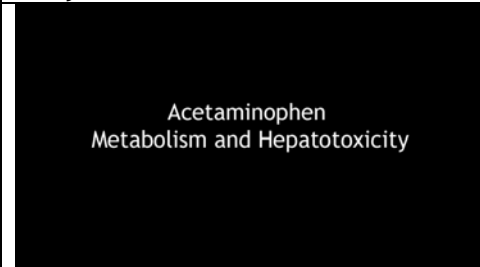

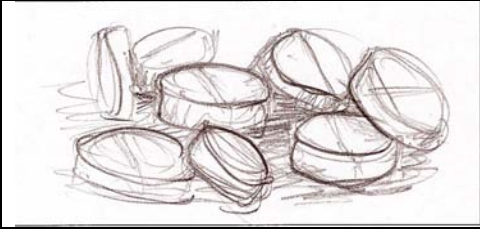


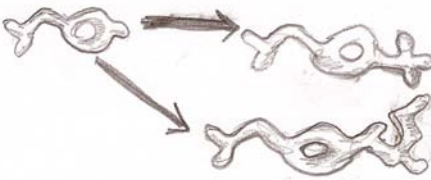


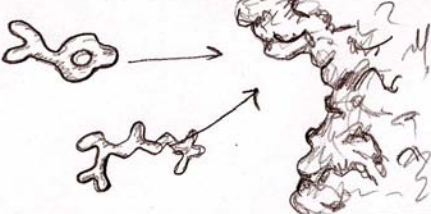

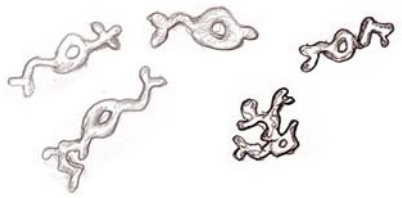

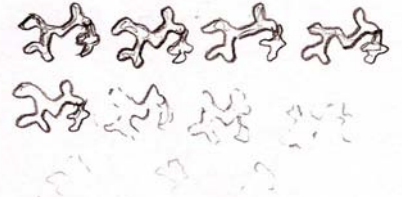



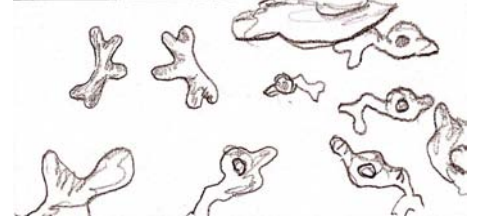
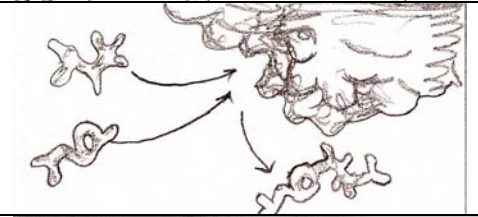

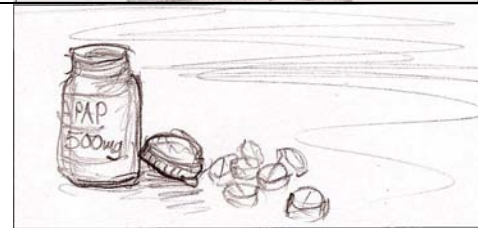


Storyboard Sketches	VO - Word Count 258?	Text on Screen	Animation Notes
		<p>Acetaminophen Metabolism and Hepatotoxicity</p>	<p>Fade on title page. Fade out.</p>
	<p>Acetaminophen (APAP) is a widely used medication with analgesic and antipyretic properties.</p>	<p>Acetaminophen</p>	<p>Fade in. Shown is a bottle of APAP and tablets of APAP with a neutral background.</p>
	<p>The FDA recommends a maximum dose of 4 grams of APAP per day. Consuming more APAP than recommended can potentially cause severe liver damage.</p>	<p>Maximum APAP dose 4 grams per day</p>	<p>Camera pushes in to show what 4 grams of active ingredient looks like (eight 500mg tablets = 4grams).</p>
	<p>When APAP is taken orally...</p>		<p>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.</p>
	<p>...it absorbs rapidly in the upper GI tract.</p>		<p>Picture-in-picture is faded on and shows villi surface of GI tract.</p>

	<p>APAP enters the bloodstream and is carried to sites of action.</p>		<p>Picture-in-picture cross fades to show APAP passing through the surface of the villi into a blood vessel and swept away.</p>
	<p>The liver metabolizes APAP and produces metabolites required for function.</p>	<p>Liver</p>	<p>Stomach fades off and liver fades on.</p>
	<p>Many metabolic pathways occur in the liver to rid excess APAP and other substances from the body.</p>	<p>Liver Lobule</p>	<p>Cut to interior of liver. Healthy hepatocytes are arranged in a symmetrical pattern. Blood cells are flowing along arrow path.</p>
	<p>APAP is metabolized in the hepatocyte's smooth endoplasmic reticulum.</p>	<p>Hepatocyte</p>	<p>Cut to single hepatocyte that nearly fills the screen. Simple cellular contents are shown including; nucleus, endoplasmic reticulum, golgi, mitochondria etc.</p>
	<p>The majority of APAP...</p>	<p>APAP</p>	<p>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.</p>

	<p>...is conjugated by enzymes into inert sulfate and glucuronide metabolites.</p>	<p>APAP Sulfate APAP Glucuronide</p>	<p>Camera move to show scene wider. Arrows and labels appear to show the 2 metabolites.</p>
	<p>An enzyme, cytochrome P450, converts the remaining APAP...</p>	<p>APAP Cytochrome P450</p>	<p>Cut to focus on Cytochrome P450 as it drifts into view. APAP enters the active site of the enzyme.</p>
 <p>↳ ID PDB</p>	<p>...to NAPQI.</p>	<p>NAPQI</p>	<p>NAPQI exits the enzyme.</p>
	<p>NAPQI can be combined with GSH...</p>	<p>NAPQI GSH</p>	<p>Cut to another enzyme. Both NAPQI and GSH enter the active site.</p>
	<p>...to create an intermediate glutathione metabolite. Further conjugation results in mercapturate and cysteine forms.</p>	<p>APAP Glutathione APAP Mercapturate APAP Cysteine</p>	<p>APAP Glutathione exit the enzyme. Same arrow and label treatment is used for these 2 end product metabolites.</p>

	<p>Inert metabolic end products are harmlessly eliminated in the urine.</p>		<p>Camera drifts to frame up the end products. These metabolites are shown moving away from center and off frame. Fade to black.</p>
	<p>The situation changes if an excessive amount of APAP enters the system. An overdose of 7-10 grams of APAP in one day...</p>	<p>Excess APAP</p>	<p>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.</p>
	<p>...quickly exhausts the GSH available for NAPQI deactivation.</p>	<p>APAP overdose 7-10grams</p>	<p>GSH molecules are shown but there are not enough to pair with all the NAPQI.</p>
	<p>NAPQI is toxic to cellular proteins and nucleic acids.</p>	<p>NAPQI</p>	<p>Cut to show single NAPQI.</p>
	<p>Damage to intracellular structures causes irreversible harm to the hepatocyte.</p>		<p>Cut to NAPQI moving away from the area to structures nearby which lose color and look ill.</p>

	<p>Spreading hepatocyte destruction can lead to hepatic failure and patient death.</p>	<ul style="list-style-type: none"> • Hepatocyte Destruction • Hepatic Failure • Patient Death 	<p>Cross fade to liver lobule now with obvious damage. Show 3 bullet points in time to VO. Blow out to white.</p>
	<p>There are ways to avoid such consequences. N-acetylcysteine, called NAC is the antidote for APAP overdose.</p>	<p>N-acetylcysteine</p>	<p>Fade in from white to ambiguous cellular environment. NAC pathway is shown with 3D molecules. Excess NAPQI is in the environment.</p>
	<p>If NAC is given in time, it converts to GSH for deactivation of excess NAPQI...</p>	<p>NAPQI GSH</p>	<p>NAPQI is converted by the enzyme into the inert form.</p>
	<p>...before hepatotoxicity can occur.</p>		<p>Cut to show undamaged liver. Same liver as earlier. Fade out.</p>
	<p>Increasing general awareness of appropriate APAP usage could help prevent overdoses from occurring.</p>		<p>Cut to pill bottle of APAP and tablets. Same scene as the beginning. Screen fades to black. The end!</p>