE 5 mL of a solution containing epinephrine 1 mg/mL, no change after mixing (Kim et al, 1992al)
- 9) Epinephrine 1 mg/mL with iopamidol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989aa)
- 10) Epinephrine 1 mg/mL with iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992ar)
- 11) Epinephrine 1 mg/mL with iothalamate meglumine 5 mL of a solution containing 282 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ak)
- 12) DIATRIZOATE SODIUM 5 mL of a solution containing epinephrine 1 mg/mL, no change after mixing (Kim et al, 1992al)
- 13) DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg **iodine**/mL with epinephrine 1 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989v)

### 3.5.5.1.A.13 Erythromycin Gluceptate

#### a) Compatible

- 1) Iohexol (5 mL of a solution containing 300 mg 10 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989)
- 2) Erythromycin gluceptate (10 mg/mL with 5 mL of a diatrizoate meglumine and diatrizoate sodium solution containing **iodine** temperature) (Irving & Burbridge, 1989p)
- 3) Erythromycin gluceptate (10 mg/mL with 5 mL of a diatrizoate meglumine solution containing **iodine** 283 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989p)
- 4) Erythromycin gluceptate (10 mg/mL with iopamidol 5 mL of a solution containing 300 mg

- iodine**/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989af)
- 5)** Erythromycin gluceptate (10 mg/mL with 5 mL of an iothalamate meglumine solution containing **iodine** 282 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989ao)
- 6)** DIATRIZOATE MEGLUMINE (5 mL of a solution containing 283 mg erythromycin gluceptate 10 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989)
- 7)** Iothalamate meglumine (5 mL of a solution containing 282 mg erythromycin gluceptate 10 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989)
- 8)** Erythromycin gluceptate 10 mg/mL with 5 mL of an ioxaglate meglumine and ioxaglate sodium solution containing 320 mg temperature (Irving & Burbridge, 1989ay)
- 9)** Erythromycin gluceptate (10 mg/mL with iohexol 5 mL of a solution containing 300 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989az)
- 10)** DIATRIZOATE SODIUM AND DIATRIZOATE MEGLUMINE (5 mL of a solution containing 292.5 mg **iodine**/mL with erythromycin gluceptate 10 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989)
- 11)** Iopamidol (5 mL of a solution containing 300 mg gluceptate 10 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989)

#### 3.5.5.1.A.14 Gentamicin

##### a) Conflicting Data

##### 1) Incompatible

- a)** Ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg **iodine**/mL with gentamicin 800 mcg/mL, a transient precipitate was reported which cleared within 5 minutes at room temperature (Irving & Burbridge, 1989n)
- b)** Gentamicin 40 mg/mL with ioxaglate 5 mL of a solution containing mg/mL, precipitate persisting after centrifugation (Kim et al, 1992cn)

##### 2) Compatible

- a)** Gentamicin 40 mg/mL with iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992c)
- b)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg gentamicin 800 mcg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989d)
- c)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing gentamicin 40 mg/mL, no change after mixing (Kim et al, 1992o)
- d)** DIATRIZOATE SODIUM 5 mL of a solution containing gentamicin 40 mg/mL, no change after mixing (Kim et al, 1992o)
- e)** DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg **iodine** hours at room temperature (Irving & Burbridge, 1989d)
- f)** Gentamicin 800 mcg/mL with iothalamate meglumine 5 mL of a solution containing 282 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989q)
- g)** Gentamicin 40 mg/mL with iohexol 5 mL of solution containing no change after mixing (Kim et al, 1992bm)
- h)** Gentamicin 800 mcg/mL with iohexol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989am)
- i)** Gentamicin 800 mcg/mL with iopamidol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989an)
- j)** Gentamicin 40 mg/mL with iopamidol 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992bo)



**3.5.5.1.A.15 Heparin****a) Compatible**

- 1) DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg heparin sodium 5,000 U/0.5 mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989y)
- 2) DIATRIZOATE MEGLUMINE 5 mL of a solution containing heparin 1000 U/mL, no change after mixing (Kim et al, 1992aq)
- 3) DIATRIZOATE SODIUM 5 mL of a solution containing 1000 U/mL, no change after mixing (Kim et al, 1992aq)
- 4) Heparin 1000 U/mL with ioxaglate 5 mL of a solution containing change after mixing (Kim et al, 1992aw)
- 5) Heparin 1000 U/mL with iothalamate 5 mL of a solution containing no change after mixing (Kim et al, 1992bn)
- 6) Heparin 1000 U/mL with iohexol 5 mL of solution containing change after mixing (Kim et al, 1992cd)
- 7) Heparin 1000 U/mL with iopamidol 5 mL of a solution containing change after mixing (Kim et al, 1992ch)

**3.5.5.1.A.16 Heparin Sodium****a) Compatible**

- 1) Heparin sodium 5,000 U/0.5 mL with iothalamate meglumine 5 mL of a solution containing 282 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989f)
- 2) Heparin sodium 5,000 U/0.5 mL with iopamidol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ar)
- 3) Heparin sodium 5,000 U/0.5 mL with iohexol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989bd)
- 4) Heparin sodium 5,000 units/0.5 mL with 5 mL of an ioxaglate meglumine and ioxaglate sodium solution containing 320 mg temperature (Irving & Burbridge, 1989); another source, however, describes conditions under which these 2 drugs were found to be incompatible (Shah & Gerlock, 1987d)

**3.5.5.1.A.17 Hydrocortisone Sodium Succinate****a) Compatible**

- 1) Hydrocortisone sodium succinate 167.09 mg/mL with ioxaglate 5 mL of a solution containing **iodine** 320 mg/mL, no change after mixing (Kim et al, 1992x)
- 2) Hydrocortisone sodium succinate 10 mg/mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg room temperature (Irving & Burbridge, 1989h)
- 3) DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM 5 mL of a solution containing 292.5 mg **iodine**/mL with hydrocortisone sodium succinate 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989s)
- 4) Hydrocortisone sodium succinate 167.09 mg/mL with iothalamate 5 mL of a solution containing **iodine** 282 mg/mL, no change after mixing (Kim et al, 1992ak)
- 5) Hydrocortisone sodium succinate 10 mg/mL with iopamidol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989w)
- 6) Hydrocortisone sodium succinate 167.09 mg/mL with iopamidol 5 mL of a solution containing **iodine** 300 mg/mL, no change after mixing (Kim et al, 1992ap)
- 7) DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg hydrocortisone sodium succinate 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989s)
- 8) DIATRIZOATE MEGLUMINE 5 mL of a solution containing

- hydrocortisone sodium succinate 167.09 mg/mL, no change after mixing (Kim et al, 1992bc)
- 9)** DIATRIZOATE SODIUM 5 mL of a solution containing hydrocortisone sodium succinate 167.09 mg/mL, no change after mixing (Kim et al, 1992bc)
- 10)** Hydrocortisone sodium succinate 10 mg/mL with iohalamate meglumine 5 mL of a solution containing 282 mg **iodine** (Irving & Burbridge, 1989ap)
- 11)** Hydrocortisone sodium succinate 10 mg/mL with iohexol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989be)
- 12)** Hydrocortisone sodium succinate 167.09 mg/mL with iohexol 5 mL of solution containing **iodine** 300 mg/mL, no change after mixing (Kim et al, 1992cl)

### 3.5.5.1.A.18 Iohexol

#### a) Compatible

- 1)** Iohexol 5 mL of solution containing change after mixing (Kim et al, 1992b)
- 2)** Iohexol (5 mL of a solution containing 300 mg 10 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989)
- 3)** Diphenhydramine 50 mg/mL with iohexol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989a)
- 4)** Diphenhydramine 50 mg/mL with iohexol 5 mL of solution containing no change after mixing (Kim et al, 1992e)
- 5)** Cimetidine 150 mg/mL with iohexol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989c)
- 6)** Cimetidine 100 mg/mL with iohexol 5 mL of solution containing change after mixing (Kim et al, 1992f)
- 7)** Iohexol 5 mL of solution containing change after mixing (Kim et al, 1992n)
- 8)** Epinephrine 1 mg/mL with iohexol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989o)
- 9)** Epinephrine 1 mg/mL with iohexol 5 mL of solution containing change after mixing (Kim et al, 1992ac)
- 10)** Iohexol 5 mL of solution containing no change after mixing (Kim et al, 1992ad)
- 11)** Iohexol 5 mL of solution containing change after mixing (Kim et al, 1992af)
- 12)** Iohexol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989t)
- 13)** Iohexol 5 mL of solution containing change after mixing (Kim et al, 1992ag)
- 14)** Iohexol 5 mL of solution containing change after mixing (Kim et al, 1992as)
- 15)** Ampicillin 30 mg/mL with iohexol 5 mL of a solution containing visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ai)
- 16)** Ampicillin 100 mg/mL with iohexol 5 mL of solution containing change after mixing (Kim et al, 1992bi)
- 17)** Gentamicin 40 mg/mL with iohexol 5 mL of solution containing change after mixing (Kim et al, 1992bm)
- 18)** Gentamicin 800 mcg/mL with iohexol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989am)
- 19)** Alprostadil 4 U/mL with iohexol 5 mL of solution containing change after mixing (Kim et al, 1992br)
- 20)** Diazepam 5 mg/mL with iohexol 5 mL of solution containing change after mixing (Kim et al, 1992bt)
- 21)** Chloramphenicol 33 mg/mL with iohexol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989aq)

- 22) Iohexol 5 mL of solution containing change after mixing (Kim et al, 1992by)
- 23) Iohexol (Omnipaque(R)) 5 mL of a solution containing methylprednisolone sodium succinate (Solu- Medrol(R)) 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ax)
- 24) Erythromycin gluceptate (10 mg/mL with iohexol 5 mL of a solution containing 300 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989az)
- 25) Iohexol 5 mL of solution containing change after mixing (Kim et al, 1992cc)
- 26) Iohexol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ba)
- 27) Heparin 1000 U/mL with iohexol 5 mL of solution containing change after mixing (Kim et al, 1992cd)
- 28) Chloramphenicol sodium succinate 200 mg/mL with iohexol 5 mL of solution containing **iodine** 300 mg/mL, no change after mixing (Kim et al, 1992ci)
- 29) Heparin sodium 5,000 U/0.5 mL with iohexol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989bd)
- 30) Hydrocortisone sodium succinate 10 mg/mL with iohexol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989be)
- 31) Hydrocortisone sodium succinate 167.09 mg/mL with iohexol 5 mL of solution containing **iodine** 300 mg/mL, no change after mixing (Kim et al, 1992cl)
- 32) Iohexol 5 mL of solution containing mixing (Kim et al, 1992cq)

#### 3.5.5.1.A.19 Iopamidol

##### a) Compatible

- 1) Iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992i)
- 2) Iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992l)
- 3) Diphenhydramine 50 mg/mL with iopamidol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989e)
- 4) Diphenhydramine 50 mg/mL with iopamidol 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992r)
- 5) Iopamidol 5 mL of a solution containing change after mixing (Kim et al, 1992v)
- 6) Iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992y)
- 7) Cimetidine 150 mg/mL with iopamidol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989j)
- 8) Cimetidine 100 mg/mL with iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992aa)
- 9) Ampicillin 30 mg/mL with iopamidol 5 mL of a solution containing visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989k)
- 10) Ampicillin 100 mg/mL with iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992ab)
- 11) Iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992am)
- 12) Hydrocortisone sodium succinate 10 mg/mL with iopamidol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989w)
- 13) Hydrocortisone sodium succinate 167.09 mg/mL with iopamidol 5 mL of a solution containing **iodine** 300 mg/mL, no change after mixing (Kim et al, 1992ap)
- 14) Epinephrine 1 mg/mL with iopamidol 5 mL of a solution containing 300 mg

- visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989aa)
- 15)** Epinephrine 1 mg/mL with iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992ar)
- 16)** Alprostadil 4 U/mL with iopamidol 5 mL of a solution containing change after mixing (Kim et al, 1992at)
- 17)** Iopamidol 5 mL of a solution containing mcg/mL, no change after mixing (Kim et al, 1992az)
- 18)** Erythromycin gluceptate (10 mg/mL with iopamidol 5 mL of a solution containing 300 mg **iodine**/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989af)
- 19)** Iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992bd)
- 20)** Iopamidol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ag)
- 21)** Iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992be)
- 22)** Iopamidol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ah)
- 23)** Gentamicin 800 mcg/mL with iopamidol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989an)
- 24)** Gentamicin 40 mg/mL with iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992bo)
- 25)** Chloramphenicol sodium succinate 200 mg/mL with iopamidol 5 mL of a solution containing **iodine** 300 mg/mL, no change after mixing (Kim et al, 1992bu)
- 26)** Heparin sodium 5,000 U/0.5 mL with iopamidol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ar)
- 27)** Iopamidol (Isovue(R)) 5 mL of a solution containing methylprednisolone sodium succinate (Solu-Medrol(R)) 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989at)
- 28)** Chloramphenicol 33 mg/mL with iopamidol 5 mL of a solution containing 300 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989aw)
- 29)** Iopamidol 5 mL of a solution containing no change after mixing (Kim et al, 1992ca)
- 30)** Heparin 1000 U/mL with iopamidol 5 mL of a solution containing change after mixing (Kim et al, 1992ch)
- 31)** Diazepam 5 mg/mL with iopamidol 5 mL of a solution containing change after mixing (Kim et al, 1992cj)
- 32)** Iopamidol (5 mL of a solution containing 300 mg gluceptate 10 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989)

#### 3.5.5.1.A.20 Iothalamate

- a) Conflicting Data
- 1) Incompatible
    - a) Iothalamate 5 mL of a solution containing mg/mL, precipitate persisting after centrifugation (Kim et al, 1992co)
  - 2) Compatible
    - a) Iothalamate 5 mL of a solution containing U/mL, no change after mixing (Kim et al, 1992a)
    - b) Gentamicin 40 mg/mL with iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992c)
    - c) Iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992j)
    - d) Ampicillin 100 mg/mL with iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992t)

- e) Heparin sodium 5,000 U/0.5 mL with iothalamate meglumine 5 mL of a solution containing 282 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989f)
- f) Epinephrine 1 mg/mL with iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992ah)
- g) Hydrocortisone sodium succinate 167.09 mg/mL with iothalamate 5 mL of a solution containing **iodine** 282 mg/mL, no change after mixing (Kim et al, 1992ak)
- h) Chloramphenicol sodium succinate 200 mg/mL with iothalamate 5 mL of a solution containing **iodine** 282 mg/mL, no change after mixing (Kim et al, 1992an)
- i) Iothalamate 5 mL of a solution containing U/mL, no change after mixing (Kim et al, 1992ao)
- j) Iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992av)
- k) Iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992bb)
- l) Iothalamate meglumine 5 mL of a solution containing 282 mg papaverine 32 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ae)
- m) Diphenhydramine 50 mg/mL with iothalamate 5 mL of a solution containing 282 mg/mL, no change after mixing (Kim et al, 1992bh)
- n) Iothalamate 5 mL of a solution containing mcg/mL, no change after mixing (Kim et al, 1992bl)
- o) Heparin 1000 U/mL with iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992bn)
- p) Alprostadil 4 U/mL with iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992bq)
- q) Iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992bz)
- r) Diazepam 5 mg/mL with iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992ce)
- s) Cimetidine 100 mg/mL with iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992cp)
- t) Iothalamate 5 mL of a solution containing no change after mixing (Kim et al, 1992cr)

#### 3.5.5.1.A.21 Iothalamate Meglumine

##### a) Compatible

- 1) Iothalamate meglumine 5 mL of a solution containing 282 mg 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989i)
- 2) Gentamicin 800 mcg/mL with iothalamate meglumine 5 mL of a solution containing 282 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989q)
- 3) Chloramphenicol 33 mg/mL with IOTHALAMATE MEGLUMINE 5 mL of a solution containing 282 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ab)
- 4) Iothalamate meglumine (Conray-60(R)) 5 mL of a solution containing with methylprednisolone sodium succinate (Solu-Medrol(R)) 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ad)
- 5) Iothalamate 5 mL of a solution containing no change after mixing (Kim et al, 1992bb)
- 6) Iothalamate meglumine 5 mL of a solution containing 282 mg 32 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ae)
- 7) Epinephrine 1 mg/mL with iothalamate meglumine 5 mL of a solution containing 282 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ak)
- 8) Diphenhydramine 1 mL with IOTHALAMATE MEGLUMINE (60%) - Conray(R) - 1, 2, 5, 10, 20 or 40 mL, concentration not specified, no precipitate detected within 48 hours in

- direct admixture in syringe; temperature not specified (Marshall et al, 1965a; Trissel, 1988a)
- 9)** Diphenhydramine 12.5 mg/0.25 mL with iothalamate meglumine (60%) - Conray(R) 5 mL of a solution containing 282 mg temperature (Irving & Burbridge, 1989al)
- 10)** Diphenhydramine 1 mL with iothalamate meglumine (80%) - Angio-Conray(R) - 1, 2, 5, 10, 20 or 40 mL, concentration not specified, no precipitate detected within 48 hours in direct admixture in syringe; temperature not specified (Marshall et al, 1965a; Trissel, 1988a)
- 11)** Diphenhydramine, concentration not specified, with iothalamate meglumine, % unspecified, 5 mL, no precipitate formation was detected in direct admixture in syringe; duration not specified (Stevens, 1975; Trissel, 1988a)
- 12)** Erythromycin gluceptate (10 mg/mL with 5 mL of an iothalamate meglumine solution containing **iodine** 282 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989ao)
- 13)** Hydrocortisone sodium succinate 10 mg/mL with iothalamate meglumine 5 mL of a solution containing 282 mg **iodine** (Irving & Burbridge, 1989ap)
- 14)** Cimetidine 150 mg/mL with iothalamate meglumine 5 mL of a solution containing 282 mg **iodine**/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989av)
- 15)** Iothalamate meglumine (5 mL of a solution containing 282 mg erythromycin gluceptate 10 mg/mL visually compatible for 2 hours at room temperature) (Irving & Burbridge, 1989)
- 16)** Ampicillin 30 mg/mL with iothalamate meglumine 5 mL of an solution containing 282 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989bh)

#### 3.5.5.1.A.22 Ioxaglate

##### a) Conflicting Data

##### 1) Incompatible

- a)** Ioxaglate 5 mL of a solution containing mg/mL, resulted a white suspension that persisted longer than 1 minute (Kim et al, 1992m)
- b)** Ioxaglate 5 mL of a solution containing resulted a white suspension that disappeared within 1 minute (Kim et al, 1992q)
- c)** Cimetidine 100 mg/mL with Ioxaglate 5 mL of a solution containing mg/mL, precipitate persisting after centrifugation (Kim et al, 1992ax)
- d)** Ioxaglate 5 mL of a solution containing mg/mL, precipitate persisting after centrifugation (Kim et al, 1992bg).
- e)** Diphenhydramine 50 mg/mL with Ioxaglate 5 mL of a solution containing mg/mL, precipitate persisting after centrifugation (Kim et al, 1992cg)
- f)** Gentamicin 40 mg/mL with Ioxaglate 5 mL of a solution containing mg/mL, precipitate persisting after centrifugation (Kim et al, 1992cn)

##### 2) Compatible

- a)** Diazepam 5 mg/mL with Ioxaglate 5 mL of a solution containing no change after mixing (Kim et al, 1992d)
- b)** Ioxaglate 5 mL of a solution containing U/mL, no change after mixing (Kim et al, 1992g)
- c)** Chloramphenicol sodium succinate 200 mg/mL with Ioxaglate 5 mL of a solution containing **iodine** 320 mg/mL, no change after mixing (Kim et al, 1992h)
- d)** Ampicillin 100 mg/mL with Ioxaglate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992k)
- e)** Ioxaglate 5 mL of a solution containing resulted a white suspension that disappeared within 1 minute (Kim et al, 1992s)
- f)** Hydrocortisone sodium succinate 167.09 mg/mL with Ioxaglate 5 mL of a solution containing **iodine** 320 mg/mL, no change after mixing (Kim et al, 1992x)
- g)** Epinephrine 1 mg/mL with Ioxaglate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992ai)

- h)** Ioxaglate 5 mL of a solution containing U/mL, no change after mixing (Kim et al, 1992aj)
- i)** Heparin 1000 U/mL with ioxaglate 5 mL of a solution containing no change after mixing (Kim et al, 1992aw)
- j)** Ioxaglate 5 mL of a solution containing mcg/mL, no change after mixing (Kim et al, 1992bp)
- k)** Alprostadil 4 U/mL with ioxaglate 5 mL of a solution containing no change after mixing (Kim et al, 1992bs)
- l)** Ioxaglate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992bx)
- m)** Ioxaglate 5 mL of a solution containing no change after mixing (Kim et al, 1992ck)

### 3.5.5.1.A.23 Ioxaglate Meglumine

#### a) Conflicting Data

##### 1) Incompatible

- a)** Ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg **iodine**/mL with gentamicin 800 mcg/mL, a transient precipitate was reported which cleared within 5 minutes at room temperature (Irving & Burbridge, 1989n)
- b)** Diphenhydramine 12.5 mg/0.25 mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg was reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989u)
- c)** Diphenhydramine 50 mg/1 mL with ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL, formation of a dense, cloudy precipitate was reported (Shah & Gerlock, 1987a)
- d)** Ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL of a solution containing 320 mg **iodine**/mL with papaverine 32 mg/mL, immediate formation of a precipitate was reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989x)
- e)** Ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL with papaverine 30 mg/1 mL, undiluted, formation of a dense, cloudy, white precipitate was reported (Shah & Gerlock, 1987b); however, ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL with papaverine 30 mg/1 mL diluted in 10 mL of Sodium chloride 0.9%, formation of a white suspension though minimal precipitate formation was reported (Shah & Gerlock, 1987b)
- f)** Cimetidine 150 mg/1 mL with ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL, formation of a thread-like precipitate was reported (Shah & Gerlock, 1987c)
- g)** Cimetidine 150 mg/mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989au)

##### 2) Compatible

- a)** Hydrocortisone sodium succinate 10 mg/mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg at room temperature (Irving & Burbridge, 1989h)
- b)** Epinephrine 1 mg/mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg temperature (Irving & Burbridge, 1989i)
- c)** Epinephrine 1 mg/1 mL with ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL, clear solution reported; conditions not specified (Shah & Gerlock, 1987)
- d)** Erythromycin gluceptate 10 mg/mL with 5 mL of an ioxaglate meglumine and ioxaglate sodium solution containing 320 mg at room temperature (Irving & Burbridge, 1989ay)
- e)** Chloramphenicol 33 mg/mL with 5 mL of an ioxaglate meglumine and ioxaglate sodium solution containing 320 mg

temperature (Irving & Burbridge, 1989bc)

**f)** Heparin sodium 5,000 units/0.5 mL with 5 mL of an ioxaglate meglumine and ioxaglate sodium solution containing 320 mg at room temperature (Irving & Burbridge, 1989); another source, however, describes conditions under which these 2 drugs were found to be incompatible (Shah & Gerlock, 1987d)

**g)** Ampicillin 30 mg/mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing **iodine** 320 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989bf).

**h)** Ioxaglate meglumine and ioxaglate sodium solution 5 mL containing 320 mg **iodine**/mL with methylprednisolone sodium succinate 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989bg)

#### 3.5.5.1.A.24 Ioxaglate Meglumine/Ioxaglate Sodium

##### a) Incompatible

**1)** Ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg **iodine**/mL with protamine 10 mg/mL, immediate formation of a precipitate was reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989bb)

#### 3.5.5.1.A.25 Ioxaglate Sodium

##### a) Conflicting Data

##### 1) Incompatible

**a)** Ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg **iodine**/mL with gentamicin 800 mcg/mL, a transient precipitate was reported which cleared within 5 minutes at room temperature (Irving & Burbridge, 1989n)

**b)** Diphenhydramine 12.5 mg/0.25 mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg was reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989u)

**c)** Diphenhydramine 50 mg/1 mL with ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL, formation of a dense, cloudy precipitate was reported (Shah & Gerlock, 1987a)

**d)** Ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL of a solution containing 320 mg **iodine**/mL with papaverine 32 mg/mL, immediate formation of a precipitate was reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989x)

**e)** Ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL with papaverine 30 mg/1 mL, undiluted, formation of a dense, cloudy, white precipitate was reported (Shah & Gerlock, 1987b); however, ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL with papaverine 30 mg/1 mL diluted in 10 mL of Sodium chloride 0.9%, formation of a white suspension though minimal precipitate formation was reported (Shah & Gerlock, 1987b).

**f)** Cimetidine 150 mg/1 mL with ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL, formation of a thread-like precipitate was reported (Shah & Gerlock, 1987c)

**g)** Cimetidine 150 mg/mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989au)

##### 2) Compatible

**a)** Hydrocortisone sodium succinate 10 mg/mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg at room temperature (Irving & Burbridge, 1989h)

**b)** Epinephrine 1 mg/mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg temperature (Irving & Burbridge, 1989i)



- c)** Epinephrine 1 mg/1 mL with ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL, clear solution reported; conditions not specified (Shah & Gerlock, 1987)
- d)** Erythromycin gluceptate 10 mg/mL with 5 mL of an ioxaglate meglumine and ioxaglate sodium solution containing 320 mg at room temperature (Irving & Burbridge, 1989ay)
- e)** Chloramphenicol 33 mg/mL with 5 mL of an ioxaglate meglumine and ioxaglate sodium solution containing 320 mg temperature (Irving & Burbridge, 1989bc)
- f)** Heparin sodium 5,000 units/0.5 mL with 5 mL of an ioxaglate meglumine and ioxaglate sodium solution containing 320 mg at room temperature (Irving & Burbridge, 1989); another source, however, describes conditions under which these 2 drugs were found to be incompatible (Shah & Gerlock, 1987d)
- g)** Ampicillin 30 mg/mL with ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing **iodine** 320 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989bf).
- h)** Ioxaglate meglumine and ioxaglate sodium solution 5 mL containing 320 mg **iodine**/mL with methylprednisolone sodium succinate 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989bg)

#### 3.5.5.1.A.26 Lidocaine

##### a) Compatible

- 1)** Iopamidol 5 mL of a solution containing change after mixing (Kim et al, 1992v)
- 2)** Iohexol 5 mL of solution containing change after mixing (Kim et al, 1992as)
- 3)** DIATRIZOATE SODIUM 5 mL of a solution containing 5 mg/mL, no change after mixing (Kim et al, 1992bf)
- 4)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing lidocaine 5 mg/mL, no change after mixing (Kim et al, 1992bf)
- 5)** Ioxaglate 5 mL of a solution containing change after mixing (Kim et al, 1992ck)
- 6)** Iothalamate 5 mL of a solution containing change after mixing (Kim et al, 1992cr)

#### 3.5.5.1.A.27 Meperidine

##### a) Conflicting Data

- 1) Incompatible**
  - a)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing meperidine 25 mg/mL, precipitate persisting after centrifugation (Kim et al, 1992u)
  - b)** DIATRIZOATE SODIUM 5 mL of a solution containing meperidine 25 mg/mL, precipitate persisting after centrifugation (Kim et al, 1992u)
- 2) Compatible**
  - a)** Iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992j)
  - b)** Iopamidol 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992y)
  - c)** Ioxaglate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992bx)
  - d)** Iohexol 5 mL of solution containing after mixing (Kim et al, 1992cq)

#### 3.5.5.1.A.28 Methylprednisolone Sodium Succinate

##### a) Compatible

- 1) DIATRIZOATE MEGLUMINE (Hypaque 60%(R)) 5 mL of a solution containing**

- 283 mg/mL with methylprednisolone sodium succinate (Solu-Medrol(R)) 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989m)
- 2) Iothalamate meglumine (Conray-60(R)) 5 mL of a solution containing methylprednisolone sodium succinate (Solu-Medrol(R)) 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ad)
- 3) Iopamidol (Isovue(R)) 5 mL of a solution containing methylprednisolone sodium succinate (Solu- Medrol(R)) 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989at)
- 4) Iohexol (Omnipaque(R)) 5 mL of a solution containing methylprednisolone sodium succinate (Solu- Medrol(R)) 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ax)
- 5) Ioxaglate meglumine and ioxaglate sodium solution 5 mL containing 320 mg with methylprednisolone sodium succinate 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989bg)
- 6) DIATRIZOATE MEGLUMINE and DIATRIZOATE SODIUM (MD-60(R)) 5 mL of a solution containing **iodine** 292.5 mg/mL with methylprednisolone sodium succinate (Solu-Medrol(R)) 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989m)

#### 3.5.5.1.A.29 Metrizamide

##### a) Compatible

###### 1) Metrizamide 48.25% **iodine**

mg/mL, no precipitate observed, observation time and other conditions not specified (Pilla et al, 1986)

#### 3.5.5.1.A.30 Nitroglycerin

##### a) Compatible

- 1) DIATRIZOATE MEGLUMINE 5 mL of a solution containing nitroglycerin 120 mcg/mL, no change after mixing (Kim et al, 1992z)
- 2) DIATRIZOATE SODIUM 5 mL of a solution containing nitroglycerin 120 mcg/mL, no change after mixing (Kim et al, 1992z)
- 3) Iohexol 5 mL of solution containing change after mixing (Kim et al, 1992ad)
- 4) Iopamidol 5 mL of a solution containing mcg/mL, no change after mixing (Kim et al, 1992az)
- 5) Iothalamate 5 mL of a solution containing mcg/mL, no change after mixing (Kim et al, 1992bl)
- 6) Ioxaglate 5 mL of a solution containing mcg/mL, no change after mixing (Kim et al, 1992bp)

#### 3.5.5.1.A.31 Papaverine

##### a) Conflicting Data

###### 1) Incompatible

- a) Ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL of a solution containing 320 mg **iodine**/mL with papaverine 32 mg/mL, immediate formation of a precipitate was reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989x)
- b) Ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL with papaverine 30 mg/1 mL, undiluted, formation of a dense, cloudy, white precipitate was reported (Shah & Gerlock, 1987b); however, ioxaglate meglumine (39.3%) and ioxaglate sodium (19.6%) 5 mL with papaverine 30 mg/1 mL diluted in 10 mL of Sodium chloride 0.9%, formation of a white suspension though minimal precipitate formation was reported (Shah & Gerlock, 1987b) .
- c) Diatrizoate sodium and diatrizoate meglumine 5 mL of a solution containing 292.5 mg **iodine**/mL with papaverine 32 mg/mL, a transient precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 2 hours at room

temperature (Irving & Burbridge, 1989z)

**d)** DIATRIZOATE SODIUM 5 mL of a solution containing papaverine 30 mg/mL, resulted a white suspension that disappeared within 1 minute (Kim et al, 1992ba)

**e)** Ioxaglate 5 mL of a solution containing mg/mL, precipitate persisting after centrifugation (Kim et al, 1992bg).

**f)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing papaverine 30 mg/mL, precipitate persisting after centrifugation (Kim et al, 1992ba)

**g)** Diatrizoate meglumine 5 mL of a solution containing 283 mg papaverine 32 mg/mL, a transient precipitate formed which cleared within 5 minutes at room temperature (Irving & Burbridge, 1989z)

**2) Compatible**

**a)** Iohexol 5 mL of solution containing no change after mixing (Kim et al, 1992af)

**b)** Iohexol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989t)

**c)** Diatrizoate sodium and diatrizoate meglumine 5 mL of a solution containing 292.5 mg **iodine**/mL with papaverine 32 mg/mL, a transient precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 2 hours at room temperature (Irving & Burbridge, 1989ac)

**d)** Iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992bb)

**e)** Iothalamate meglumine 5 mL of a solution containing 282 mg papaverine 32 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ae)

**f)** Iopamidol 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992be)

**g)** Iopamidol 5 mL of a solution containing 300 mg mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ah)

**h)** Diatrizoate meglumine 5 mL of a solution containing 283 mg papaverine 32 mg/mL, a transient precipitate formed which cleared within 5 minutes at room temperature (Irving & Burbridge, 1989ac) DIATRIZOATE SODIUM AND DIATRIZOATE MEGLUMINE

**i)** Diatrizoate sodium and diatrizoate meglumine 5 mL of a solution containing 292.5 mg **iodine**/mL with papaverine 32 mg/mL, a transient precipitate formed which cleared within 5 minutes, but delayed precipitation was observed in 2 hours at room temperature (Irving & Burbridge, 1989ac)

**3.5.5.1.A.32 Papaverine Hydrochloride**

**a) Compatible**

**1) Metrizamide 48.25% iodine**

mg/mL, no precipitate observed, observation time and other conditions not specified (Pilla et al, 1986)

**3.5.5.1.A.33 Phentolamine**

**a) Conflicting Data**

**1) Incompatible**

**a)** Ioxaglate 5 mL of a solution containing mg/mL, resulted a white suspension that persisted longer than 1 minute (Kim et al, 1992m)

**b)** DIATRIZOATE SODIUM 5 mL of a solution containing phentolamine 10 mg/mL, resulted a white suspension that disappeared within 1 minute (Kim et al, 1992cm)

**c)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing phentolamine 10 mg/mL, resulted a white suspension that disappeared within 1 minute

(Kim et al, 1992cm)

**d)** Iothalamate 5 mL of a solution containing mg/mL, precipitate persisting after centrifugation (Kim et al, 1992co)

**2) Compatible**

**a)** Iopamidol 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992l)

**b)** Iohexol 5 mL of solution containing no change after mixing (Kim et al, 1992n)

**3.5.5.1.A.34 Protamine**

**a) Conflicting Data**

**1) Incompatible**

**a)** DIATRIZOATE SODIUM AND DIATRIZOATE MEGLUMINE 5 mL of a solution containing 292.5 mg **iodine** precipitate was reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989b)

**b)** DIATRIZOATE SODIUM 5 mL of a solution containing protamine 10 mg/mL, precipitate persisting after centrifugation (Kim et al, 1992bk)

**c)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing protamine 10 mg/mL, precipitate persisting after centrifugation (Kim et al, 1992bk).

**d)** DIATRIZOATE MEGLUMINE (Renografin(R) - 76), reported to form a thick, gelatinous precipitate when prepared in a 1 to 1 admixture in serum (Martin & Taylor, 1976); precipitate formation reported if the dye is not flushed out of the catheter prior to administration of the protamine (Iannone, 1975)

**e)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing 283 mg protamine 10 mg/mL, immediate formation of a precipitate was reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989b)

**f)** Ioxaglate meglumine and ioxaglate sodium 5 mL of a solution containing 320 mg **iodine**/mL with protamine 10 mg/mL, immediate formation of a precipitate was reported which persisted for a 2-hour study period at room temperature (Irving & Burbridge, 1989bb)

**2) Compatible**

**a)** Iothalamate meglumine 5 mL of a solution containing 282 mg protamine 10 mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989l)

**b)** Iothalamate 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992av)

**c)** Iopamidol 5 mL of a solution containing mg/mL, no change after mixing (Kim et al, 1992bd)

**d)** Iopamidol 5 mL of a solution containing 300 mg mg/mL, visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ag)

**e)** Iohexol 5 mL of solution containing change after mixing (Kim et al, 1992cc)

**f)** Iohexol 5 mL of a solution containing 300 mg visually compatible for 2 hours at room temperature (Irving & Burbridge, 1989ba)

**3.5.5.1.A.35 Tolazoline**

**a) Conflicting Data**

**1) Incompatible**

**a)** Ioxaglate 5 mL of a solution containing resulted a white suspension that disappeared within 1 minute (Kim et al, 1992q)

**2) Compatible**

**a)** DIATRIZOATE MEGLUMINE 5 mL of a solution containing tolazoline 25 mg/mL, no change after mixing (Kim et al, 1992p)

**b)** DIATRIZOATE SODIUM 5 mL of a solution containing

tolazoline 25 mg/mL, no change after mixing (Kim et al, 1992p)

**c)** loxaglate 5 mL of a solution containing  
resulted a white suspension that disappeared within 1 minute (Kim et al, 1992s)

**d)** lohexol 5 mL of solution containing  
change after mixing (Kim et al, 1992by)

**e)** lothalamate 5 mL of a solution containing  
mg/mL, no change after mixing (Kim et al, 1992bz)

**f)** lopamidol 5 mL of a solution containing  
no change after mixing (Kim et al, 1992ca)

#### 3.5.5.1.A.36 Urokinase

##### a) Compatible

1) DIATRIZOATE SODIUM 5 mL of a solution containing  
1200 U/mL, no change after mixing (Kim et al, 1992)

2) lothalamate 5 mL of a solution containing  
no change after mixing (Kim et al, 1992a)

3) lohexol 5 mL of solution containing  
change after mixing (Kim et al, 1992b)

4) DIATRIZOATE MEGLUMINE 5 mL of a solution containing  
urokinase 1200 U/mL, no change after mixing (Kim et al, 1992)

5) loxaglate 5 mL of a solution containing  
change after mixing (Kim et al, 1992g)

6) lopamidol 5 mL of a solution containing  
no change after mixing (Kim et al, 1992i)

#### 3.5.5.1.A.37 Vasopressin

##### a) Compatible

1) DIATRIZOATE SODIUM 5 mL of a solution containing  
vasopressin 20 U/mL, no change after mixing (Kim et al, 1992ae)

2) lohexol 5 mL of solution containing  
change after mixing (Kim et al, 1992ag)

3) DIATRIZOATE MEGLUMINE 5 mL of a solution containing  
vasopressin 20 U/mL, no change after mixing (Kim et al, 1992ae)

4) loxaglate 5 mL of a solution containing  
change after mixing (Kim et al, 1992aj)

5) lopamidol 5 mL of a solution containing  
change after mixing (Kim et al, 1992am)

6) lothalamate 5 mL of a solution containing  
no change after mixing (Kim et al, 1992ao)

#### 3.5.5.1.B Sodium Iodide

Aminophylline

Anileridine Hydrochloride

Carbenicillin

Codeine

Codeine Phosphate

Dextran 70

Erythromycin Lactobionate

Levorphanol  
Magnesium Sulfate  
Meperidine  
Meperidine Hydrochloride  
Metaraminol Bitartrate  
Methadone  
Methicillin  
Methylprednisolone  
Methylprednisolone Sodium Succinate  
Morphine  
Norepinephrine  
Penicillin G Potassium  
Pentobarbital  
Procaine  
Procaine Hydrochloride  
Sodium Bicarbonate  
Thiopental  
Trimethaphan Camsylate

#### **3.5.5.1.B.1 Aminophylline**

##### **a) Compatible**

- 1) Aminophylline 500 mg/L with sodium iodide 1 g/L, physically compatible; conditions not specified (Parker, 1970b)
- 2) Aminophylline 500 or 1000 mg with methylprednisolone sodium succinate (Solu-Medrol(R)) 40 or 80 mg and Sodium iodide 500 or 1000 mg in Dextrose 5% in water 500 or 1000 mL, visually compatible with a clear solution for up to 24 hours; conditions not specified (Tech Info Solu-Medrol(R), 1978)(Trissel, 1988b)
- 3) Aminophylline 1 g/L with sodium iodide 1 g/L and methylprednisolone sodium succinate 80 mg/L or aminophylline 500 mg/L with sodium iodide 500 mg/L and methylprednisolone sodium succinate 40 mg/L, visually compatible for 24 hours in Dextrose 5% in water; temperature not specified (Trissel, 1988b)
- 4) Aminophylline 1 g/L with sodium iodide 1 g/L and methylprednisolone sodium succinate 80 mg/L or aminophylline 500 mg/L with sodium iodide 500 mg/L and methylprednisolone sodium succinate 40 mg/L, visually compatible for 24 hours in Dextrose 5% in water; temperature not specified (Trissel, 1988c)
- 5) Methylprednisolone 40 mg/L with sodium iodide 500 mg/L and aminophylline 500 mg/L give clear solutions for 24 hours; temperature not specified (Trissel, 1988d)
- 6) Methylprednisolone 80 mg/L with sodium iodide 1 g/L and aminophylline 1 g/L give clear solutions for 24 hours; temperature not specified (Trissel, 1988d).

#### **3.5.5.1.B.2 Anileridine Hydrochloride**

##### **a) Incompatible**

- 1) Anileridine hydrochloride incompatible with sodium iodide; conditions not specified

(Kramer et al, 1971)

#### **3.5.5.1.B.3 Carbenicillin**

##### **a) Incompatible**

- 1) Carbenicillin with sodium iodide, carbenicillin deteriorates when mixed either by drip or Soluset(R); conditions not specified (VanDerLinde et al, 1977a)

#### **3.5.5.1.B.4 Codeine**

##### **a) Incompatible**

- 1) Codeine stated to be physically incompatible with sodium iodide; conditions not specified (Patel & Phillips, 1966i)

#### **3.5.5.1.B.5 Codeine Phosphate**

##### **a) Incompatible**

- 1) Sodium iodide (physically incompatible with codeine phosphate; conditions not specified) (Patel & Phillips, 1966f)

#### **3.5.5.1.B.6 Dextran 70**

##### **a) Compatible**

- 1) Sodium iodide 1 g/L with dextran 70 6% in Dextrose 5% in water or Sodium chloride 0.9% physically compatible for 24 hours; conditions not specified (Kirkland et al, 1961a; Smith, 1965)

#### **3.5.5.1.B.7 Erythromycin Lactobionate**

##### **a) Compatible**

- 1) Erythromycin lactobionate 1 g/L with sodium iodide 1 g/L, physically compatible and erythromycin stable for 24 hours at 25 degrees C in Dextrose 5% in water (Parker, 1969a)

#### **3.5.5.1.B.8 Levorphanol**

##### **a) Incompatible**

- 1) Levorphanol with sodium iodide, incompatible; conditions not specified (Bogash, 1955)

#### **3.5.5.1.B.9 Magnesium Sulfate**

##### **a) Incompatible**

- 1) Magnesium sulfate with sodium iodide, incompatible with concentrated solutions of sodium iodide; conditions not specified (VanDerLinde et al, 1977)

#### **3.5.5.1.B.10 Meperidine**

##### **a) Incompatible**

- 1) Sodium iodide (physically incompatible with meperidine; drug concentrations not specified) (Patel & Phillips, 1966j)

#### **3.5.5.1.B.11 Meperidine Hydrochloride**

##### **a) Incompatible**

- 1) Meperidine hydrochloride (Demerol(R)) stated to be physically incompatible with sodium iodide; conditions not specified (Patel & Phillips, 1966a)

#### **3.5.5.1.B.12 Metaraminol Bitartrate**

**a) Incompatible**

- 1) Metaraminol bitartrate with sodium iodide, may form precipitate; conditions not specified (VanDerLinde et al, 1977b)

**3.5.5.1.B.13 Methadone****a) Incompatible**

- 1) Methadone with sodium iodide, physically incompatible; no conditions specified (Patel & Phillips, 1966)

**3.5.5.1.B.14 Methicillin****a) Compatible**

- 1) Methicillin 1 g/L with sodium iodide 1 g/L, stated to be physically compatible; conditions not specified (Parker, 1970f)

**3.5.5.1.B.15 Methylprednisolone****a) Compatible**

- 1) Methylprednisolone 40 mg/L with sodium iodide 500 mg/L and aminophylline 500 mg/L give clear solutions for 24 hours; temperature not specified (Trissel, 1988d)
- 2) Methylprednisolone 80 mg/L with sodium iodide 1 g/L and aminophylline 1 g/L give clear solutions for 24 hours; temperature not specified (Trissel, 1988d).

**3.5.5.1.B.16 Methylprednisolone Sodium Succinate****a) Compatible**

- 1) Aminophylline 500 or 1000 mg with methylprednisolone sodium succinate (Solu-Medrol(R)) 40 or 80 mg and Sodium iodide 500 or 1000 mg in Dextrose 5% in water 500 or 1000 mL, visually compatible with a clear solution for up to 24 hours; conditions not specified (Tech Info Solu-Medrol(R), 1978)(Trissel, 1988b)
- 2) Aminophylline 1 g/L with sodium iodide 1 g/L and methylprednisolone sodium succinate 80 mg/L or aminophylline 500 mg/L with sodium iodide 500 mg/L and methylprednisolone sodium succinate 40 mg/L, visually compatible for 24 hours in Dextrose 5% in water; temperature not specified (Trissel, 1988b)
- 3) Aminophylline 1 g/L with sodium iodide 1 g/L and methylprednisolone sodium succinate 80 mg/L or aminophylline 500 mg/L with sodium iodide 500 mg/L and methylprednisolone sodium succinate 40 mg/L, visually compatible for 24 hours in Dextrose 5% in water; temperature not specified (Trissel, 1988c)

**3.5.5.1.B.17 Morphine****a) Incompatible**

- 1) Morphine stated to be physically incompatible with sodium iodide; conditions not specified (Patel & Phillips, 1966d)
- 2) Sodium iodide (stated to be physically incompatible with morphine; no conditions specified) (Patel & Phillips, 1966e; Kramer et al, 1971a)

**3.5.5.1.B.18 Norepinephrine****a) Incompatible**

- 1) Norepinephrine with sodium iodide, stated to be physically incompatible; conditions not specified (Patel & Phillips, 1966g)
- 2) Norepinephrine (levarterenol) with sodium conditions not stated (VanDerLinde et al, 1977d)
- 3) Sodium iodide (stated to be physically incompatible with norepinephrine; conditions not specified) (Patel & Phillips, 1966h)



**3.5.5.1.B.19 Penicillin G Potassium****a) Compatible**

- 1) Penicillin G potassium 5 million U/L with sodium iodide 1 g/L, physically compatible; conditions not specified; penicillin G potassium 1 million U/L with sodium iodide 1 g/L, penicillin activity retained for 24 hours at 25 degrees C; solution not specified (Parker, 1969d)

**3.5.5.1.B.20 Pentobarbital****a) Compatible**

- 1) Pentobarbital 500 mg/10 mL with sodium iodide 1 g/10 mL, physically compatible in syringe; conditions not specified (Jones et al, 1961a)

**3.5.5.1.B.21 Procaine****a) Conflicting Data****1) Incompatible**

- a) Sodium iodide (with procaine physically incompatible; conditions not specified) (Patel & Phillips, 1966b)

**2) Compatible**

- a) Sodium iodide (1 g/L with procaine 1 g/L physically compatible in Sodium chloride 0.9%; conditions not specified) (Kirkland et al, 1961)

**3.5.5.1.B.22 Procaine Hydrochloride****a) Incompatible**

- 1) Procaine hydrochloride stated to be physically incompatible with sodium iodide; conditions not specified (Patel & Phillips, 1966c)

**3.5.5.1.B.23 Sodium Bicarbonate****a) Compatible**

- 1) Sodium bicarbonate 2.4 mEq/L with sodium iodide 1 g/L, physically compatible for 24 hours in Dextrose 5% in water; temperature not specified (Trissel, 1990)

**3.5.5.1.B.24 Thiopental****a) Compatible**

- 1) Sodium iodide (1 g/10 mL with thiopental 75 mg/3 mL physically compatible in syringe) (Jones et al, 1961)

**3.5.5.1.B.25 Trimethaphan Camsylate****a) Incompatible**

- 1) Sodium iodide with trimethaphan camsylate, reported incompatible; conditions not stated (VanDerLinde et al, 1977c)

**3.5.5.2 Solutions**

Iodine

Sodium Iodide

**3.5.5.2.A Iodine**

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**3.5.5.2.A.1 SODIUM CHLORIDE****a) Compatible**

- 1) Sodium chloride 0.9% compatible with sodium iodide; conditions not specified (Fowler, 1967)

**3.5.5.2.B Sodium Iodide**

DEXTROSE 10% IN SODIUM CHLORIDE 0.9%

DEXTROSE 10% IN WATER

DEXTROSE 5% IN SODIUM CHLORIDE 0.225%

DEXTROSE 5% IN SODIUM CHLORIDE 0.45%

DEXTROSE 5% IN SODIUM CHLORIDE 0.9%

DEXTROSE 5% IN WATER

Fructose 10% (Levugen(R) 10%) in water

Invert sugar 10% (Travert(R) 10%) in electrolyte 1

Invert sugar 10% (Travert(R) 10%) in electrolyte 2

Sodium lactate 1/6 M

TOTAL PARENTERAL NUTRITION

**3.5.5.2.B.1 DEXTROSE 10% IN SODIUM CHLORIDE 0.9%****a) Compatible**

- 1) DEXTROSE 10% IN SODIUM CHLORIDE 0.9% compatible with sodium iodide; conditions not specified (Fowler, 1967a)

**3.5.5.2.B.2 DEXTROSE 10% IN WATER****a) Compatible**

- 1) DEXTROSE 10% IN WATER compatible with sodium iodide; conditions not specified (Fowler, 1967a)

**3.5.5.2.B.3 DEXTROSE 5% IN SODIUM CHLORIDE 0.225%****a) Compatible**

- 1) DEXTROSE 5% IN SODIUM CHLORIDE 0.225% compatible with sodium iodide; conditions not specified (Fowler, 1967a)

**3.5.5.2.B.4 DEXTROSE 5% IN SODIUM CHLORIDE 0.45%****a) Compatible**

- 1) DEXTROSE 5% IN SODIUM CHLORIDE 0.45% compatible with sodium iodide; conditions not specified (Fowler, 1967a)

**3.5.5.2.B.5 DEXTROSE 5% IN SODIUM CHLORIDE 0.9%****a) Compatible**

- 1) DEXTROSE 5% IN SODIUM CHLORIDE 0.9% compatible with sodium iodide; conditions not specified (Fowler, 1967a)

**3.5.5.2.B.6 DEXTROSE 5% IN WATER**

## a) Compatible

- 1) DEXTROSE 5% IN WATER compatible with sodium iodide; conditions not specified (Fowler, 1967a)

**3.5.5.2.B.7 Fructose 10% (Levugen(R) 10%) in water**

## a) Compatible

- 1) Fructose 10% (Levugen(R) 10%) in water with sodium iodide 2 g/1000 mL, visually compatible for 24 hours; conditions not specified (Dixon & Weshalek, 1972)

**3.5.5.2.B.8 Invert sugar 10% (Travert(R) 10%) in electrolyte 1**

## a) Compatible

- 1) Invert sugar 10% (Travert(R) 10%) in electrolyte 1 with sodium iodide 2 g/1000 mL, visually compatible for 24 hours; conditions not specified (Dixon & Weshalek, 1972a)

**3.5.5.2.B.9 Invert sugar 10% (Travert(R) 10%) in electrolyte 2**

## a) Compatible

- 1) Invert sugar 10% (Travert(R) 10%) in electrolyte 2 with sodium iodide 2 g/1000 mL, visually compatible for 24 hours; conditions not specified (Dixon & Weshalek, 1972a)

**3.5.5.2.B.10 Sodium lactate 1/6 M**

## a) Compatible

- 1) Sodium iodide 2 g/1000 mL in 1/6 molar sodium lactate in water, visually compatible for 24 hours; conditions not specified (Dixon & Weshalek, 1972b)

**3.5.5.2.B.11 TOTAL PARENTERAL NUTRITION**

## a) Compatible

- 1) Sodium iodide 100 mg/L with total parenteral nutrition (ProcalAmine(R)), visually compatible with no precipitate (conditions not specified); composition of total parenteral nutrition listed below (Prod Info ProcalAmine(R), 1985):

Amino acids	3%
Glycerol	3%
Electrolytes	present

**4.0 Clinical Applications**

Monitoring Parameters

Patient Instructions

Place In Therapy

Mechanism of Action / Pharmacology

## Therapeutic Uses

### Comparative Efficacy / Evaluation With Other Therapies

#### 4.1 Monitoring Parameters

- A) Therapeutic
  - 1) Physical Findings
    - a) Patients should be monitored for prompt wound healing, or the absence of infection.
- B) Toxic
  - 1) Physical Findings
    - a) Patients should be monitored for hypersensitivity, or for the development of

#### 4.2 Patient Instructions

- A) Potassium Iodide (By mouth)  
Potassium Iodide

Loosens mucus in your chest and lungs. Also protects your thyroid gland from radiation.

##### When This Medicine Should Not Be Used:

You should not use this medicine if you have had an allergic reaction to potassium iodide. You should not use this medicine if you have an overactive thyroid or goiter (due to lack of

##### How to Use This Medicine:

###### Liquid

Your doctor will tell you how much of this medicine to use and how often. Do not use more medicine or use it more often than your doctor tells you to.

Measure the oral liquid medicine with a marked measuring spoon, oral syringe, or medicine cup.

Drink half a glass (4 ounces) of water when you take this medicine.

##### If a Dose is Missed:

If you miss a dose or forget to use your medicine, use it as soon as you can. If it is almost time for your next dose, wait until then to use the medicine and skip the missed dose. Do not use extra medicine to make up for a missed dose.

##### How to Store and Dispose of This Medicine:

Store the medicine in a closed container at room temperature, away from heat, moisture, and direct light. Keep the bottle tightly closed after use.

Ask your pharmacist, doctor, or health caregiver about the best way to dispose of any leftover medicine after you have finished your treatment. You will also need to throw away old medicine after the expiration date has passed.

Keep all medicine away from children and never share your medicine with anyone.

##### Drugs and Foods to Avoid:

Ask your doctor or pharmacist before using any other medicine, including over-the-counter medicines, vitamins, and herbal products.

##### Warnings While Using This Medicine:

Make sure your doctor knows if you are pregnant or breast feeding.

##### Possible Side Effects While Using This Medicine:

Call your doctor right away if you notice any of these side effects:

Allergic reaction: Itching or hives, swelling in your face or hands, swelling or tingling in your mouth or throat, chest tightness, trouble breathing.

Confusion, weakness, uneven heartbeat, shortness of breath, or numbness or tingling in your hands, feet or lips.

If you notice these less serious side effects, talk with your doctor:

- Lumps in your armpits or neck.
- Metallic taste in your mouth.
- Mild nausea, vomiting, or diarrhea.
- Mild skin rash.
- Pain in your joints.
- Skin rash.
- Stomach pain.

If you notice other side effects that you think are caused by this medicine, tell your doctor.

#### 4.3 Place In Therapy

##### A) Iodine

1) **Iodine** solutions are widely used in the treatment of superficial wounds. The toxicity profile of the lowest of all the topical antiseptics. It is highly effective in the decontamination of intact skin and minor wounds, and these factors combined with its low cost make it a useful addition to most formularies. However, the routine use of older **iodine** preparations has probably been superseded by the advent of povidone-preparations, which retain antiseptic activity in the presence of body secretions, tissue fluids, and surfactants.

##### B) Potassium Iodide

- 1) Potassium iodide is used preoperatively to reduce vascularity of the thyroid gland prior to thyroidectomy, as an antithyroid agent in the management of thyroid storm, and after radioactive disease.
- 2) Potassium iodide is used to treat erythematous dermatoses, including erythema nodosum, erythema multiforme, and nodular vasculitis.
- 3) Potassium iodide is the drug of choice for treatment of lymphocutaneous sporotrichosis.
- 4) Potassium iodide is used as a thyroid blocking agent following exposure to radioisotopes of from a nuclear reactor accident.
- 5) Potassium iodide is used for adjunctive treatment as an expectorant in respiratory tract disorders such as chronic obstructive pulmonary disease (bronchitis, emphysema, and bronchial asthma), cystic fibrosis, and chronic sinusitis and to help prevent postsurgical atelectasis. Objective evidence of clinical efficacy as an expectorant is lacking. Because of the availability of more effective and safer expectorants, other agents usually are preferred.

#### 4.4 Mechanism of Action / Pharmacology

##### A) Iodine

###### 1) MECHANISM OF ACTION

- a) Free **iodine** captures electrons to form iodide ions. oxidizing carbohydrates, lipids, amino acids, and proteins, thus killing the organism (AMA Department of Drugs, 1986).
- b) Elemental **iodine** is a very effective antimicrobial agent. Sufficient concentrations and contact time will kill all bacteria, fungi, protozoa, viruses, and yeasts (AMA Department of Drugs, 1986). Spores, however, are highly resistant to aqueous solutions, but alcoholic solutions of against spores (Osol, 1980).
- c) **Iodine** cannot penetrate tissue without rapid conversion to iodide ions, which are devoid of antimicrobial activity. Thus, **iodine** solutions (with the exception of povidone-the tissue surface (AMA Department of Drugs, 1986).

##### B) Potassium Iodide

###### 1) MECHANISM OF ACTION

- a) Iodides are readily absorbed from the gastrointestinal tract and concentrated primarily in respiratory tract secretions. They enhance secretion of respiratory fluids, thus decreasing mucus viscosity, and also may stimulate breakdown of fibrinoid material in inflammatory exudate. Objective evidence of clinical efficacy is lacking (Olin, 1990).
- b) In erythematous dermatoses, the antiinflammatory effect of potassium iodide may be due to an immunosuppressive effect mediated by heparin (Schulz & Whiting, 1976).
- c) When administered after exposure to radioisotopes of accumulation of iodide by the thyroid. Mechanisms of action include saturation of the iodide transport

system of the thyroid, inhibition of intrathyroidal organification of iodide, and dilution of the isotope atoms with nonradioactive **iodine** atoms. It also increases the rate of urinary excretion of I-131 iodide atoms and thus decreases whole-body radiation dose (Becker, 1987).

## 2) REVIEW ARTICLES

a) A review article discussing the use of potassium iodide for the treatment of inflammatory dermatoses; also addresses pharmacology and adverse effects (Sterling & Heymann, 2000).

## 4.5 Therapeutic Uses

Iodine

Potassium Iodide

### 4.5.A Iodine

Disinfection

Endemic goiter

Skin ulcer

Thyroid storm

Total parenteral nutrition

#### 4.5.A.1 Disinfection

FDA Labeled Indication

##### a) Overview

FDA Approval: Adult, yes; Pediatric, yes

Efficacy: Adult, Effective; Pediatric, Effective

Recommendation: Adult, Class IIa; Pediatric, Class IIa

Strength of Evidence: Adult, Category B; Pediatric, Category B

See Drug Consult reference: RECOMMENDATION AND EVIDENCE RATINGS

##### b) Summary:

**IODINE** is an effective antiseptic agent for use on intact skin

Tincture of 2% **IODINE** should be used, not the older, stronger 7% tincture (which has been known to cause burns)

##### c) Adult:

1) **IODINE** 2% tincture is the preferred preparation for decontamination of intact skin prior to venipuncture because it dries faster (AMA Department of Drugs, 1986b; Osol, 1980a). The alcoholic vehicle facilitates spreading and penetration (Goodman & Gilman, 1970).

2) Although the older 7% tincture is also effective, it has caused severe burns, and should probably not be used for this purpose (AMA Department of Drugs, 1986b).

#### 4.5.A.2 Endemic goiter

##### a) Overview

FDA Approval: Adult, no; Pediatric, no

Efficacy: Adult, Evidence favors efficacy; Pediatric, Evidence favors efficacy

Recommendation: Adult, Class IIa; Pediatric, Class IIa

Strength of Evidence: Adult, Category B; Pediatric, Category B

See Drug Consult reference: RECOMMENDATION AND EVIDENCE RATINGS

##### b) Summary:

**IODINE** may be effective treatment for endemic goiter caused by

Reduction in goiter size has occurred following

##### c) Adult:

1) A 400-microgram daily dose of **IODINE**

patients with endemic GOITER due to **IODINE** in the size of diffuse goiters (Hintze et al, 1989).

**2) Iodine** supplementation of euthyroid subjects with endemic goiter normalized thyroid volume but resulted in reversible thyroid dysfunction and autoimmunity in some subjects. Sixty-two subjects with untreated endemic goiter were given either

The mean reduction in goiter size was 38% with I treatment, which was sustained at 18 months. Serum TSH and T3 levels were stable in both groups, but T4 rose with I treatment. Thyroglobulin levels declined during I therapy and rose again during follow-up. Three subjects taking I developed thyroid microsomal autoantibody titers; 2 of the 3 manifested I-induced hypothyroidism, the other hyperthyroidism. Thyroid dysfunctions and antibody titers decreased after I withdrawal (Kahaly et al, 1997a).

**d) Pediatric:**

**1) Iron deficiency anemia** reduces the efficacy of

endemic goiter in the Ivory Coast, 51 children with endemic goiter and adequate iron status (group 1) and 53 children with endemic goiter and iron deficiency anemia (group 2) were given a single oral dose of iodized poppy seed oil providing 200 milligrams of dosing, thyroid volume decreased in both groups, but significantly more so in group 1 (45% vs 22%, p less than 0.001). At 15 and 30 weeks post-dose, the prevalence of goiter was 62% and 64%, respectively, in group 2 and 31% and 12%, respectively, in group 1. The regression of hemoglobin and percentage change in thyroid volume was significant ( $r(2)=0.606$ , p less than 0.001) (Zimmerman et al, 2000).

#### 4.5.A.3 Skin ulcer

**a) Overview**

FDA Approval: Adult, no; Pediatric, no  
Efficacy: Adult, Evidence is inconclusive  
Recommendation: Adult, Class III  
Strength of Evidence: Adult, Category B

See Drug Consult reference: RECOMMENDATION AND EVIDENCE RATINGS

**b) Summary:**

**IODINE**-containing ointment was beneficial for treatment of diabetic ulcers of the lower extremities in one small study  
The cost of **IODINE** therapy was lower than standard therapy

**c) Adult:**

**1) The results of a small study involving 12 diabetic patients with cavity foot ulcers indicate that cadexomer iodine ointment is as effective as standard topical therapy (gentamicin solution, streptodornase/streptokinase, dry saline gauze) in the treatment of exuding diabetic cavity foot ulcers and at a lower cost. Cadexomer iodine ointment contains 0.9% modified starch matrix. This ointment has been shown to be highly fluid-absorbing, antibacterial, and able to dissolve debris and necrotic tissue (Apelqvist & Ragnarson Tennvall, 1996).**

#### 4.5.A.4 Thyroid storm

FDA Labeled Indication

**a) Overview**

FDA Approval: Adult, yes; Pediatric, no  
Efficacy: Adult, Effective  
Recommendation: Adult, Class I  
Strength of Evidence: Adult, Category B

See Drug Consult reference: RECOMMENDATION AND EVIDENCE RATINGS

**b) Summary:**

**IODINE** (as Lugol's Solution, potassium iodide, or sodium iodide) has been effective in combination with other agents in managing thyroid storms (Carter et al, 1975; Duncan & Jones, 1973)

**IODINE** is rapid acting and should be used only on a short-term basis in patients with thyroid storm

**4.5.A.5 Total parenteral nutrition**

See Drug Consult reference: TRACE MINERAL SUPPLEMENTATION IN TPN

**4.5.B Potassium Iodide**

Cutaneous sporotrichosis

Erythematous condition

Implementation of protective measures to prevent injury due to radiation sources, Thyroid gland; Prophylaxis

Induction of involution of thyroid

Iodine deficiency; Treatment and Prophylaxis

Livedoid vasculitis

Lymphocutaneous sporotrichosis

**4.5.B.1 Cutaneous sporotrichosis****a) Overview**

FDA Approval: Adult, no; Pediatric, no

Efficacy: Adult, Evidence favors efficacy; Pediatric, Evidence favors efficacy

Recommendation: Adult, Class IIb; Pediatric, Class IIb

Strength of Evidence: Adult, Category B; Pediatric, Category B

See Drug Consult reference: RECOMMENDATION AND EVIDENCE RATINGS

**b) Summary:**

Saturated solution of potassium iodide (SSKI) is recommended in adults and children as an alternative treatment for patients not responding to itraconazole for cutaneous sporotrichosis (Kauffman et al, 2007).

**c) Adult:**

**1)** Saturated solution of potassium iodide (SSKI) is recommended as an alternative treatment for patients not responding to itraconazole for cutaneous sporotrichosis. Treatment should be continued for 2 to 4 weeks after all lesions have healed, usually a total of 3 to 6 months. Adverse effects such as metallic taste, nausea, abdominal pain and rash are frequent among patients treated with SSKI. Cure rates ranging from 80% to 100% have been reported with SSKI in clinical trials and case reports (Kauffman et al, 2007).

**d) Pediatric:**

**1)** Saturated solution of potassium iodide (SSKI) is recommended as an alternative treatment for patients not responding to itraconazole for cutaneous sporotrichosis. Treatment should be continued for 2 to 4 weeks after all lesions have healed, usually a total of 3 to 6 months. Adverse effects such as metallic taste, nausea, abdominal pain and rash are frequent among children treated with SSKI. Cure rates ranging from 80% to 100% have been reported with SSKI in clinical trials and case reports (Kauffman et al, 2007).

**4.5.B.2 Erythematous condition****a) Overview**

FDA Approval: Adult, no; Pediatric, no

Efficacy: Adult, Evidence is inconclusive

Recommendation: Adult, Class IIb

Strength of Evidence: Adult, Category C

See Drug Consult reference: RECOMMENDATION AND EVIDENCE RATINGS

**b) Summary:**

Has been used for erythematous dermatoses, including erythema nodosum, nodular vasculitis, and erythema multiforme



#### 4.5.B.3 Implementation of protective measures to prevent injury due to radiation sources, Thyroid gland; Prophylaxis

FDA Labeled Indication

##### a) Overview

FDA Approval: Adult, yes; Pediatric, yes

Efficacy: Adult, Effective; Pediatric, Effective

Recommendation: Adult, Class IIa; Pediatric, Class IIa

Strength of Evidence: Adult, Category B; Pediatric, Category B

See Drug Consult reference: RECOMMENDATION AND EVIDENCE RATINGS

##### b) Summary:

Potassium iodide is used following radiation exposure (eg, nuclear reactor accident) to block uptake by the thyroid of radioactive

risk of radiation-induced thyroid neoplasms

Combination therapy of potassium iodide, methimazole, and thyroxine protected thyroid function better than did potassium iodide alone in children being treated with metaiodobenzylguanidine for neuroblastoma

##### c) Adult:

##### 1) General Information

Potassium iodide (KI) reduces the risk of thyroid cancer in radiation emergencies involving the release of radioactive **iodine**. KI protects the thyroid in radiation emergencies by saturating the gland with non-radioactive **iodine**. This blocks the uptake of radioactive or contaminated water, milk, or other foods. The Food and Drug Administration (FDA) recommends that state and local public health officials should consider the use of KI depending on the measured radiation exposure, and the age of the person exposed.

There is an inverse relationship between the risk of thyroid cancer and age. Younger individuals are at higher risk for thyroid cancer than older individuals. The FDA recommends the following KI doses based on age, predicted thyroid exposure, and pregnancy and lactation status:

AGE	
Adults over 40 yrs	
Adults over 18 through 40 yrs	
Pregnant or lactating women	
Children over 3 through 18 years(**)	
Children over 1 month through 3 yrs	
Birth through 1 month	
(*)...A centigray (cGY) is a unit of measure of radiation exposure in humans; 1cGy=1 REM	
(**)...Adolescents approaching adult size (70 kilograms or greater) should receive an adult dose (130 mg)	
(&)...mg = milligrams	

These doses can block approximately 90% of radioiodine absorption if the first dose is taken a few hours before or immediately after exposure. Even if the dose is taken 3 to 4 hours after exposure, the drug can still block about 50% of radioiodine absorption. The recommended dose should be taken daily until the risk of exposure to radioiodines no longer exists. The protective effects of KI last approximately 24 hours. Potassium iodide does not reduce body uptake of other radioactive substances nor provide protection against other effects of radiation exposure. KI, though generally well tolerated, has been associated with some side effects including mild gastrointestinal distress (more frequent in children), and rash. Transient hypothyroidism was observed in 0.37% of the neonates treated with KI following Chernobyl. Due to the potential consequences of transient hypothyroidism on brain development, the FDA recommends that all neonates treated with KI be monitored by measuring TSH and treating hypothyroidism should it develop. It is also recommended that repeat dosing be avoided in pregnant and lactating women, and neonates to minimize the risk of hypothyroidism.

KI in a tablet form or as a fresh saturated solution should be used. The solution can be diluted in milk, water, or formula. KI is also available as an ingredient in prescription drugs for treating

asthma and other lung disorders; however, these prescription products are not suitable for use in a radiation emergency. The high dosage in prescription tablets, for example, exceeds that approved for thyroid blocking. Also, the enteric coating on these tablets delays absorption and may impede the effectiveness in a radiation emergency.

The safe and effective use of KI as a thyroid blocking agent depends on a determination by local public health authorities that a radiation emergency has occurred that is likely to release radioactivity, and that the benefits of using KI outweigh its risks. Since the use of KI is not without risk, special labeling for the consumer must accompany the drug, stating that it should be taken only when directed by public health authorities (FDA, 2001; Becker, 1987a; Becker et al, 1984; Crocker, 1984).

**d) Pediatric:**

**1)** Combination therapy with thyroxine, methimazole, and potassium iodide (referred to as DBR prophylaxis: dilute, block, and replace) afforded better protection of the thyroid gland than did potassium iodide alone when children with neuroblastoma were being diagnosed and/or treated with metaiodobenzylguanidine (MIBG). A cohort of 34 children (age range 0.5 to 128 months) with confirmed or suspected neuroblastoma were given daily thyroxine 100 micrograms/meter(2) in 1 dose, methimazole 0.5 milligrams/kilogram body mass in 2 doses, and potassium iodide 90 milligrams in 3 doses. All were administered orally. Thyroxine and methimazole were started 1 day before MIBG, and potassium iodide was started on the morning of administration of MIBG. Thyroid protection was given for 3 days when 123I- MIBG was administered (diagnosis). For patients receiving 131I-MIBG (treatment), thyroxine and methimazole were given for 4 weeks and potassium iodide for 2 weeks. Protection was continued between times of administration of MIBG. Thyrotropin elevation was used as a measure of thyroid damage. At the end of follow-up, which ranged from 1 to 34 months (mean 19 months), 15 (65%) of the 23 evaluable patients had no thyrotropin elevation (TE), 4 (17%) had transient TE, and 4 (17%) had permanent TE. In a historic control group who received only potassium iodide for thyroid protection while receiving MIBG, 29 of 42 (48%) had no TE, 4 (9%) had transient TE, and 18 (43%) had permanent TE. Of patients receiving DBR, the proportion with permanent TE was significantly less than corresponding proportion of patients who received only potassium iodide ( $p=0.038$ ). In the entire DBR group ( $n=34$ ), 11 patients (33.5%) showed radiiodide uptake on at least 1 occasion, compared to 35 of 42 patients (83%) who received only potassium iodide ( $p=0.000$  by Pearson chi-square test). DBR was associated with no liver toxicity, bone marrow toxicity, or other side effects. There were no signs of hyperthyroidism, and all thyroid parameters returned to normal within 2 months (van Santen et al, 2003).

**4.5.B.4 Induction of involution of thyroid**

**a) Overview**

FDA Approval: Adult, no; Pediatric, no  
 Efficacy: Adult, Effective; Pediatric, Effective  
 Recommendation: Adult, Class IIa; Pediatric, Class IIa  
 Strength of Evidence: Adult, Category B; Pediatric, Category B

See Drug Consult reference: RECOMMENDATION AND EVIDENCE RATINGS

**b) Summary:**

Potassium iodide is used concurrently with an antithyroid agent to induce thyroid involution prior to thyroidectomy. (Feek et al, 1980)  
 Potassium iodide 15 milligrams/day up to 250 milligrams 3 times a day is used 10 to 14 days preoperatively to reduce vascularity of the thyroid gland prior to thyroidectomy (Reynolds, 1990)  
 It is given in doses of 100 to 150 milligrams orally prior to administration of  
 to saturate the thyroid gland when uptake of radioiodine by the thyroid is not desired; potassium iodine also is given for up to 2 weeks after radioiodine treatment (Reynolds, 1990)

**4.5.B.5 Iodine deficiency; Treatment and Prophylaxis**

**a) Overview**

FDA Approval: Adult, no; Pediatric, no  
 Efficacy: Pediatric, Evidence favors efficacy  
 Recommendation: Pediatric, Class IIb  
 Strength of Evidence: Pediatric, Category B

See Drug Consult reference: RECOMMENDATION AND EVIDENCE RATINGS

**b) Summary:**

Potassium iodide is used for prophylaxis and treatment of areas where diet is deficient in **iodine**

It is given as iodized salt (Reynolds, 1990)

**c) Pediatric:**

**1)** A 10% potassium iodide solution administered as 8.7 milligrams (mg) 29.7 mg every month corrected **iodine** deficiency more effectively than did larger, less frequent doses. School children (n=305), aged 7 to 13 years, in an area of Zimbabwe known to have a high rate of **iodine** deficiency diseases, were given one of 5 dosages of solution: 8.7 mg every 2 weeks, 29.7 mg every month, 148.2 mg every 3 months, 382 mg every 6 months, and 993 mg once. The study extended for 13 months. At 6 months, thyroglobulin had decreased in all groups and had normalized in the first 2 groups to levels of populations. At 13 months, standardized thyroid volume (taking increased body height into account) was less than baseline volumes in the first 2 groups and remained unchanged in the other 3 groups. Although total annual dose of **iodine** was greater in the groups with the less frequent administration, the smaller, more frequent doses were more effective. Potassium iodide given at intervals greater than 3 months is less effective than is **iodine**

#### 4.5.B.6 Livedoid vasculitis

**a) Overview**

FDA Approval: Adult, no; Pediatric, no

Efficacy: Adult, Evidence favors efficacy

Recommendation: Adult, Class IIb

Strength of Evidence: Adult, Category C

See Drug Consult reference: RECOMMENDATION AND EVIDENCE RATINGS

**b) Summary:**

Oral potassium iodide cured livedo vasculitis in a reported case

**c) Adult:**

**1)** Oral potassium iodide resolved the skin lesions of a 25-year-old woman with livedo vasculitis that had been refractory to treatment with steroids and an immunosuppressant. The woman presented with multiple small ulcers, white atrophic scars, telangiectasias, hyperpigmentation, and erythematous nodules on her lower legs and ankles. Histological evidence of ischemic necrosis of the epidermis, vascular occlusion of the small arterioles with fibrinoid deposition in the walls, fresh microthrombi in capillaries with perivascular lymphocytic infiltrate, and mild chronic panniculitis led to the diagnosis of lived vasculitis. Six months of treatment with steroids alone or steroids plus an immunosuppressant brought no improvement. After institution of oral potassium iodide treatment 300 milligrams 3 times per day, a good response was evident at 4 weeks, with complete cure of the skin ulcers in 2 months (Abraham et al, 2003).

#### 4.5.B.7 Lymphocutaneous sporotrichosis

**a) Overview**

FDA Approval: Adult, no; Pediatric, no

Efficacy: Adult, Evidence favors efficacy; Pediatric, Evidence favors efficacy

Recommendation: Adult, Class IIb; Pediatric, Class IIb

Strength of Evidence: Adult, Category B; Pediatric, Category B

See Drug Consult reference: RECOMMENDATION AND EVIDENCE RATINGS

**b) Summary:**

Saturated solution of potassium iodide (SSKI) is recommended in adults and children as an alternative treatment for patients not responding to itraconazole for lymphocutaneous sporotrichosis (Kauffman et al, 2007).

**c) Adult:**

**1)** Saturated solution of potassium iodide (SSKI) is recommended as an alternative treatment for patients not responding to itraconazole for lymphocutaneous sporotrichosis. Treatment should be continued for 2 to 4 weeks after all lesions have healed, usually a total of 3 to 6 months. Adverse effects such as metallic taste, nausea, abdominal pain and rash are frequent among patients treated

with SSKI. Cure rates ranging from 80% to 100% have been reported with SSKI in clinical trials and case reports (Kauffman et al, 2007).

**d) Pediatric:**

**1)** Saturated solution of potassium iodide (SSKI) is recommended as an alternative treatment for patients not responding to itraconazole for lymphocutaneous sporotrichosis. Treatment should be continued for 2 to 4 weeks after all lesions have healed, usually a total of 3 to 6 months. Adverse effects such as metallic taste, nausea, abdominal pain and rash are frequent among children treated with SSKI. Cure rates ranging from 80% to 100% have been reported with SSKI in clinical trials and case reports (Kauffman et al, 2007).

## 4.6 Comparative Efficacy / Evaluation With Other Therapies

Levothyroxine

Povidone Iodine

### 4.6.A Levothyroxine

#### 4.6.A.1 Goiter

**a)** A daily dose of **iodine** (400 micrograms), as di-iodotyrosine, or a combination of levothyroxine(75 mcg) and **iodine** (200 mcg) is at least as effective as levothyroxine (150 mcg/day) alone in the treatment of endemic goiter due to **iodine** deficiency (Hintze & Emrich D Kobberling, 1989). All 3 therapies, initially, produced a significant reduction in the size of diffuse goiters; however, only the levothyroxine-treated group experienced a rebound increase in goiter size.

**b)** JUVENILE GOITERS, in children 13 to 15 years of age, respond rapidly to daily treatment with either 150 mcg of iodide, 100 mcg of levothyroxine, or 50 mcg of levothyroxine plus 100 mcg of iodide (Einenkel et al, 1992). However, treatment with levothyroxine alone only temporarily blocked the thyroid's tendency to enlarge and withholding or reducing the dose resulted in relapse.

### 4.6.B Povidone Iodine

#### 4.6.B.1 Disinfection, Skin

**a)** Tincture of **iodine** (2% **iodine** tincture in 47% alcohol) was superior to povidone disinfecting skin prior to phlebotomy. The tincture of isopropyl alcohol applicator to be used for a 1- minute scrub before using the gauze pad containing tincture of **iodine**. One or the other of the disinfecting methods was used for the collection of 3,851 blood samples by trained and experienced phlebotomists. The rates of infection of blood samples by skin flora were 3.8% for povidone **iodine** and 2.4% for

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