

**“Liver Failure and Spoiled Spaghetti”**

Fulminant Liver Failure in Association with the Emetic Toxin of *Bacillus cereus*

NEJM (1997) 336:1142-1148

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**Cognitive Learning Objectives**

- Identify the potential contributing factors to the death of a food-poisoned patient.
- Summarize the major functions of the liver.
- List many common causes of liver failure.
- Correlate abnormal laboratory tests results with liver failure.

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**Affective Learning Objectives**

- Human interest story: Humans are frail and life is short. Should we not each strive to become more gentle and nurturing each day (yet without trashing the biosphere (other life forms).
- Public health: Let’s exit together in awe of mammalian physiology, including the liver and its functions. Let’s take better care of our livers.

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### Food Poisoning and Liver Failure

- The principal causes of fulminant liver failure are viral infections and drugs.
- Food poisoning rarely causes liver failure, and most documented cases arise from the consumption of toxic mushrooms (such as *Amanita* species).
- Foodborne bacterial toxins most often cause acute gastroenteritis and are only rarely associated with liver injury.

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### Bacterial food poisoning...

- ...is common, has an economic impact, and is rarely fatal in previously healthy persons
- *Bacillus cereus*...
  - is widely recognized as a foodborne pathogen
  - causes a self-limiting gastroenteritis requiring only symptomatic treatment
  - releases at least two exotoxins
    - diarrheal toxin (enterotoxin)
    - emetic toxin (cereulide)
  - caused three reported cases of fatal food poisoning (as of 1997)

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### Case History: Summary

- A 17-year-old and his father had acute gastroenteritis after eating spaghetti and pesto\* prepared four days earlier.
- Adolescent outcome: fulminant liver failure, rhabdomyolysis, and death within three days.
- Adult outcome: hyperbilirubinemia and rhabdomyolysis followed by recovery.

\*\*Pesto\* refers to a sauce made especially of fresh basil, garlic, oil, pine nuts, and grated cheese.

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### Case History: Details

- G-I symptoms developed in a previously healthy 17-year-old and his father (a physician), 30 minutes after they ate spaghetti with homemade pesto.
- The food had been prepared four days earlier and refrigerated, although on several occasions it had been left in a pan at room temperature for one or more hours and then reheated.
- On day four, the food had an unusual smell but was eaten completely. The 17-year-old consumed more.
- Both ate the food on the day and day after preparation without experiencing symptoms.

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### Emergency Department Treatment

- Thirty minutes after consuming the food on day four, the father had abdominal pain and diarrhea, yet his overall condition remained satisfactory with symptomatic treatment (antiemetics and charcoal).
- In contrast, the son had no diarrhea and vomited a dose of charcoal despite anti-emetic treatment.

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### Major Liver Functions

- Synthesizes most blood proteins (all major ones except antibodies)
- Synthesizes bile acids and bile salts
- Stores and appropriately “doles out” nutrients (carbohydrates, lipids, proteins/amino acids, iron, fat soluble vitamins)

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## Major Liver Functions

- Metabolizes and excretes thyroid and steroids hormones
- Detoxifies/purifies the blood (bilirubin, ammonia, excess dietary copper, exogenous toxins, medicinal drugs)

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## Some Common Causes of Liver Failure

- Acetaminophen overdose
- Excessive alcohol intake
- Viral hepatitis (Hep B, Hep C)
- Autoimmune, hereditary and metabolic conditions (including iron or copper overload)
- Non-alcoholic fatty liver disease
- Hepatic cancer

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## Both patients returned home.

- The son's condition gradually deteriorated at home during the next two days, and he became listless and later, somnolent (very drowsy).
- During this period, he was treated symptomatically by his father with aspirin (total dose, 1 g), acetaminophen (total dose, 1 g), thiethylperazine\*, meclizine\*, and domperidone\*.

\*anti-emetics

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Two days after departing the ED, the son returned to the hospital

- When he became somnolent, he was admitted to a district hospital, where he was found to be icteric and afebrile, with tachycardia but otherwise normal cardiac function, a blood pressure of 115/70 mm Hg, and pain in the upper right quadrant of the abdomen.
- Prothrombin ratio: 12 % (normal: 80 to 100 %)

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### Laboratory Results

- AST: 2140 U/L (normal: <18), ALT: 5270 U/L (normal: <22), ALP: 378 U/L (normal: 60 to 170)
- Bilirubin: 7.0 mg/dl (normal: <1)
- CK: 2560 U/L (normal: 10 to 50 [MB fraction normal])
- Creatinine: 4.9 mg/dl (normal: 0.6 to 1.3)
- Metabolic acidosis (arterial pH: 7.27)
- Normal hemoglobin, WBC, PLT, ESR

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### The son's diagnosis

- Fulminant hepatic failure
- Rhabdomyolysis
- Acute renal failure
  
- Transferred immediately to the University Hospital of Zurich.

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The father continued to have episodes of abdominal pain and diarrhea but was otherwise in a satisfactory condition.

- Serum bilirubin: 3.3 mg/dl
  - Serum AST: 55 U/L (normal: <18)
  - Serum ALT: 18 U/L (normal: <22)
  - Serum CK: 1920 U/L (normal: <270)
  - Prothrombin ratio: 91% (normal: >70%)
- Two weeks later, the symptoms had resolved, and all laboratory values were within the normal ranges. (Yet, his life was forever changed.)

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At University Hospital, the son could not walk or respond to simple commands.

- Pupils unreactive to light.
- Severe, intermittent extensor spasms.
- Prothrombin ratio remained low (12%)
- Coagulation factor II, V, and VII activities were 22%, 10%, and 11% of normal, respectively
- Plasma ammonia: 250 µg/dl (normal: 27 to 82)
- Serum lactate: 14.4 mmol/L (normal: 0.6 to 2.4).

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### Further testing

- Urinalysis: RBCs, hemoglobinuria, myoglobinuria, and proteinuria.
- No hepatic toxins detected in plasma or urine (e.g., acetaminophen, carbon tetrachloride, amatoxins, amphetamine, opiates, or cocaine)
- Multiple blood cultures for bacteria and fungi were negative, as were serologic assays for hepatitis A, B, C, and E, Epstein-Barr virus, and herpesvirus.

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The patient was immediately scheduled for liver transplantation.

- Supportive treatment for fulminant liver failure including antibiotic prophylaxis was initiated.
- However, brain edema developed with increased intracranial pressure, and the patient died the day after hospitalization.

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### Small Group Discussion

- Why were the father's and son's outcomes profoundly different? (Multiple causes are likely.)
- Create a list of potential causes for the different father and son outcomes by considering potential genetic, medical history and social history differences between them, and also by carefully reviewing details of the case history.

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### Postmortem findings

- Diffuse edema and oligemia of the brain, thrombotic microangiopathy in small renal arteries, and vacuolar degeneration of renal tubular epithelia.
- 100 ml of clear ascitic fluid in the abdominal cavity
- Liver was yellowish and enlarged (weight, 1800 g).
- Microscopic architecture of the liver was intact.
- Plugged bile ducts but no major cellular infiltrates.
- Diffuse microvesicular steatosis of the whole liver parenchyma

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### Microvesicular steatosis of hepatocytes (MSH)

- Normally associated with:
  - acute fatty liver of pregnancy
  - valproate- or hypoglycin-induced toxicity
  - Reye's syndrome
- Results from reduced fatty-acid metabolism by hepatic mitochondria, which can be caused by impaired (beta)-oxidation or impaired activity of the mitochondrial electron-transport chain.
- Development of MSH is often associated with severe liver injury and is frequently fatal in the absence of liver transplantation.

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### Summary of case history

- After eating food contaminated with *B. cereus* and its toxins, a father and son had G-I symptoms, including nausea and emesis followed by liver injury and rhabdomyolysis
- The father made a complete recovery while the son died of fulminant liver failure.

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### Interpretation of Liver Enzyme Tests – A Rapid Guide

By A. Fraser  
NZFP (2007) 34:194-196

The next two slides summarize information from Dr. Fraser's elegant review. See:  
[www.rnzcgp.org.nz/news/nzfp/June2007/Fraser\\_June\\_07.pdf](http://www.rnzcgp.org.nz/news/nzfp/June2007/Fraser_June_07.pdf)

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**Single “Liver Test” Elevation  
(Other “Liver Tests” Apparently Normal)**

- GGT: Ethanol consumption, therapeutic drugs, or fatty liver
- ALP: Bone abnormality or rapid bone growth
- ALT: Obesity, mild chronic hepatitis
- AST: Muscle abnormality
- Bilirubin: Gilbert’s syndrome

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**If Several Abnormal “Liver Tests”,  
Which Are More Pronounced?**

- ALT/AST indicates hepatocellular lysis
  - Greater than 500 IU? Acute viral hepatitis or toxin exposure very likely
  - Lesser elevation that remains after one month? Chronic hepatitis very likely
- ALP/GGT indicates cholestasis
  - Ultrasound imaging now becomes key
  - Pain and jaundice suggestive of gallstones
  - Obstruction resulting from malignancy?

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