Acetaminophen Metabolism and Hepatotoxicity

Storyboards

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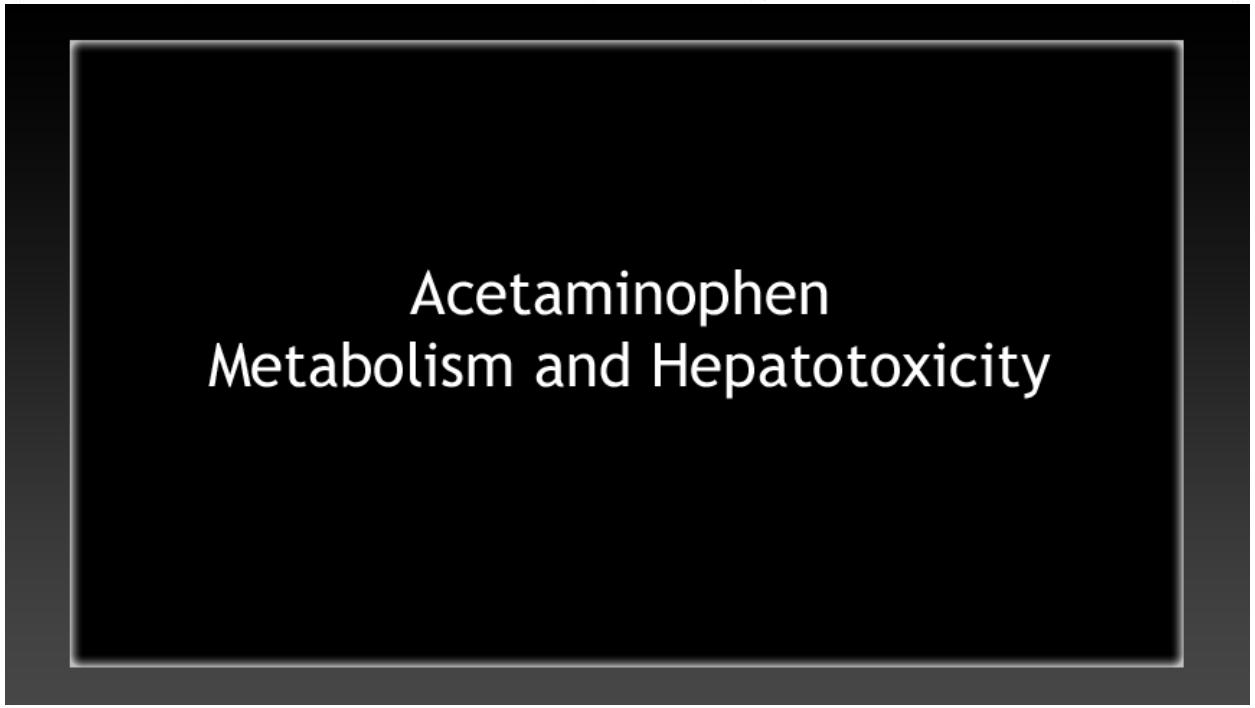
UIC UNIVERSITY OF ILLINOIS AT CHICAGO

Acetaminophen Metabolism and Hepatotoxicity



Voice Over:

Animation Notes:

Fade on title page.
Fade out.

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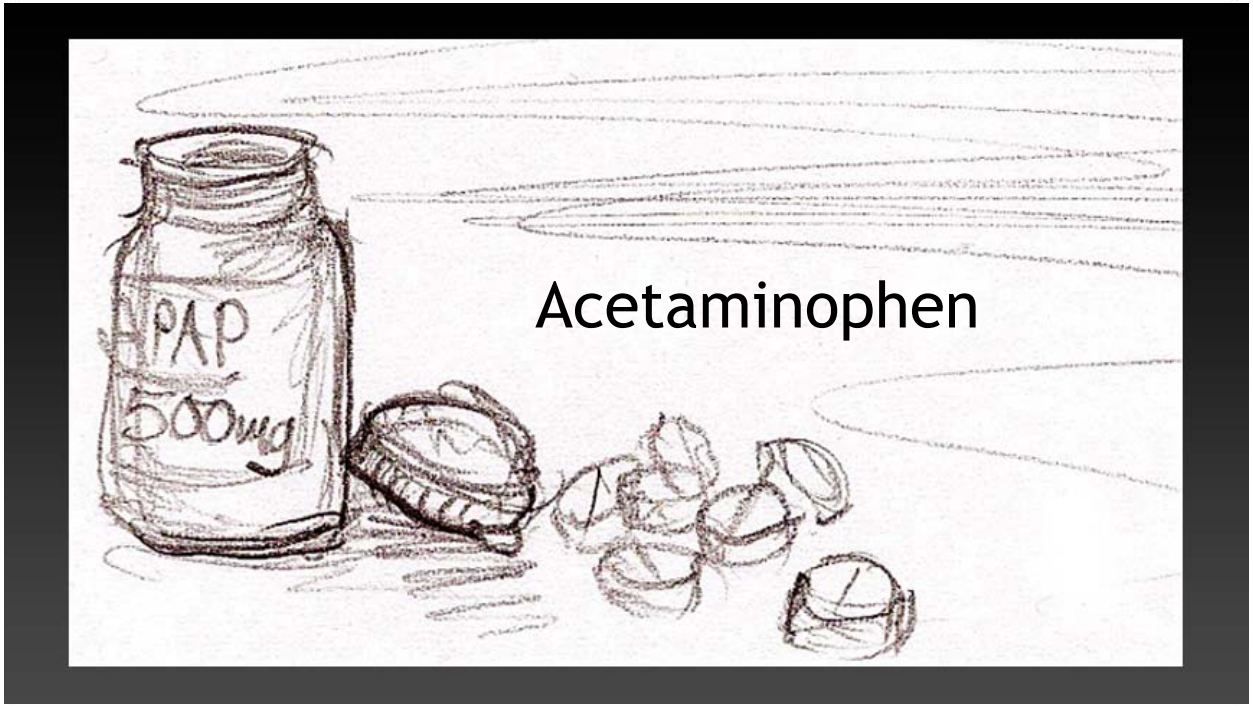
Acetaminophen Metabolism and Hepatotoxicity



Animation Notes:

Fade in.
Shown is a bottle of APAP and tablets of APAP with a neutral background.

Voice Over:

Acetaminophen (APAP) is a widely used medication with analgesic and antipyretic properties.

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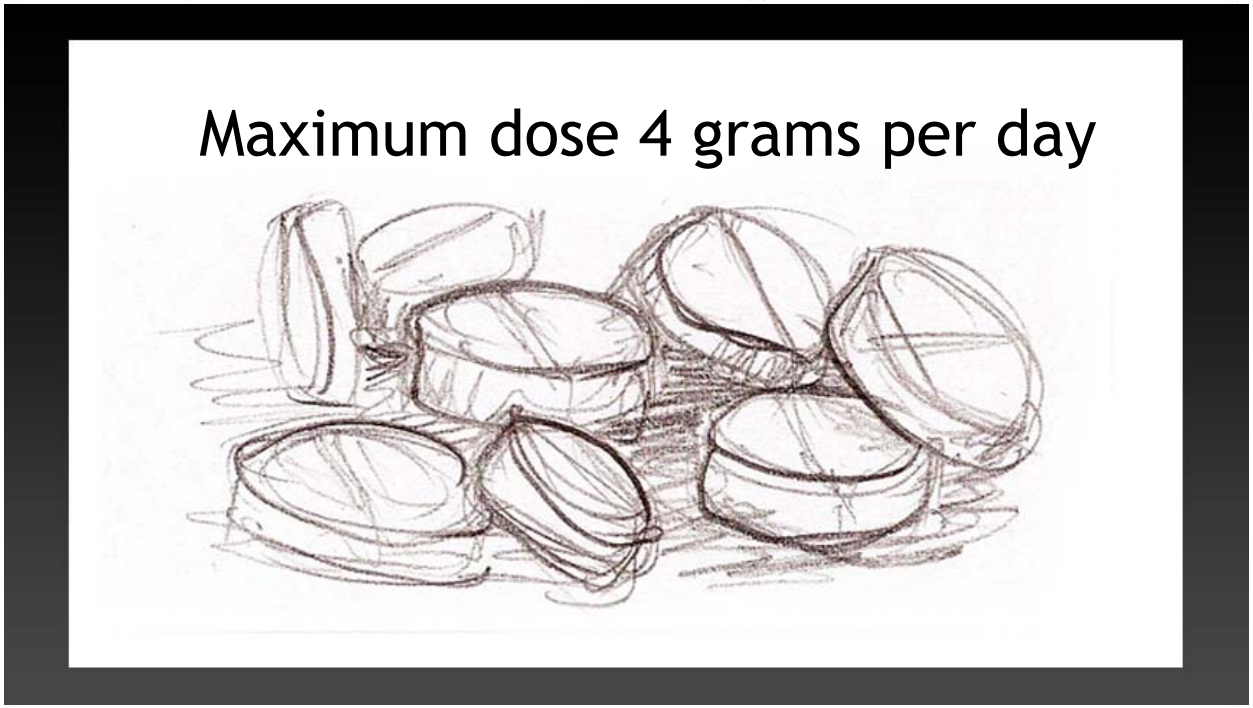
Acetaminophen Metabolism and Hepatotoxicity



Animation Notes:

Camera pushes in to show what 4 grams of active ingredient looks like (eight 500mg tablets = 4grams).

Voice Over:

The FDA recommends a maximum dose of 4 grams of APAP per day. Consuming more APAP than recommended can potentially cause severe liver damage.

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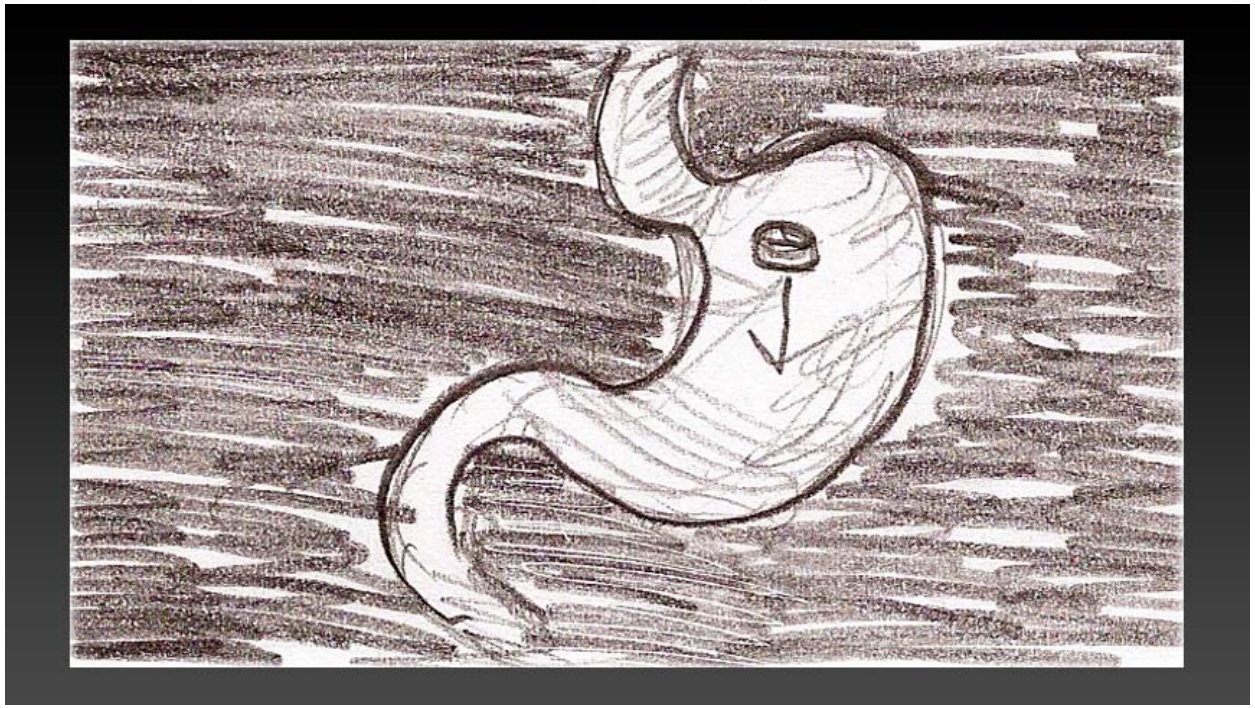
Acetaminophen Metabolism and Hepatotoxicity



Animation Notes:

Cut to a single APAP tablet moving downward in the stomach. The stomach will be simple and no other stomach contents will be shown. A visual effect will show the tablet dissipating to individual particles representing APAP molecules.

Voice Over:

When APAP is taken orally…

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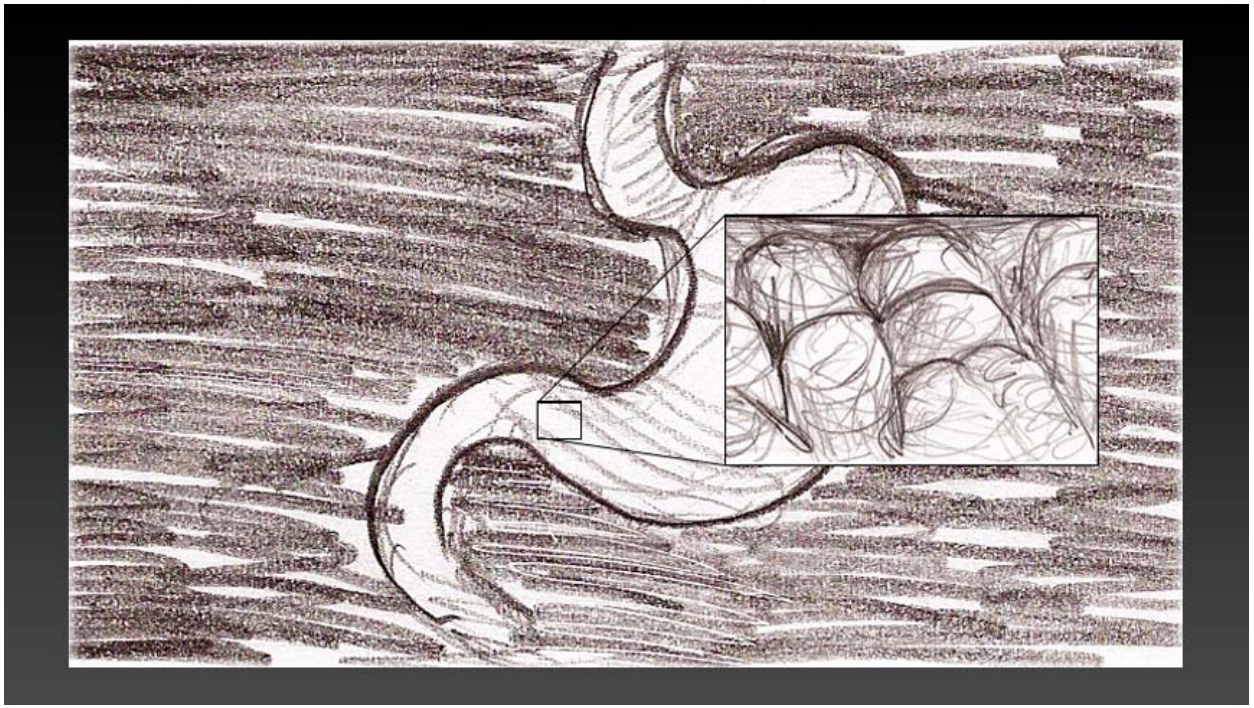
Acetaminophen Metabolism and Hepatotoxicity



Animation Notes:

Picture-in-picture is faded on and shows villi surface of GI tract.

Voice Over:

…it absorbs rapidly in the upper GI tract.

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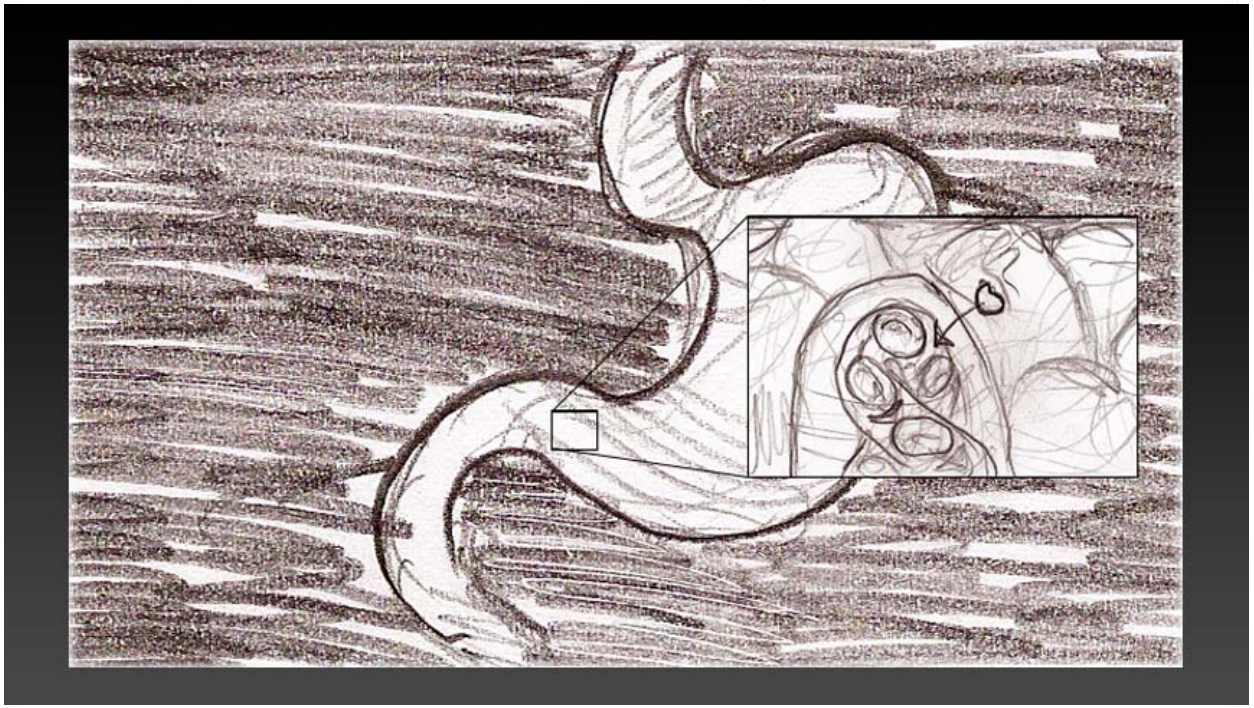

Animation Notes:

Picture-in-picture cross fades to show APAP passing though the surface of the villi into a blood vessel and swept away.

Voice Over:

APAP enters the bloodstream and is carried to sites of action.

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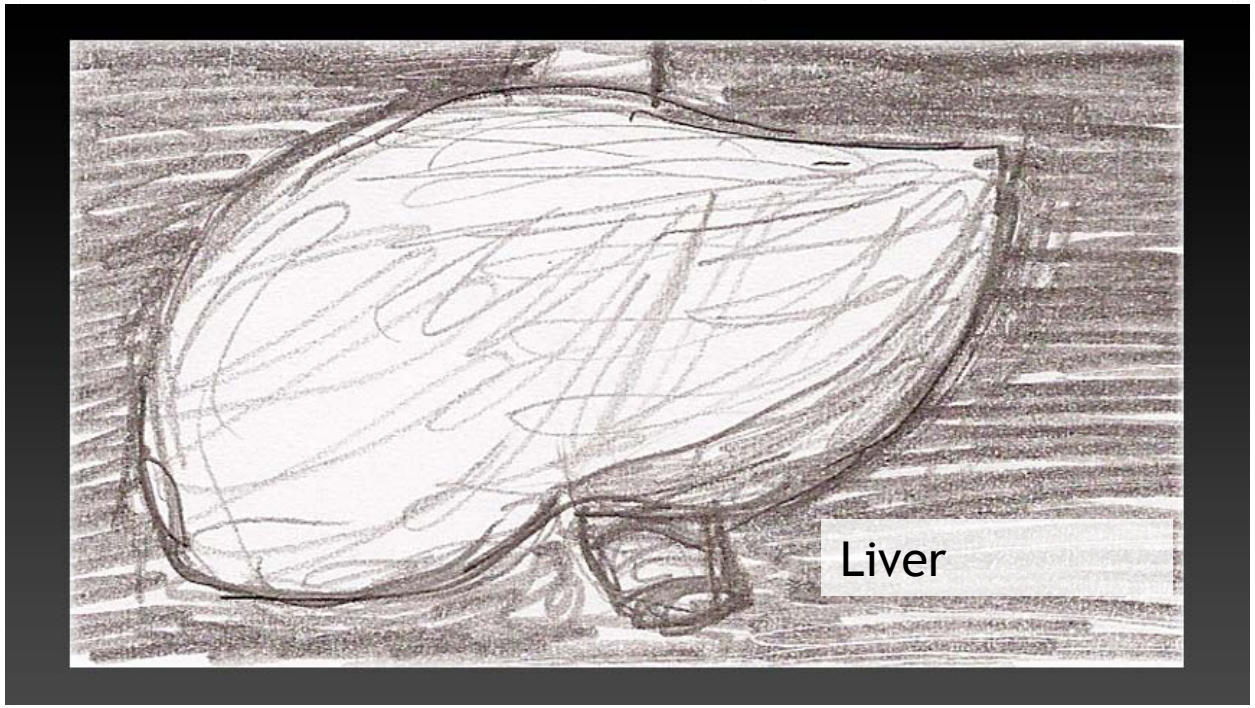

Animation Notes:

Stomach fades off and liver fades on.

Voice Over:

The liver metabolizes APAP and produces metabolites required for function.

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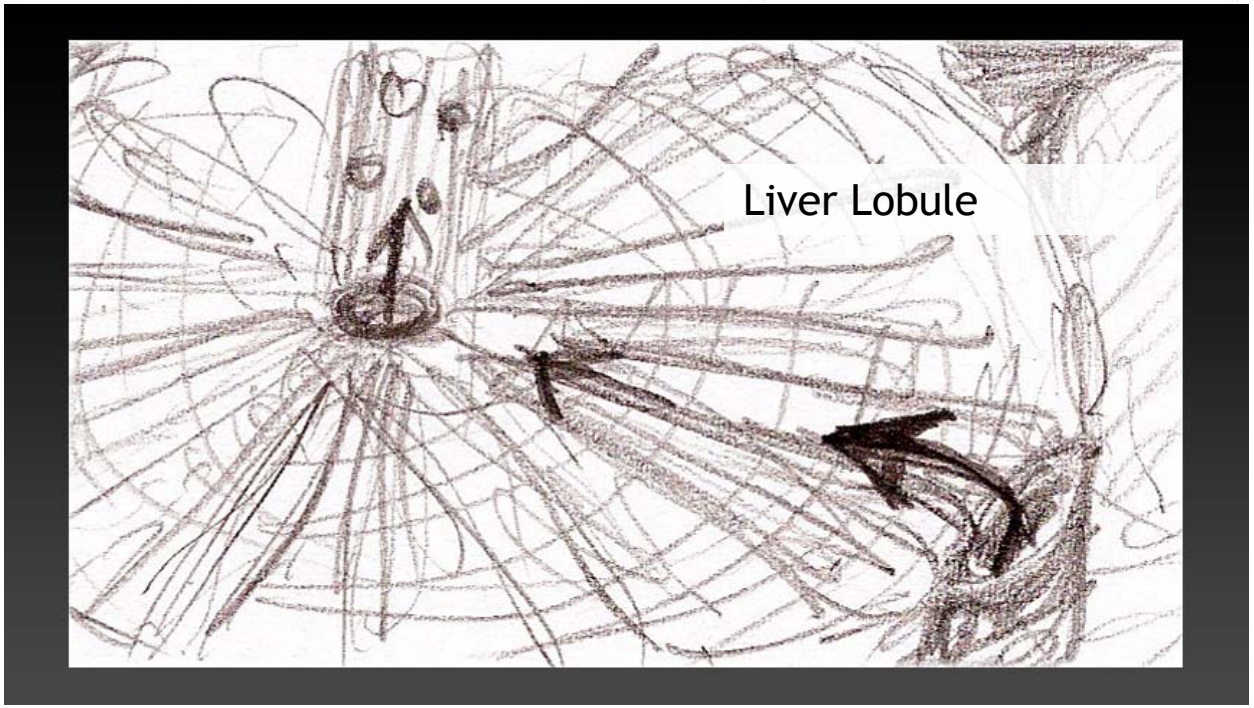


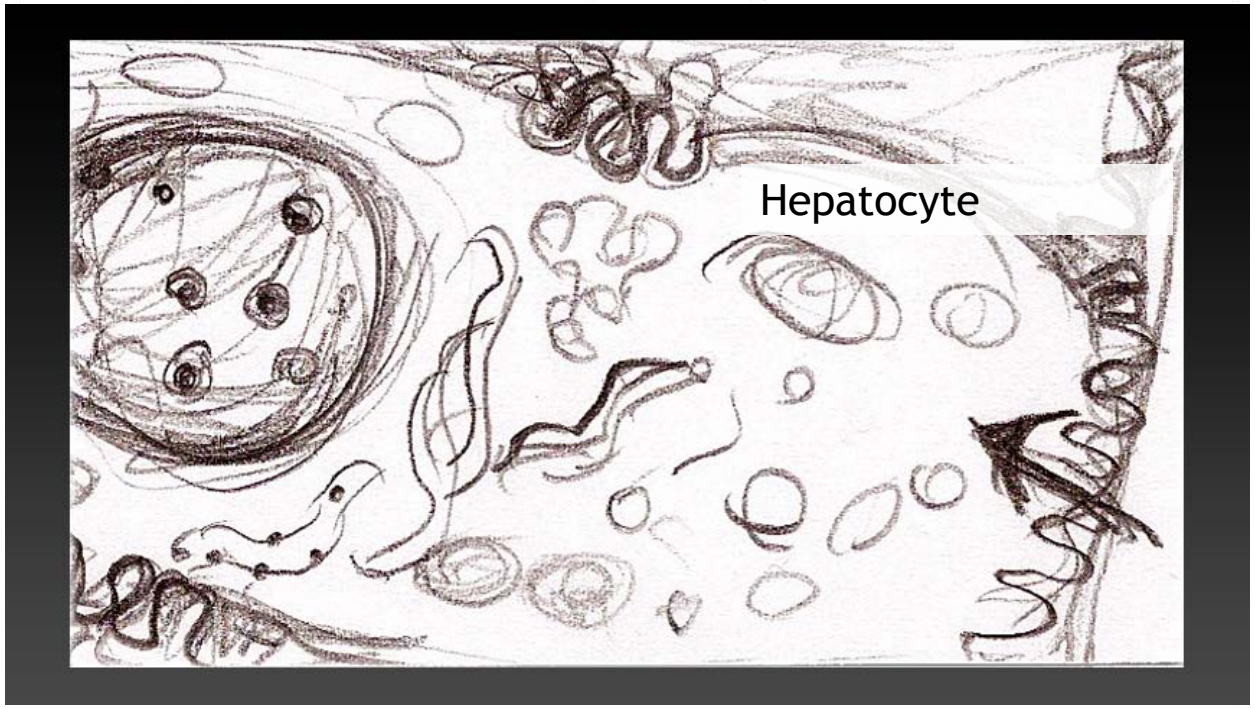
Animation Notes:

Cut to interior of liver. Healthy hepatocytes are arranged in a symmetrical pattern. Blood cells are flowing along arrow path.

Voice Over:

Many metabolic pathways occur in the liver to rid excess APAP and other substances from the body.

Acetaminophen Metabolism and Hepatotoxicity



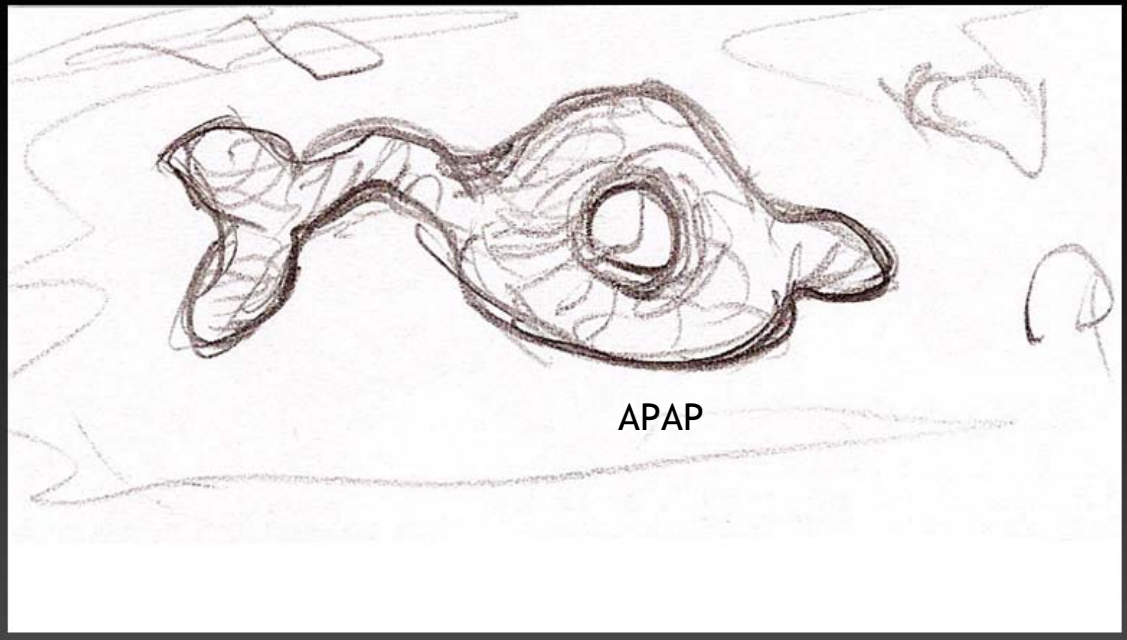
Animation Notes:

Cut to single hepatocyte that nearly fills the screen. Simple cellular contents are shown including; nucleus, endoplasmic reticulum, golgi, mitochondria etc.

Voice Over:

APAP is metabolized in the hepatocyte's smooth endoplasmic reticulum.

Acetaminophen Metabolism and Hepatotoxicity



Animation Notes:

Cut to a simple intracellular space environment, the same color of the smooth endoplasmic reticulum. The APAP molecule structure is shown.
More molecules will be seen in the background throughout all molecular shots.

Voice Over:

The majority of APAP…

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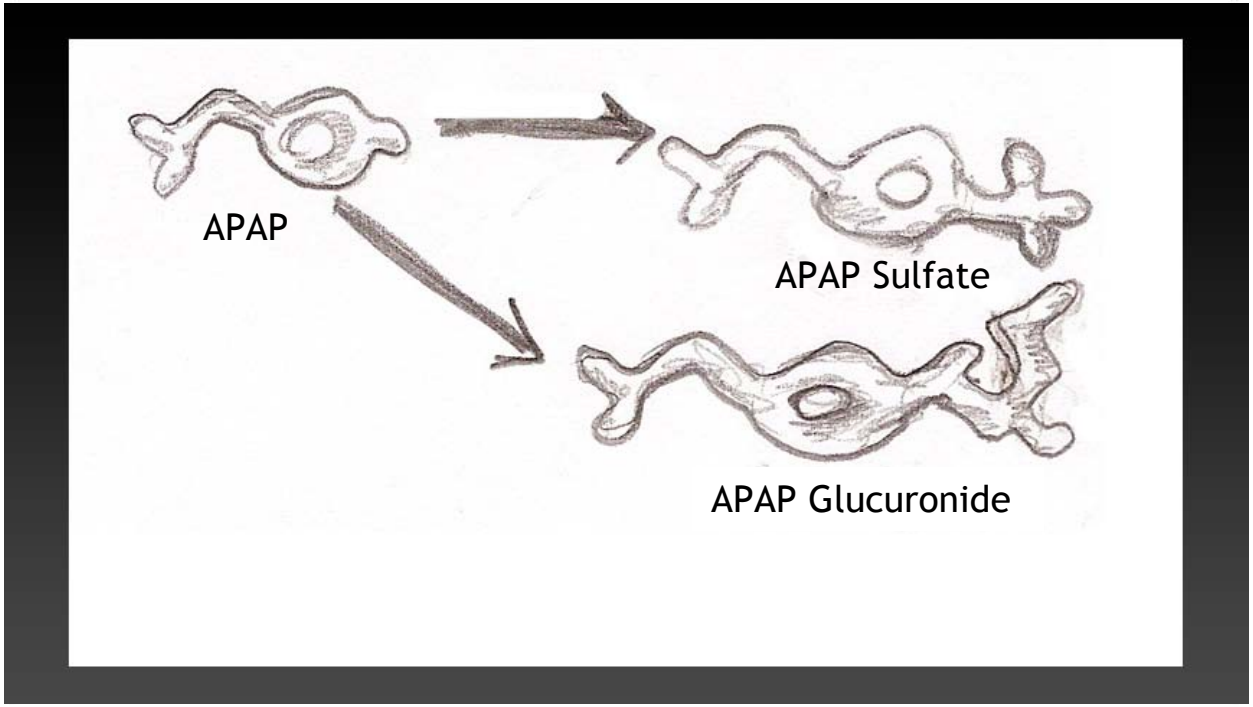


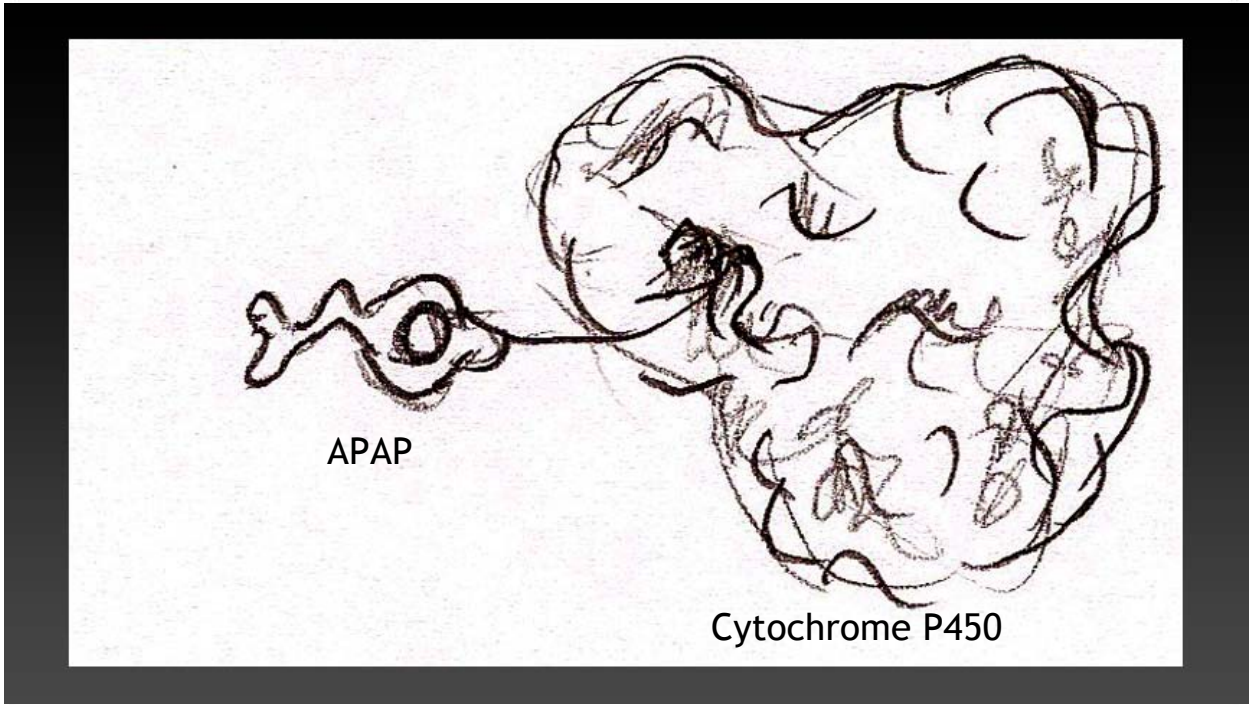
Animation Notes:

Camera move to show scene wider. Arrows and labels appear to show the 2 metabolites.

Voice Over:

…is conjugated by enzymes into inert sulfate and glucuronide metabolites.

Acetaminophen Metabolism and Hepatotoxicity



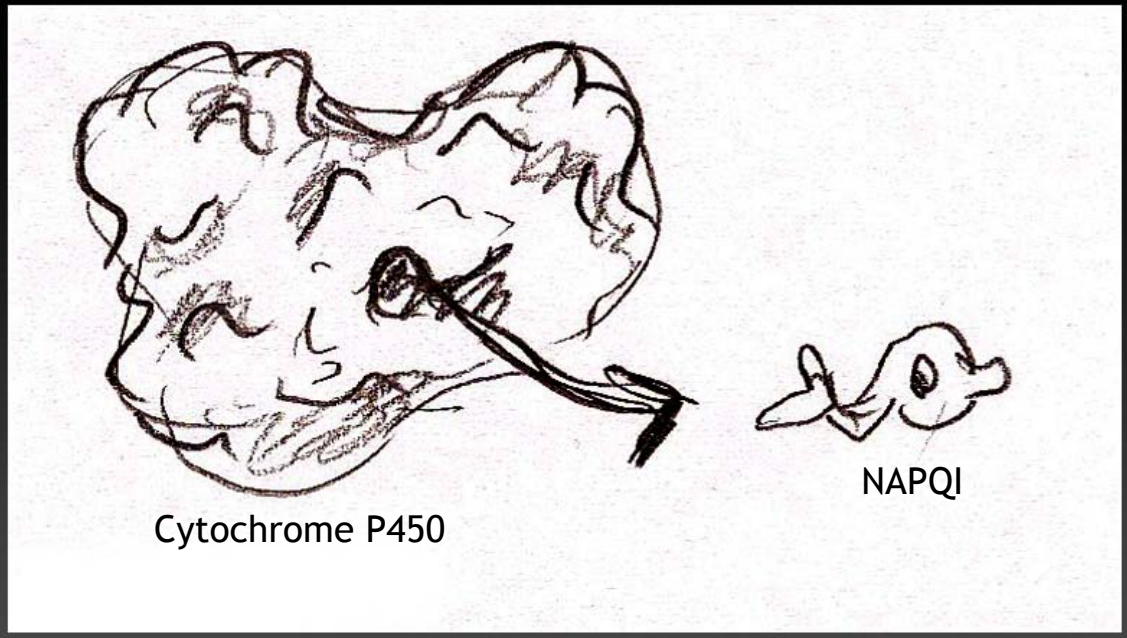
Animation Notes:

Cut to focus on Cytochrome P450 as it drifts into view. APAP enters the active site of the enzyme.

Voice Over:

An enzyme, cytochrome P450, converts the remaining APAP…

Acetaminophen Metabolism and Hepatotoxicity



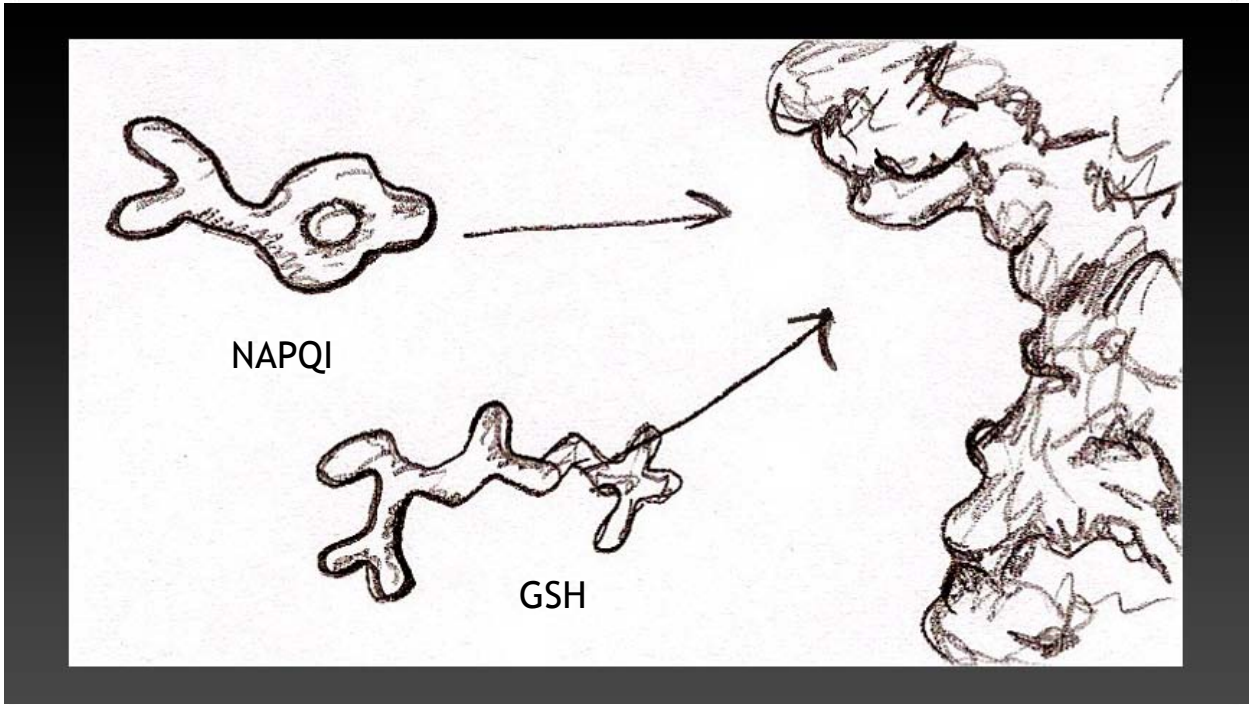
Animation Notes:

NAPQI exits the enzyme.

Voice Over:

...to NAPQI.

Acetaminophen Metabolism and Hepatotoxicity



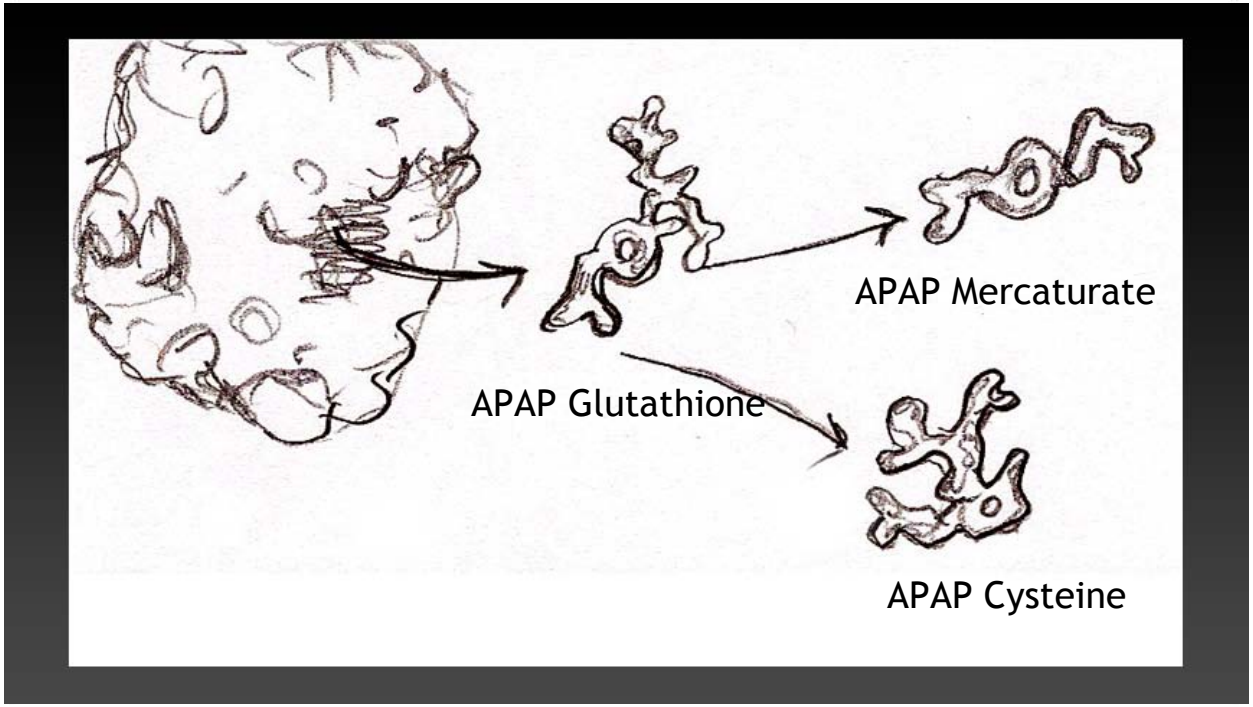
Animation Notes:

Cut to another enzyme. Both NAPQI and GSH enter the active site.

Voice Over:

NAPQI can be combined with GSH…

Acetaminophen Metabolism and Hepatotoxicity



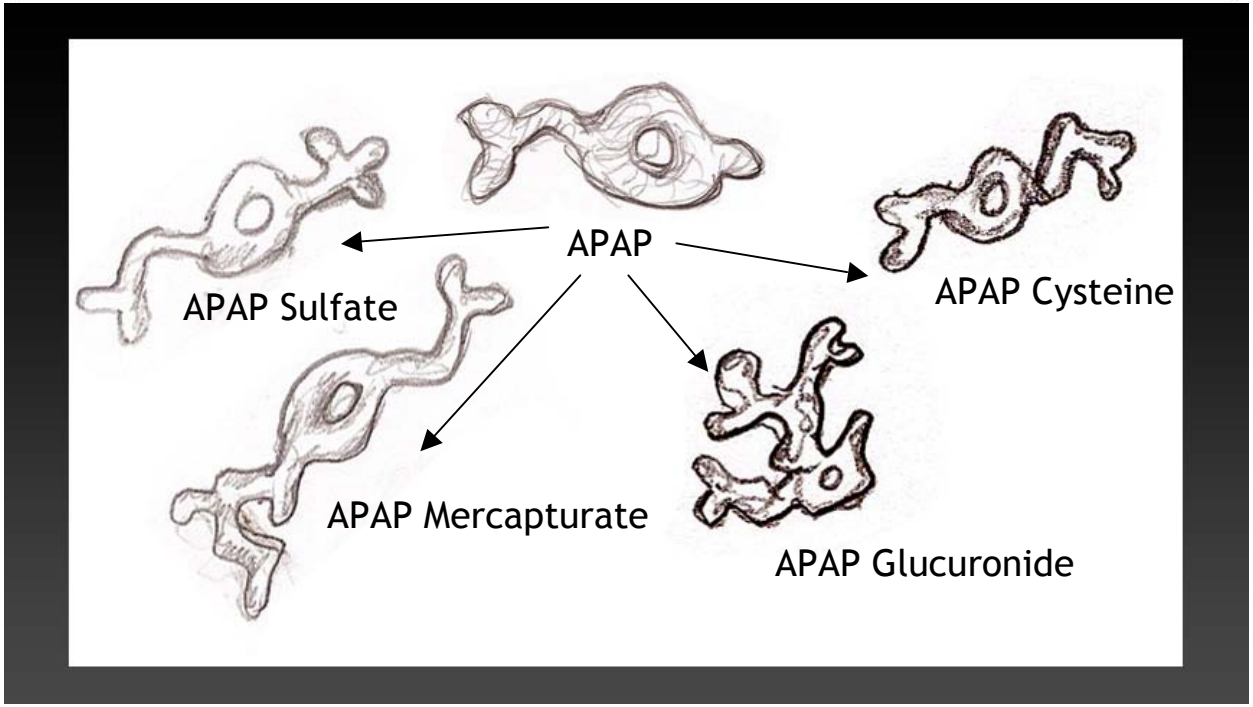
Animation Notes:

APAP Glutathione exit the enzyme. Same arrow and label treatment is used for these 2 end product metabolites.

Voice Over:

...to create an intermediate glutathione metabolite.
Further conjugation results in mercapturate and cysteine forms.

Acetaminophen Metabolism and Hepatotoxicity



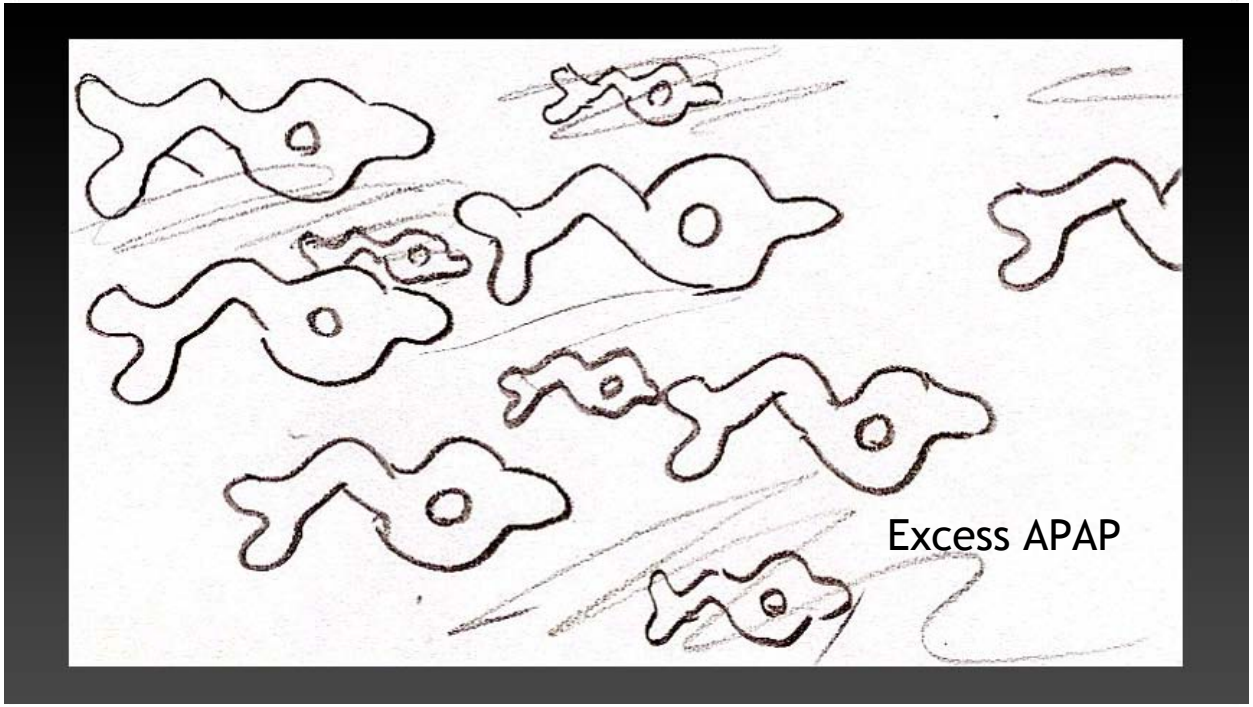
Voice Over:

Inert metabolic end products are harmlessly eliminated in the urine.

Animation Notes:

Camera drifts to frame up the end products. These metabolites are shown moving away from center and off frame. Fade to black.

Acetaminophen Metabolism and Hepatotoxicity



Animation Notes:

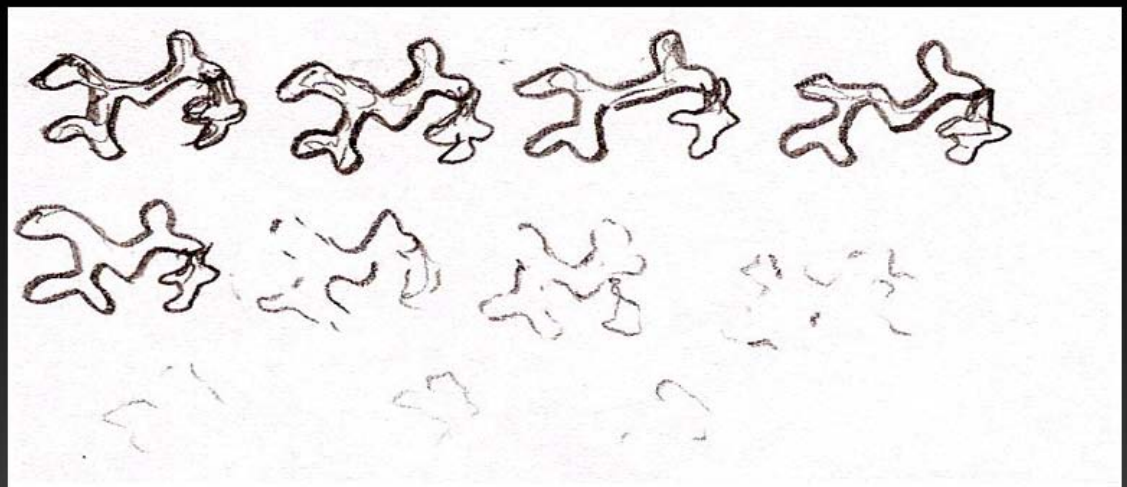
Fade in to slightly different (color) cellular environment. More APAP molecules are seen. Some in background convert to the first 2 metabolites. Most convert to NAPQI.

Voice Over:

The situation changes if an excessive amount of APAP enters the system.

An overdose of 7-10 grams of APAP in one day…

Acetaminophen Metabolism and Hepatotoxicity



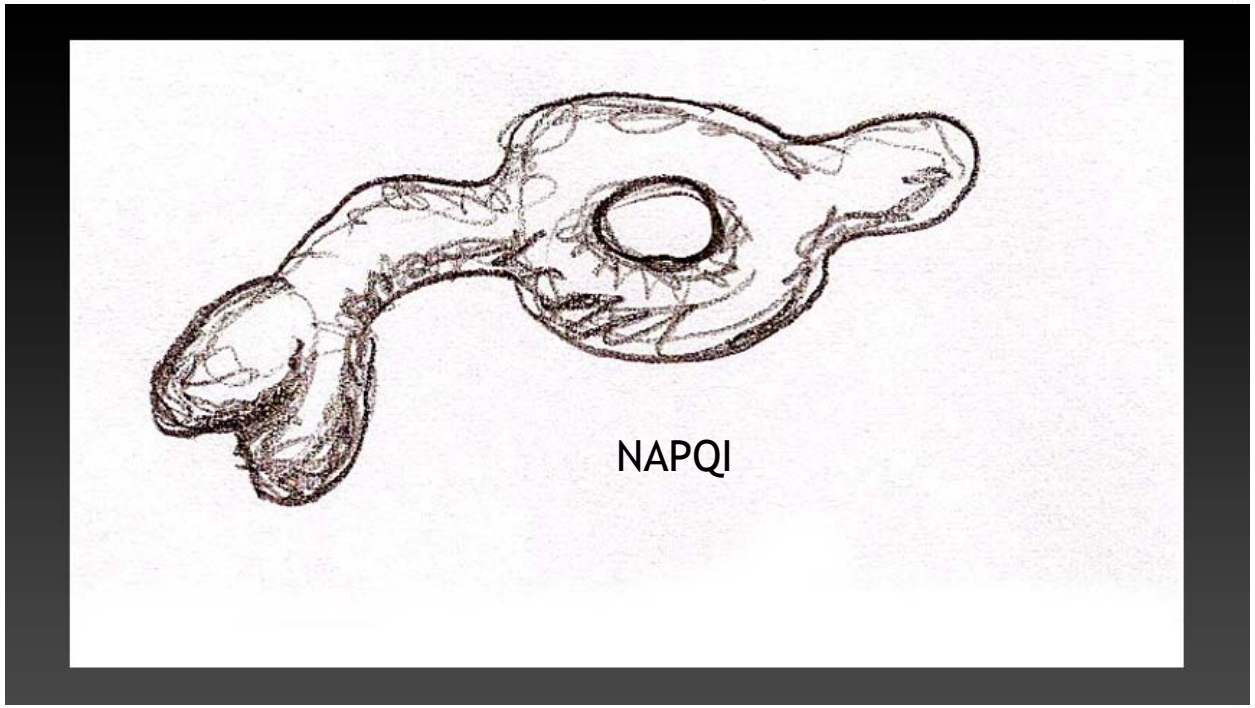
Animation Notes:

GSH molecules are shown but there are not enough to pair with all the NAPQI.

Voice Over:

…quickly exhausts the GSH available for NAPQI deactivation.

Acetaminophen Metabolism and Hepatotoxicity



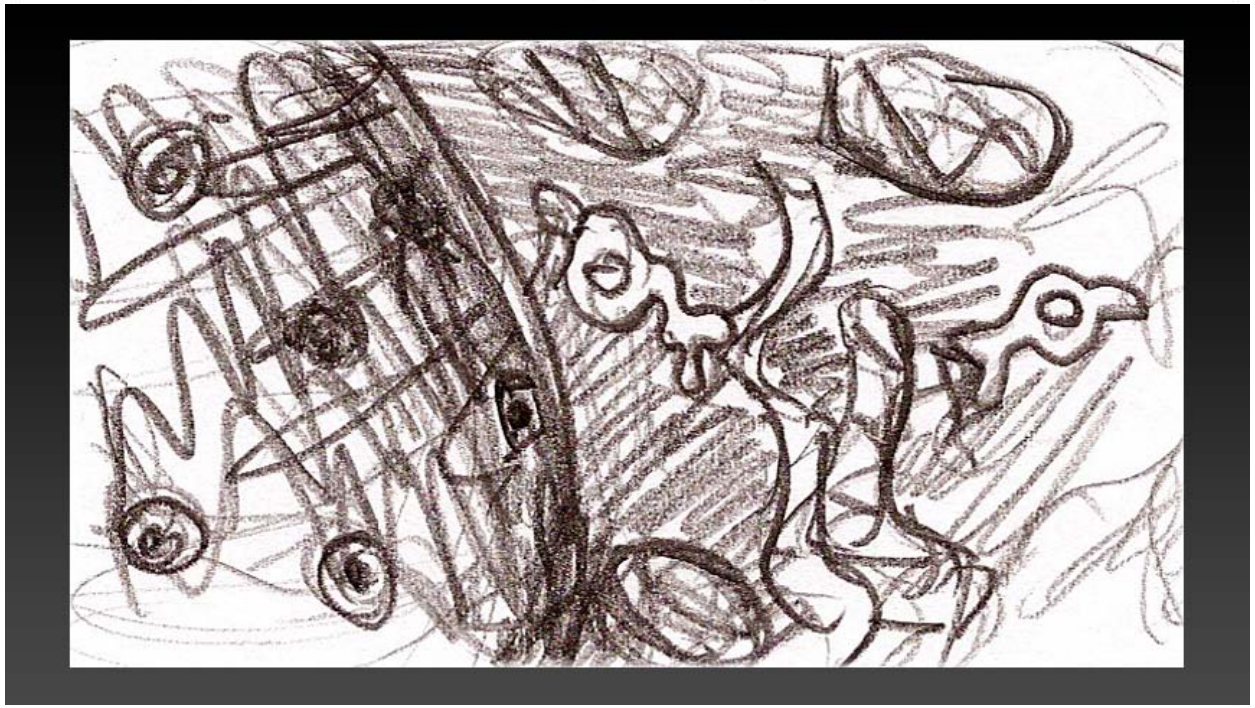
Animation Notes:

Cut to show single NAPQI.

Voice Over:

NAPQI is toxic to cellular proteins and nucleic acids.

Acetaminophen Metabolism and Hepatotoxicity



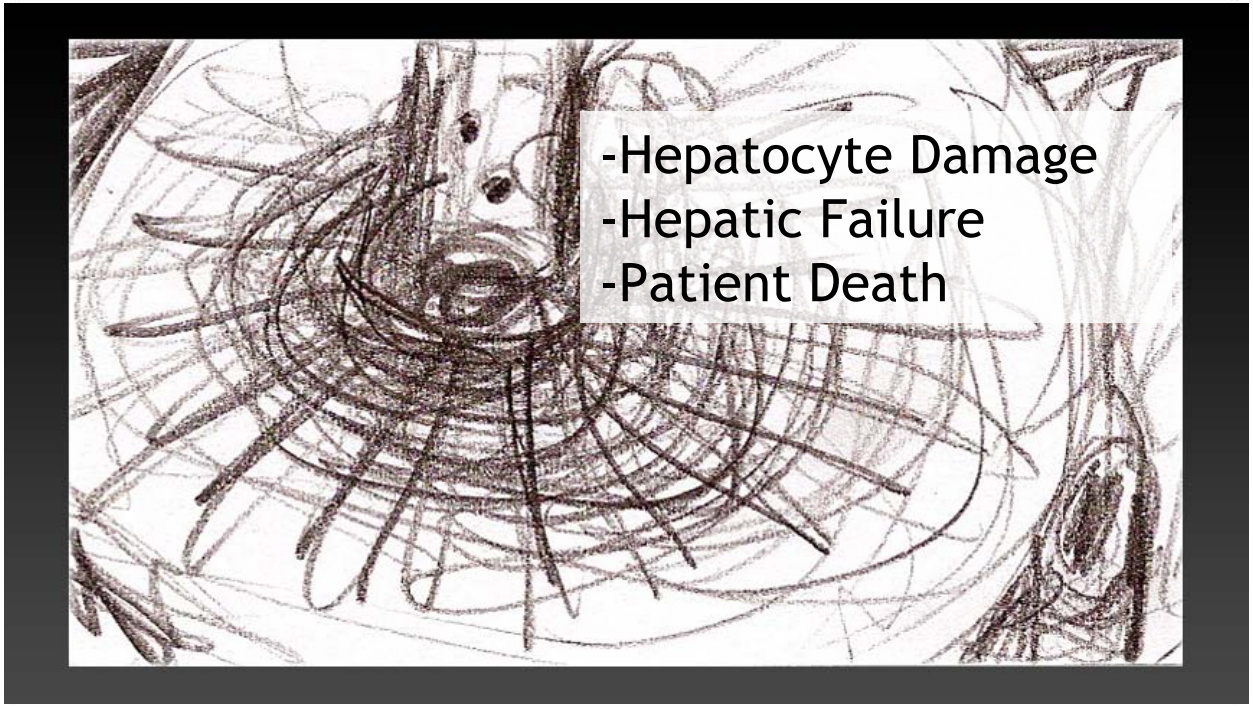
Animation Notes:

Cut to NAPQI moving away from the area to structures nearby which lose color and look ill.

Voice Over:

Damage to intracellular structures causes irreversible harm to the hepatocyte.

Acetaminophen Metabolism and Hepatotoxicity



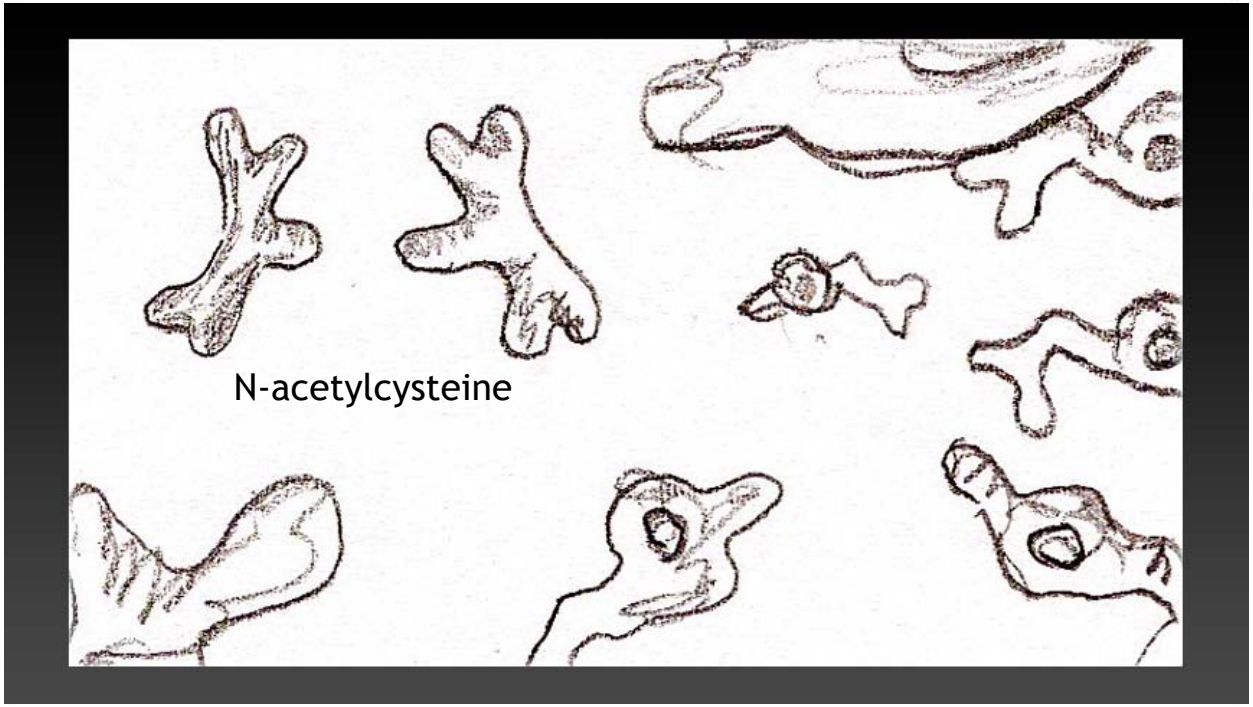
Animation Notes:

Cross fade to liver lobule now with obvious damage. Show 3 bullet points in time to VO. Blow out to white.

Voice Over:

Spreading hepatocyte destruction can lead to hepatic failure and patient death.

Acetaminophen Metabolism and Hepatotoxicity



Animation Notes:

Fade in from white to ambiguous cellular environment. NAC pathway is shown with 3D molecules. Excess NAPQI is in the environment.

Voice Over:

There are ways to avoid such consequences. N-acetylcysteine, called NAC is the antidote for APAP overdose.

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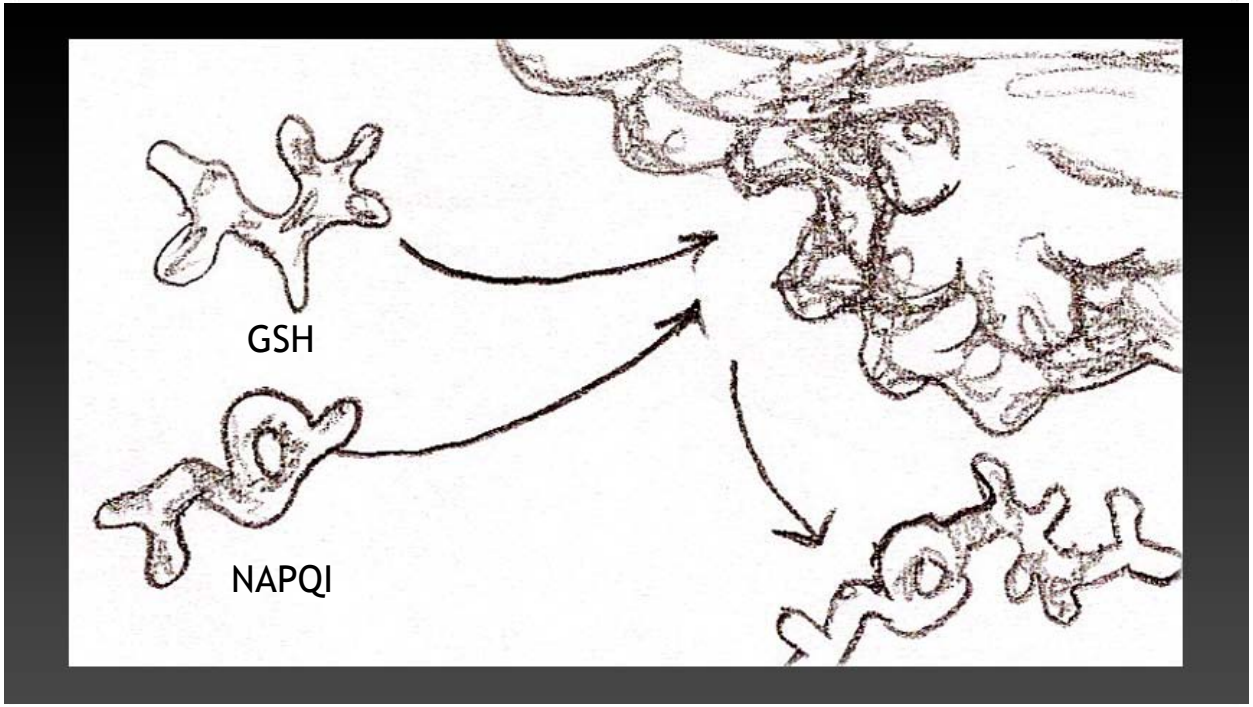
Acetaminophen Metabolism and Hepatotoxicity



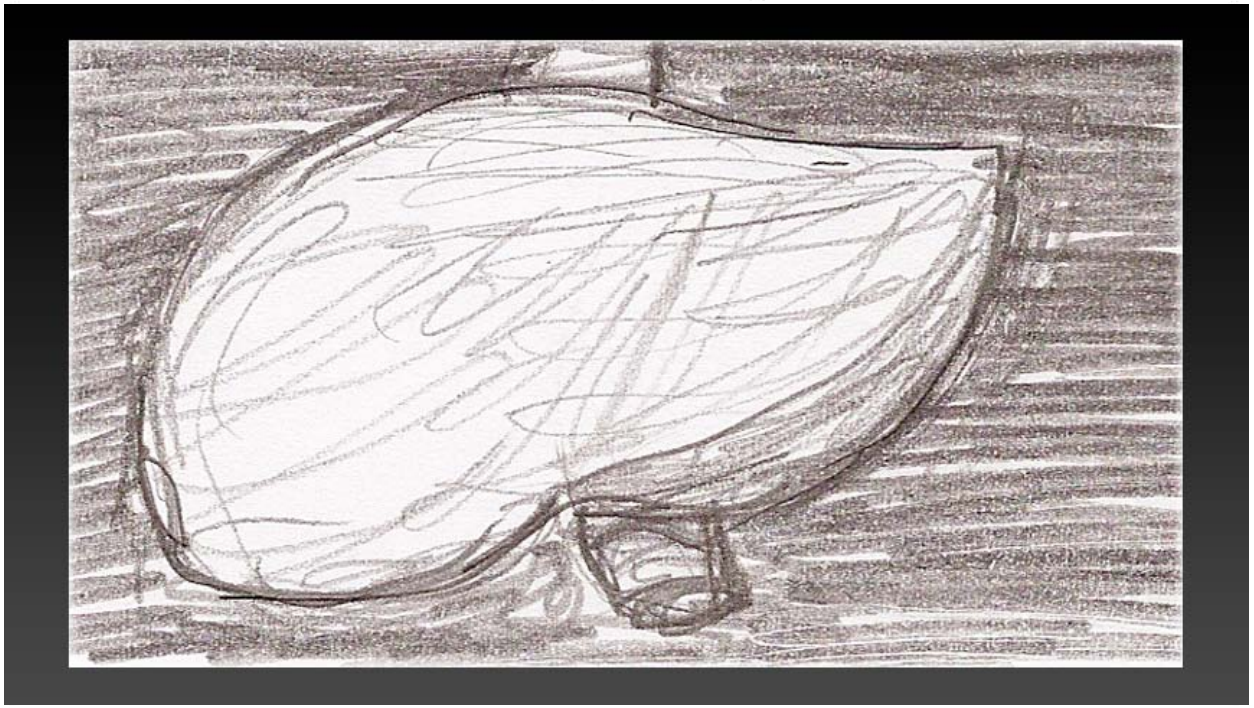
Animation Notes:

NAPQI is converted by the enzyme into the inert form.

Voice Over:

If NAC is given in time, it converts to GSH for deactivation of excess NAPQI…

Acetaminophen Metabolism and Hepatotoxicity



Animation Notes:

Cut to show undamaged liver. Same liver as earlier.
Fade out.

Voice Over:

…before hepatotoxicity can occur.

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Acetaminophen Metabolism and Hepatotoxicity

Animation Notes:

Cut to pill bottle of APAP and tablets. Same scene as the beginning. Screen fades to black.

Voice Over:

Increasing general awareness of appropriate APAP usage could help prevent overdoses from occurring.

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Voice Over:

Animation Notes:

The end!

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