

# Problems with Acetaminophen (Tylenol/paracetamol)

By Edward J. Petrus, M.D.

Acetaminophen (best known by the brand name Tylenol), or paracetamol, as it is known in much of the rest of the world, is a widely used over-the-counter analgesic (pain reliever) and antipyretic (fever reducer), and has little anti-inflammatory activity of NSAIDs, such as aspirin and ibuprofen. Paracetamol was first used in Europe, but because of side effects was replaced by phenacetin. Paracetamol was first marketed in the U.S. in 1953, and popularized by McNeil Labs in 1955 as Tylenol, a contraction of para-acetylaminophenol. Johnson & Johnson acquired McNeil in 1959, and started a safer-than-aspirin pitch, complimented by a massive giveaway of Tylenol to doctors and hospitals, creating market share by an irresistible financial force, as reported by Fred Gardner, in his article “The Big Bucks in Tylenol, The Long War on Aspirin.”

## Reye’s Syndrome

In 1963, Ralph Reye, a pathologist from Sydney Australia described a disease in children now called Reye’s syndrome (liver and brain damage after viral infection) There is no evidence for an increased use of aspirin in the 1970s and 1980s when cases of Reyes syndrome were identified. Interestingly, aspirin has been shown to be a potent anti-influenza agent not only in cell culture experiments but in animals. In many cases it turned out the symptoms attributed to Reye’s were actually manifestations of inborn errors of metabolism, where the body could not make enough of a certain enzyme. In 1987, a researcher named Orłowski reviewed the records of 20 patients diagnosed with Reye’s and found that only one had been administered aspirin, and this patient had a zero salicylate level when admitted. In 1999, Orłowski found that most of the surviving Reye’s cases had inborn metabolic disorders. Orłowski noted that aspirin was used to alleviate fever and pain since the beginning of the 20<sup>th</sup> century, but Reye’s syndrome was not reported until the early 1950s. Reye’s syndrome disappeared from countries like France and Belgium that continued to give aspirin throughout the 1970s, 80s and 90s.

In his book, *Acetylsalicylic Acid*, 2009, Wiley-Blackwell, Karsten Schror reported that “there is not one single article that has ever established a causal relationship between Reye’s syndrome and the intake of aspirin.”

In the 1970s, Counterpunch ([www.counterpunch.org](http://www.counterpunch.org)) reports, “J&J sales reps began solemnly informing healthcare professionals that aspirin had been associated with Reye’s syndrome.” “J&J failed to warn about Tylenol’s lethal risk, and Ralph Nader pressured the government to issue warning about aspirin, but not about Tylenol.” “ In 1982 the Surgeon General issued a warning based on J&J’s false claim, and in 1986 the FDA required all aspirin products in the U.S. to carry a warning label stating “children and teenagers who have or are recovering from chicken pox, flu symptoms or flu should not use this product.”

## Acute Liver Failure

Acetaminophen is the leading cause for calls to Poison Control Centers (more than 100,000/year) and is now the leading cause of acute liver failure in the United States. Of those who develop

acetaminophen-related liver failure, 30% die (*Hepatology*,2005 ;42(6) :1364-72). According to Counterpunch, “J&J has paid out countless millions of dollars over the years to settle suits by Tylenol victims and minimize publicity.”

The Center for Drug Evaluation and Research (CDER) of the Food and Drug Administration (FDA) prepared a study of Recommendations for FDA interventions to decrease acetaminophen hepatotoxicity for Janet Woodcock, M.D.in 2008, and noted the following issues. In 1990, acetaminophen was a major cause of acute liver failure (ALF). Acetaminophen has a narrow therapeutic-to-toxic ratio, and symptoms of overdose may not appear for 3 days, so people may continue to take the drug and increase the damage. In contrast, doubling the OTC dose of NSAIDS, such as aspirin for several days exposes the consumer to a prescription-level dose, which only slightly increases the risk of gastrointestinal bleeding. Acetaminophen leads the number of adverse event reports (AERS) (25,237) compared to the other analgesics (ibuprofen, naproxen, ketoprofen and aspirin) and has the highest number of deaths (5,581) and has quadrupled in the past 5 years from 201 in 2000 to 980 in 2005. The highest number of death reports are in adults between 30 and 50 years.

An interesting animal study by Yale researchers, reported in the *Journal of Clinical Investigation* (2009, Jan 26), found that aspirin significantly protected against liver damage when toxic doses of acetaminophen were given. The study suggested that aspirin may prevent liver damage in millions of people suffering from side effects of common drugs, such as acetaminophen, alcohol abuse, and obesity-related liver diseases.

### **Asthma**

According to Karsten Schror,(*Acetylsalicylic Acid*, 2009, Wiley-Blackwell), “The prevalence in childhood asthma in the United States increased by 23% from 1970 to 1980 but nearly twice as much, that is, 40%, from 1980 to 1986.” “There was a close linear correlation observed in the United States between the increasing use of acetaminophen and the prevalence of asthma in children and adolescents at the same time that aspirin use declined.” “Frequent acetaminophen usage can cause asthma attacks.” (*Thorax*, 2000;55:266-270). In a study comparing acetaminophen, aspirin and ibuprofen, it was found that acetaminophen is associated with an increased risk of asthma and chronic obstructive pulmonary disease and with decreased lung function. Acetaminophen used late in pregnancy increased the risk of wheezing in the child. Neither, aspirin or ibuprofen were associated with asthma or pulmonary disease. *Am J Respir Crit Care Med*, 2005;171:966-971.

### **Autism**

Leo Kanner first described autism (severe communication problems, repetitive behaviors and an acute lack of social interaction) in 1943. The CDC found that by 2006, more than 90 in 10,000 eight year olds in the U.S. had autism, or 1 in every 110 children. *Nature*,2011;479:22-24.

There has been an exponential rise in the incidence of autism since 1980, when acetaminophen began to replace aspirin for infants and young children. The impetus for this shift – a Centers for Disease Control and Prevention warning that aspirin was associated with Reye’s syndrome – has since been compellingly debunked. If aspirin is not to be feared as a cause of Reye’s syndrome,

and acetaminophen is to be feared as a cause of autism, can the autism epidemic be reversed by replacing acetaminophen with aspirin or other remedies? *Altern Med Rev* 2009;14(4):364-372.

“The incidence of autism has risen 10-fold since the early 1980s, with most of this rise not explainable by changing diagnostic criteria” *Medical Hypotheses* 2007;68:46-60. Until about 1980, approximately 50-60 percent of autistic children were abnormal from birth, and 40-50 percent regressed into autism at approximately 18 months. *Autism Research Institute*;2002:1-130. Pangborn concluded that most of the autistic population now appeared to have “an acquired disease caused by something that we were not doing 20 years ago.” The 1980s was also the decade when acetaminophen largely replaced aspirin for infants and young children.

In 1997 the FDA warned that acetaminophen could damage the liver. In 1982 seven people died after ingesting Tylenol capsules laced with cyanide. This precipitated sharp declines in nationwide sales of acetaminophen, accompanied by declines in the numbers of California children with autistic disorders born in 1984 and 1987.

In May 2008, Schultz et al reported an association between autism and acetaminophen (Tylenol, paracetamol), *Autism* 2008;12:293-307. Mothers of autistic children commonly suffer more bacterial and viral infections and fevers during pregnancy for which they commonly take acetaminophen. *BMC Pediatr* 2003;3:9. Large trials have shown that low-dose aspirin during pregnancy is relatively safe for mother and child. *Obstet Gynecol Surv* 2008;63:49-57.

### **Blood Cancer**

High use of acetaminophen was associated with an almost two-fold increased risk of incident hematologic malignancies (myeloid neoplasms, non-Hodgkins lymphomas, plasma cell disorders). Neither aspirin nor nonaspirin NSAIDs or ibuprofen were associated with the risk of hematologic malignancies. *J Clin Oncology* 2011;34:6546.

### **Hypertension**

Acetaminophen causes a significant increase in blood pressure in patients with pre-existing coronary artery disease. *Circulation* Oct. 18, 2010. Low-dose aspirin taken at bedtime lowered the blood pressure and could reduce stroke mortality by 30% and ischemic heart disease mortality by 20%. *J Am Col of Cardiology*2005;46(6):984-5.

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