



BETAHISTINE

The Stone Bridge, destroyed by Union General John Pope, following his crushing defeat by Robert E. Lee at the Second Battle of Bull Run, 28 - 30 August 1862. The surrounding countryside lies devastated in the path of his retreating army.

“Behold what God hath wrought!”

*Stonewall Jackson, on surveying the field of Union dead at the
Second Battle of Bull Run, August 1862*

“.....I could have walked a quarter of a mile in almost a straight line on their dead bodies without putting a foot on the ground”

*Private Ned Moore, Rockbridge Artillery,
Second Battle of Bull Run, August 1862*

Desperate for a victory, Lincoln removed McClellan and put tall bombastic John Pope in command.

Pope so often bragged that his headquarters were in the saddle, people began to say he had his headquarters where his hindquarters should have been.

Lincoln was warned at the start that Pope was not to be trusted with telling the truth. And Lincoln said, “I’ve known the Popes back in Illinois, known all of them. There’re all liars and braggarts. But I don’t know of any particular reason why a liar and braggart shouldn’t make a good general” (Shelby Foote, Civil War Historian)

Pope wasted no time charging into Northern Virginia after the rebel armies. But he was in trouble from the start. First Stonewall Jackson fought him to a stand-off at Cedar Mountain. Jeb Stuart hit him next, raiding his headquarters and getting away with 35,000 dollars in cash, and the Union commander’s dress coat. Then the rebels simply disappeared. It took Pope two days to find them, dug in along an abandoned railroad overlooking the old Bull Run battlefield.

On August 29th Pope attacked, promising to “bag the whole crowd”.

But the Confederates held. Jackson’s men hurling rocks when ammunition ran low. At 2.00 the next afternoon, Confederate General James Longstreet sent five divisions storming into the Union flank.

It was another Union disaster.

25,000 men were killed, wounded or missing at Second Bull Run, five times the figure that had so horrified the country the first time North and South fought there.

Lincoln sent Pope west to Minnesota to deal with an uprising among the Sioux and reluctantly put George McClellan back in command.

“We must use the tools we have”, Lincoln said.

McClellan told his wife, he had been called upon to save the country once again!

David McCullough and Shelby Foote in Ken Burns', "The Civil War", 1990.

Commanding the greatest and best equipped army in history, General George B. McClellan had led the Army of the Potomac, up the Virginia Peninsula to the Confederate capital at Richmond. At the head of his 125,000 men, he had been certain in the thought that he would avenge the shame of Bull Run and crush the South with overwhelming force in a single campaign that would end the Civil War. Victory had seemed assured, but at the Battle of the Seven Days, McClellan was stunningly defeated by Robert E. Lee, who at great cost drove him away from Richmond and sent him fleeing back to safety across the James River. Now seriously alarmed Lincoln, removed McClellan from overall command of the Union Armies and looked to the brash, bombastic, highly opinionated John Pope for deliverance. At the head of another newly formed army, the Army of Virginia, (not to be confused with Lee's Confederate Army of Northern Virginia), Pope proposed to lead the third invasion of the South, not via the indirect route McClellan had taken but by a more direct one via central Virginia.

Again, outnumbered by the big battalions of the North, Lee would have to take risks if he were to save the South again. His audacious plan called for a wide outflanking movement that would get around Pope's advancing army unnoticed, and then attack his supply lines to Washington. But he would have to have an exceptional commander, to carry out the plan. In Stonewall Jackson, he had just such a commander. Jackson had already defeated General Nathaniel Banks at Cedar Mountain in the opening battle of Pope's Northern Virginia Campaign.

On August 25th, Jackson set out with 23,000 men on a wide flanking march, that arced past Pope who had entrenched his army in an impregnable position on the northern banks of the Rappahannock river, facing Lee. Marching his men an astonishing 56 miles in just two days, Jackson arrived at Bristow Station, totally routing a surprised Union force there and destroying the Alexandria & Orange Rail that constituted Pope's supply line with Washington. Jackson then took the initiative by moving on Manassas Junction further north, site of a major Union supply base. Here he repeated the surprise on Union forces there, routing them and capturing an immense cache of food and equipment, such as the whole of the Southern Confederacy could not have produced in a year. Jackson's men gleefully helped themselves to thousands of food barrels scattered over acres, field ovens and bakeries of gigantic dimensions, pyramids of artillery ammunition, and medical supplies, coats and most importantly shoes. By seizing Manassas, Jackson threatened to reduce Pope's army to the usual penury circumstances of the Confederates!

By now however Pope had received reports of the disaster happening in his rear. After some hesitation he abandoned his position on the Rappahannock, which Lee had hoped for, and frantically marched his army north to crush Jackson. Lee in turn took off in hot pursuit of Pope. The hunter had now become the hunted, a salute to the genius of Robert E. Lee. Jackson on getting report of Pope's advance, gathered up all the supplies his men could possibly muster, then burning that which he could not take, lest it fall back into Union hands, left Manassas and headed still further north to Groveton. As the Confederates marched away into the darkness, they looked back over their shoulders at the reddened sky caused by immense explosions and fires at Manassas. Henry Kyd Douglas, the youngest member of Jackson's personal staff recorded, "Here one fellow bending beneath the weight of a score of boxes of cigars, smoking and joking as he went, another with as many boxes of canned fruit, another with coffee enough for a winter's encampment or a long string of shoes hung around his neck like beads!"

Pope, enraged at the devastation of Manassas and the Alexandria & Orange Rail, moved quickly, not to face Lee, but rather go after Jackson at Groveton. If Lee did not soon turn up, Jackson was now in serious trouble. He took up defensive positions near Bull Run creek, close to the old site of the first major battle of the war in 1861. What would follow would be the Second Battle of Bull Run, but this time things would be fought on a vastly greater scale than the first conflict. As the first Union skirmishers arrived they were amused to see what looked like in the distance some dishevelled country farmer on his scraggy old horse nonchalantly riding along a hill crest watching their movements, (and in all probability munching on a peach). He was within easy rifle range, but they had no interest in the harmless farmer. But within the woods horrified staffers, expecting shots to ring out at any moment, screamed frantically to Jackson to get back into the woods! Jackson calmly took heed and rode back to his men. "Here he comes, by God!", a relieved staffer sighed. Jackson unsure what the fuss was about simply said, "Gentlemen, bring up your men!"

The first clash came between the elite units of both armies, the Union Iron Brigade and the Confederate's Stonewall Brigade. Neither side flinched, the fighting occurring at virtually point blank range, casualty rates were staggering on both sides. There were 1100 casualties of the 2800 Unionists engaged, the Confederates, sustained 1200 casualties of 4500 engaged. Jackson needed Lee, and needed him fast. By the next day Pope had concentrated 30,000 men to renew his attack. Wave after wave of Union attacks were cut down. Then advanced units of Lee's army, Texans under General James Longstreet, finally began to arrive amidst Confederate cheers, but the battle only grew in intensity. "The battle now more furious than before", a Confederate would recount, "The enemy continued to pour in his fresh relays...The contest constantly grew fiercer and more bloody. Often the combatants delivered their fire against each other within ten or a dozen paces...The slaughter was too horrible and sickening".

That night, seemingly unaware of the arrival of Lee, Pope assumed Jackson would retreat. But in the morning the Confederate lines, despite their losses, seemed even longer than the previous day. Pope attacked again, and again and again, and each time was repulsed. A Confederate soldier from Louisiana gasped, "The ground was literally covered with their dead and wounded". In the evening Surgeon Maguire detailed the estimated casualty numbers. Among them was a young Private William C. Weston, the son of personal friends

of Jackson. The General became greatly affected, "His muscles were twitching convulsively", McGuire related, "and his eyes were all aglow. He gripped me by the shoulder till it hurt me, and in a savage threatening manner, asked why I left the boy. In a few seconds he recovered himself, and turned and walked off into the woods alone". By now it appeared that the Confederates would win the battle, but McGuire was also affected by the terrible losses. When Jackson returned there was silence for a minute, "General we have won this battle", he said as if to console, but then added, "by the hardest kind of fighting". "No, no" Jackson answered, "We have won it by the blessing of Almighty God"

The next day, August 30th, Pope attempted one last attack. An Alabama soldier, exclaimed, in amazement, "We dotted the ground with them, but others were sent to take their places...No amount of killing or wounding we could do would check them". But the toll on Federal morale by now had begun to tell. Their lines began to falter and fall back. An artillery gunner under Lee's command, looked on in awe of the scene before him, "As shell after shell burst into the wavering ranks" he recalled, "and round shot ploughed broad gaps among them, you could distinctly see, through the rifts of smoke, the Federal soldiers falling and flying on every side. With the dispersion of the enemy's reserve, the whole mass now broke and ran like a flock of sheep".

This was the moment that the Confederates had been praying for. General Longstreet gave the signal and 25,000 men rent the air as one with the Rebel Yell, and charged in pursuit. "Eagerly and fiercely did each brigade press forward" Jackson reported, "exhibiting in parts of the field scenes of close encounter and murderous strife not witnessed often in the turmoil of battle. The Federals gave way before our troops - fell back in disorder and fled precipitously leaving their dead and wounded on the field. During the retreat the Artillery opened with destructive power upon the fugitive masses".

Pope managed to avoid annihilation by scrambling his army across the old Stone Bridge over Bull Run Creek, then destroying it, to delay the pursuing Confederates. Though the Confederates could defeat greater Union armies in battle, they never had the manpower to fully follow up their victories. General Pope had escaped, but the victory had been total, and that was enough for the moment. In early June 1862 Richmond had been on the verge of surrender - by end of August 1862 Washington was threatened. For a second time Robert E. Lee and Stonewall Jackson had saved the South.

Following the battle a Federal civilian, probably a distinguished politician accompanying Pope, according to Shelby Foote, had been captured with a severely broken leg. Hearing that Jackson was standing just yards away, he asked to be lifted up so that he could see the legendary Rebel Commander. What he saw deeply shocked him, a dirty bedraggled mud covered man barely distinguishable from his miserable troops. His captors assured him it was no joke, it was indeed the famous Stonewall Jackson scourge of the North! After an incredulous half a minute, to the unrestrained mirth of Jackson's men, the politician exclaimed, "Oh my God, lay me down!"

The North was profoundly shocked when news reached Washington of the defeat of General Pope, and not least for the fact that total casualties were over five times the number of the First Battle of Bull Run the previous year. McDowell, McClellan, and now Pope had all been defeated in their invasions of the South. At this bleak hour there was no

immediate prospect of a fourth invasion; indeed there now seemed a very real possibility that the North itself, would be invaded. Lee was already casting his eyes toward Maryland. Lincoln knew he had the men, the material and the industrial might to crush the South... what he didn't have, however, was the commander. In desperation he turned back to George B. McClellan. "We must use the tools we have", he said.

Meniere's disease, seems a most intractable enemy. There is no medication in our arsenal by which we may gain victory over the devastating symptoms of this enigmatic condition. The best we can hope for currently is to take heed of President Lincoln's mournful sentiments on hearing of the terrible defeat at Second Bull Run, "We must use the tools we have" - in the case of Meniere's our tool - for better or worse - remains betahistine.

BETAHISTINE

Introduction

Betahistine is a vasodilating agent that has specific utility in the treatment of **Meniere's disease**.

Its principal adverse effects relate to histamine type reactions.

History

Betahistine was introduced into clinical practice in Europe in 1970 for the treatment of Ménière's disease.

Chemistry

Betahistine is a **histamine analogue**.

Preparations

Betahistine dihydrochloride as:

Tablets:

- 16 mg.

Physiology

Histamine has a vasodilating action.

Mechanism of Action

Betahistine is thought to act via a vasodilator action that improves blood flow to the labyrinth and brain stem.

Pharmacodynamics

Improvement in symptoms may be seen within a **few days** however it may also take **several weeks** of treatment before full benefit is seen.

Pharmacokinetics

Absorption:

- Betahistine is administered orally.

It is rapidly and completely absorbed from the gastrointestinal tract.

Distribution

- The degree of protein binding is unknown
- It is unknown if placental transfer occurs.
- It is unknown if betahistine is excreted into breast milk.

Metabolism and excretion:

- Betahistine is rapidly metabolized to one major metabolite, 2-pyridylacetic acid, which is excreted in the urine.
- Plasma half-life is around 3.5 hours.

Indications

Betahistine is specifically indicated for the treatment of **Meniere's disease**.

Contra-indications/precautions

These include:

1. Caution with those in whom histamine may be detrimental.

Therefore:

- Asthmatics
 - Active peptic ulcer or a history of peptic ulcer.
2. Patients taking antihistamines:
 - An antagonism between betahistine and antihistamines can be expected on a theoretical grounds, however there have no reports of clinical reactions.

3. Use in children:
 - Due to lack of clinical experience, betahistine dihydrochloride should not be used in children less than 18 years.
4. Patients with pheochromocytoma

Pregnancy

Betahistine is a category B2 drug with respect to pregnancy.

Category B2 drugs are those drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.

Reports describing the use of betahistine during pregnancy have not been located and the effects in the developing fetus are unknown.

Therefore, consider an alternative medicine during pregnancy if possible.

Breast feeding

Published information describing the use of betahistine during breastfeeding has not been located.

Betahistine is rapidly metabolized to an inactive metabolite, and the breastfed infant is unlikely to experience adverse effects.

However, consider an alternative medicine with more safety information during breastfeeding if possible.

Adverse Effects

1. Histaminergic reactions:

As betahistine is a histamine analogue, most of its adverse effects relate to histamine type reactions and therefore include:

Skin:

- Pruritus
- Urticaria
- Angioedema

CVS:

- Vasodilation, leading to with postural hypotension and tachycardia.

Respiratory:

- Bronchospasm with wheezing (rare).

Frank anaphylaxis has also been reported.

2. Gastrointestinal upset:

- Symptoms are usually mild only and may include nausea, vomiting, diarrhoea and epigastric pain.

Gastrointestinal disturbances may be relieved by reducing the dose or by taking betahistine with meals.

3. Stevens - Johnson syndrome has been reported.

Dosing

Usual adult dosing is:

- Oral 8 - 16 mg 3 times a day.

The maximum recommended daily dosage is **48 mg**.

References

1. eTG - November 2017.
2. Betahistine in Australian Medicines Handbook, Accessed February 2018.
3. Betahistine in MIMs Website, 1 January 2012
4. Betahistine in RWH Pregnancy and Breastfeeding Guidelines, 30 September 2015.

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