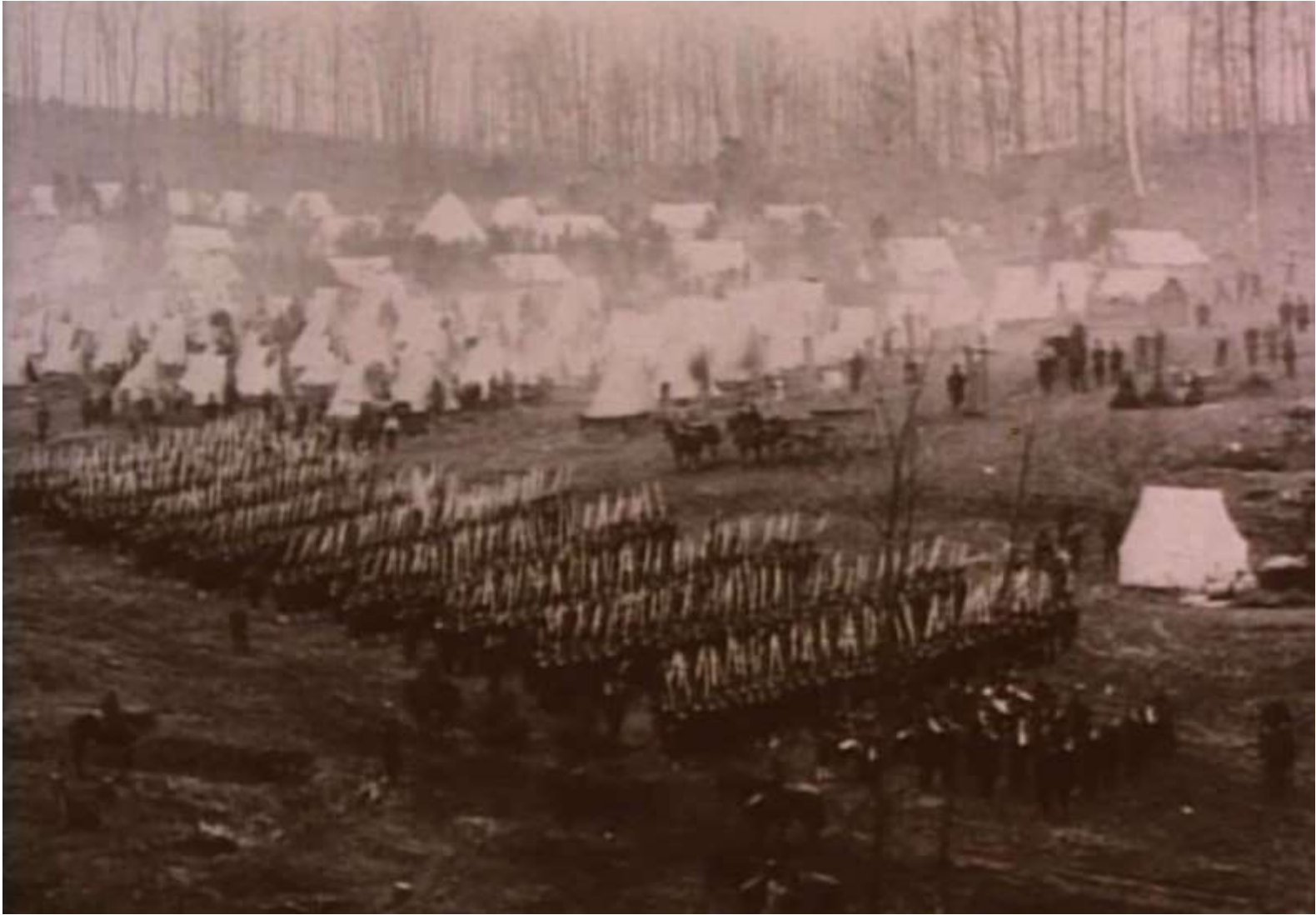


**PYRIDOXINE**



*“I have seen Him in the watch-fires of a hundred circling camps” - Union camp, Army of the Potomac, c 1863.*

*Mine eyes have seen the glory of the coming of the Lord;  
He is trampling out the vintage where the grapes of wrath are stored;  
He hath loosed the fateful lightning of His terrible swift sword:  
His truth is marching on.*

*Glory, glory, hallelujah!  
Glory, glory, hallelujah!  
Glory, glory, hallelujah!*

*His truth is marching on.*

*I have seen Him in the watch-fires of a hundred circling camps,  
They have builded Him an altar in the evening dews and damps,  
I can read His righteous sentence by the dim and flaring lamps:*

*His day is marching on.*

*Glory, glory, hallelujah!  
Glory, glory, hallelujah!  
Glory, glory, hallelujah!  
His day is marching on.*

*I have read a fiery gospel writ in burnished rows of steel  
As ye deal with my contemners, so with you my grace shall deal  
Let the Hero, born of woman, crush the serpent with his heel,  
Since God is marching on.*

*Glory, glory, hallelujah!  
Glory, glory, hallelujah!  
Glory, glory, hallelujah!  
Since God is marching on.*

*He has sounded forth the trumpet that shall never call retreat  
He is sifting out the hearts of men before His judgment-seat  
Oh, be swift, my soul, to answer Him! Be jubilant, my feet!  
His truth is marching on.*

*Glory, glory, hallelujah!  
Glory, glory, hallelujah!  
Glory, glory, hallelujah!  
Our God is marching on.*

*In the beauty of the lilies Christ was born across the sea,  
With a glory in His bosom that transfigures you and me.  
As He died to make men holy, let us die to make men free  
While God is marching on.*

*Glory, glory, hallelujah!  
Glory, glory, hallelujah!  
Glory, glory, hallelujah!  
Our God is marching on.*

*Julia Ward Howe, "Battle Hymn of the Republic"  
or "Mine Eyes have Seen the Glory"  
Published in the Atlantic Monthly,  
February 1862*

*At the Willard Hotel in Washington D.C the poet Julia Ward Howe awoke from a spectacular dream. That day she had heard a new England Regiment singing on parade and had fallen asleep with the song "John Brown's Body", ringing in her head.*

*Now in the dark, she got up and scribbled out the words with a pencil stub. She sold her poem to the Atlantic monthly for \$4.00.*

*It became the anthem of the Union.*

*Julia Ward Howe helped then lead the American woman suffrage association for 55 years. At her funeral in 1910, 4,000 mourners joined in singing Battle Hymn of the Republic.*

*"This year has brought about many changes that at the beginning would have been thought impossible. The close of the year finds me a soldier for the cause of my race. May God bless the cause and enable me in the coming year to forward it on"*

*Christian Fleetwood, Union Soldier, December 1863*

*"He who does not see the hand of God in this is blind, Sir, Blind!"*

*General T.J "Stonewall" Jackson in the Shenandoah, 1861*

*"God has been very kind to us this day"*

*General T.J "Stonewall" Jackson on surveying the field of dead in his sector at the Battle of Antietam, September 17, 1862.*

*"In great contests each party claims to act in accordance with the will of God. Both may be, but one must be wrong. God cannot be for and against the same thing at the same time"*

*Abraham Lincoln*

*It was an extremely religious age. Both sides wanted to get right with God. John Brown said he was an instrument in the hands of God to bring him to Harper's Ferry to free slaves and perhaps began the Civil War. Abraham Lincoln finally felt that he too, was an instrument in the hands of God and that God was punishing the country for the crime of slavery. Robert E. Lee said that he was an instrument in the hands of God and said at Gettysburg that it's all in God's hands and then sent the cream of his army to its doom. They really felt that providence was at work in this war. As Lincoln said, "We both pray to the same God. We both invoked Him. We both were on His side". But it wasn't until 1863, indeed at the end of the war, that it became clear where God's judgment was coming down - that was on the whole country. It must now atone in blood for its complicity in wickedness, the wickedness of slavery.*

*Stephen B. Oats, Civil War Historian*

*In the American Civil War, both Northerners and Southerners alike held firm in the belief that God was on their side. Abraham Lincoln felt that he was an instrument in the hands of God, although he conceded, that God could be on both sides, he could not see that He could be if one of those sides was in the wrong. "God cannot be for and against the same thing at the same time", he said. In a religious age it was widely thought that victory or defeat would ultimately be decided by God. What became apparent however over the course of the four horrifically bloody years of the conflict was that the Union would ultimately win by dint of attrition, a victory gained due to its overwhelming superiority in men and in industry. Though the Southerners fought with great courage, conviction and élan, by 1865 it had become apparent to all, that God was on the side of the big battalions.*

*In cases of severe isoniazid poisoning, we face a very great battle. Though we may fervently pray to our God, for ultimate victory, we must remember the lessons of the American Civil War. God is on the side of the big battalions! Ordinary therapeutic dosing will be nowhere near sufficient, we must therefore recruit as much pyridoxine as we possibly can!*



*"They have builded Him an altar in the evening dews and damps", Union soldiers, camped near Gettysburg, 1863*

# PYRIDOXINE

## Introduction

Pyridoxine is metabolized to pyridoxal – 5 - phosphate (the active form of vitamin B6).

In Emergency Medicine pyridoxine is used as the specific antidote for **coma, seizures** and **metabolic acidosis** in **isoniazid** poisoning.

It has also been used in other poisonings due to **hydrazine** compounds, found in **Gyromitra** mushrooms and some rocket and jet fuels.

When used as an antidote to isoniazid poisoning, very high doses are required, which can be problematic as standard preparations contain only small doses.

**See also separate document on Isoniazid Overdose (in Toxicology folder).**

## History

Pyridoxine was discovered in 1934 and isolated in 1938.

It was first synthesized in 1939

## Preparation

Pyridoxine as:

### Standard Ampoules:

- **50 mg in 1 ml ampoules**

### High Dose Ampoules:

These are not widely available in Australia and are only available via the Special Access Scheme:

- 100 mg in 1 ml
- 250 mg in 5 mls

### Tablets:

- 25 mg
- 100 mg

## Mechanism of Action

Pyridoxine is metabolized to **pyridoxal - 5- phosphate** (the **active form of vitamin B6**).

Vitamin B6 is an essential co-factor for the conversion of L-glutamic acid to GABA.

The hydrazines, including **isoniazid**, block the formation of P5P, as well as binding to and inactivating it, thereby resulting in depletion of GABA, and increased CNS excitability.

Large doses of pyridoxine overcome this inhibition.

## Pharmacodynamics

**Vitamin B6** is an important cofactor in over 100 known enzymatic reactions that involve amino acid metabolism.

## Pharmacokinetics

### Absorption:

- Pyridoxine can be given orally or IV
- Oral bioavailability is only around 50%.

### Distribution:

- The Vd is 0.6 L/Kg.
- The degree of protein binding in the body is unknown.
- Pyridoxine can cross the human placenta.
- Pyridoxine is excreted into human breast milk.

### Metabolism and excretion:

- Pyridoxine is rapidly metabolized at extra-hepatic sites to the active phosphate ester form.
- Elimination half-life is long at 15 - 20 days.

## Indications

Toxicological indications are:

1. Seizures or coma or metabolic acidosis induced by **hydrazine compounds**.

**Pyridoxine is mainly used to control seizures and acidosis but may also be used for prolonged coma.**

Hydrazine compounds encountered in toxicological settings include

- **Isoniazid**
  - **Gyromitra** mushroom poisoning.
  - Some jet and rocket fuels
2. As an adjunctive treatment for ethylene glycol poisoning.

Indications *outside* of the ED include:

1. Treatment and prevention of pyridoxine deficiency including the prevention of *isoniazid-induced* peripheral neuropathy.
2. Sideroblastic anaemia
3. Hyperemesis gravidarum

### **Contra-indications / Precautions**

There are no specific absolute contra-indications

### **Pregnancy**

There is a lack of information supporting the routine supplementation of pyridoxine during pregnancy.

At high doses, pyridoxine has been associated with maternal peripheral neuropathy, and case reports of neonatal anencephalopathy and alterations in the normal metabolism of pyridoxine in the infant have been described.

*However, pyridoxine has been used in the management of pregnancy-induced nausea and vomiting.*

Pyridoxine is considered safe to use if it is the medicine of choice.

### **Breastfeeding:**

Breastfeeding women have a higher requirement for pyridoxine compared to the general population, and any deficiencies should be addressed.

Pyridoxine at the recommended doses is considered safe to use during breastfeeding.



However, there is conflicting evidence as to whether high doses of pyridoxine (> 600mg/day) may suppress prolactin secretion and affect breast milk production.

Therefore, breastfeeding women are recommended not to take high doses of pyridoxine.

Consultation with a dietitian for further information is also recommended.

### Adverse Reactions

There are no serious acute adverse reactions.

*Chronic high oral dosing may lead to peripheral neuropathy.*

### Dosing

*For isoniazid poisoning:*

The dose is **1 gm IV for every 1 gm of isoniazid** ingested, up to **5 grams**.

The recommended **empirical dose** is **5 grams** pyridoxine IV, at **0.5 grams /minute** until **seizures stop**. **The remainder of the dose may then be infused more slowly over the next 4 hours.**

Note that currently pyridoxine is only **readily** available in **1 ml ampoules of 50 mg**.

Therefore **100 ampoules** will be needed to provide the ideal empirical dose of **5 gms!**

If less than 5 gms is available, give this (as 1-2 gms may be sufficient to temporarily control seizures), but then every effort must be made to secure further ampoules from sources outside the ED.

NG pyridoxine (in the form of crushed tablets) has been suggested as an alternative method, but the efficacy of this route of administration has not been established, (*personal communication Dr George Braitberg*)

*Adjunctive role of Benzodiazepines:*

The role of benzodiazepines is also important:

- Seizures are initially controlled with IV benzodiazepines while supplies of pyridoxine are secured and administered.
- In addition to the control of seizures, benzodiazepines have a beneficial **synergistic** effect with pyridoxine.
- Benzodiazepines are especially useful where isoniazid stocks fall short of optimal dosing. They should be given concurrently with pyridoxine.

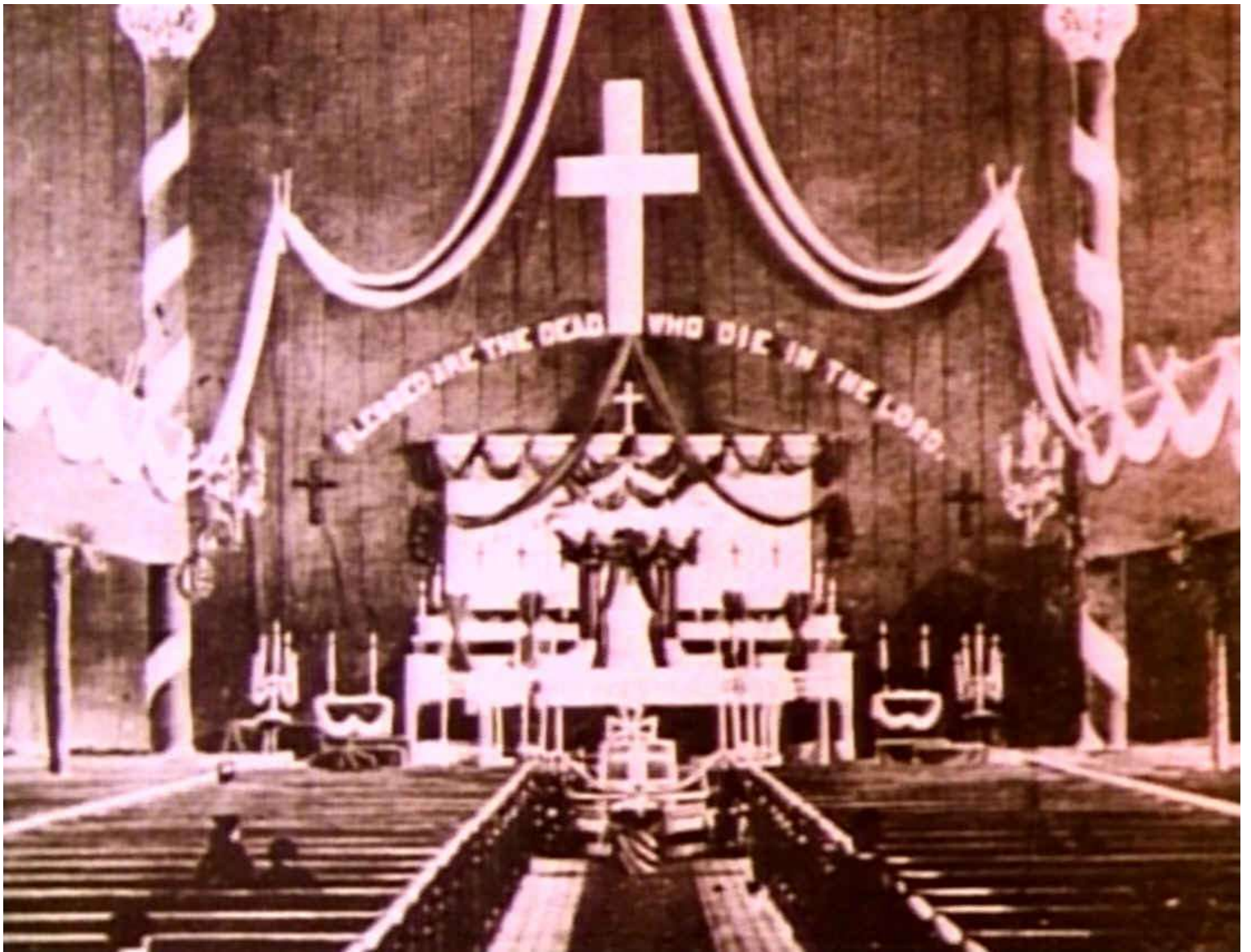


*For other Hydrazine poisoning:*

- Give an initial bolus of 25 mg/kg IV.

*For ethylene glycol poisoning:*

- Give 50 mg IV every 6 hours.



*"I have read a fiery gospel writ in burnished rows of steel", Church Hall, Civil War Period.*



*Judy Garland sings an emotional rendition of “Battle Hymn of the Republic” on national television following news of the assassination of President John F. Kennedy, in December 1963.*

*Following the Civil War, “Battle Hymn of the Republic” would become an unofficial anthem for all Americans - so sacred now that Americans would still turn to it in their darkest hours. And one of the very darkest occurred on November 1963, with the mindless assassination of one of America’s greatest - President John. F Kennedy. It was the height of the Cold War - The nation reeled in shock and disbelief - people wanted to look to someone/anyone for solace and inspiration - it would come from an unexpected source. On national television, the country watched as Judy Garland in her fidgety manner, suddenly broke with schedule announcing she wanted to dedicate her next song to the deceased President - whom she had been a personal friend of.*

*Many regard her rendition as the greatest ever of “Battle Hymn of the Republic” - following it a tearful audience stood and gave a thunderous and sustained applause.*

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Reviewed April 2018.