INTRODUCTION TO GENERAL PATHOLOGY

AUTOPSY

INVESTIGATIVE PATHOLOGY

- **Biopsies**
- **Surgical Pathology**

MANIFESTATION OF DISEASE

- **Macroscopic**
- **Microscopic**
- **Ultrastructure**

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AUTOPSY or NECROPSY

Autopsy means "see for yourself". It is a special surgical operation, performed by specially-trained physicians, on a dead body.

Its purpose is to learn the truth about the person's health during life, and how the person really died, i.e. to determine the cause of death.

Autopsy dealing with a body of our own species, a human body.

Necropsy dealing with other species.

use of general *Latin expression*

post mortem examination

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AUTOPSY anatomical pathology

Rembrandt 1632 *Anatomy*

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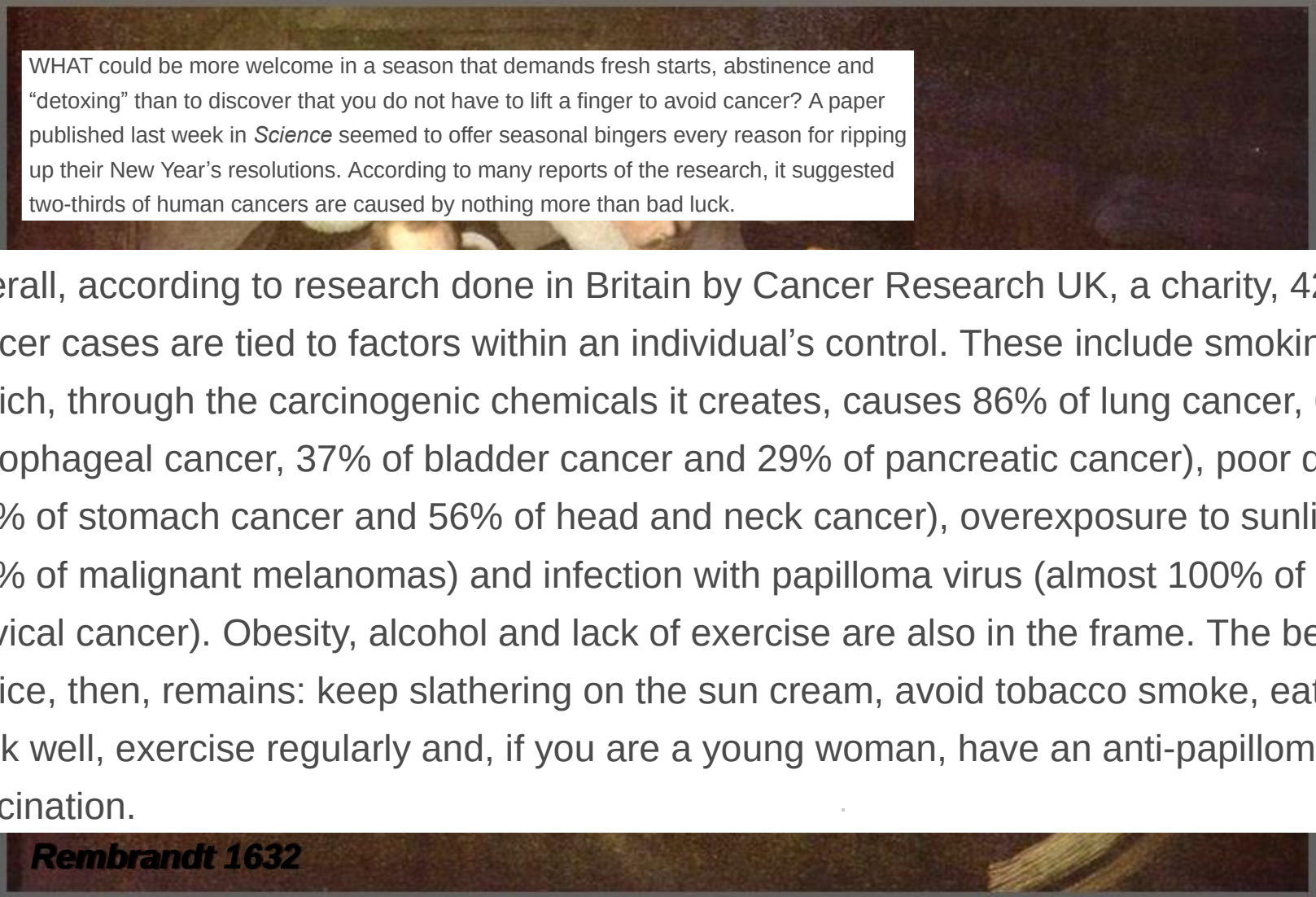
AUTOPSY anatomical pathology



WHAT could be more welcome in a season that demands fresh starts, abstinence and "detoxing" than to discover that you do not have to lift a finger to avoid cancer? A paper published last week in *Science* seemed to offer seasonal bingers every reason for ripping up their New Year's resolutions. According to many reports of the research, it suggested two-thirds of human cancers are caused by nothing more than bad luck.

Overall, according to research done in Britain by Cancer Research UK, a charity, 42% of cancer cases are tied to factors within an individual's control. These include smoking (which, through the carcinogenic chemicals it creates, causes 86% of lung cancer, 65% of oesophageal cancer, 37% of bladder cancer and 29% of pancreatic cancer), poor diet (51% of stomach cancer and 56% of head and neck cancer), overexposure to sunlight (86% of malignant melanomas) and infection with papilloma virus (almost 100% of cervical cancer). Obesity, alcohol and lack of exercise are also in the frame. The best advice, then, remains: keep slathering on the sun cream, avoid tobacco smoke, eat and drink well, exercise regularly and, if you are a young woman, have an anti-papilloma vaccination.

Rembrandt 1632

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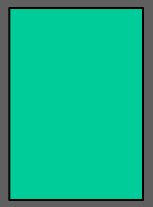
AUTOPSY anatomical pathology

we generally understand that pathology is used to explain the past

yet at times past organs were examined to predict the future



AUTOPSY

the two-handed pathologist
according to Bernhard Wagner, MD New York

Eustachi Bartolomeo 1574

PATHOLOGY and LABORATORY MEDICINE

clinical and *ante mortem* *vs post mortem*

- **needle aspirates, biopsies**
- **clinical pathology : hematology, blood chemistry, cytology, cytoscan**
- **intra-operative surgical pathology**
- **in combination with ultrasound, x-ray, mri, nmr**

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PATHOLOGY and LABORATORY MEDICINE

autopsy and *post mortem*

- external examination
- samples of body fluids, body parts
- chemical, physical analysis, x-ray, tomography, mri etc.
- laboratory tests
- histopathology, immunology, histo-chemistry
- genetics

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PATHOLOGY and LABORATORY MEDICINE

clinical and *ante mortem*

- needle aspirates, biopsies, smears
- frozen sections (e.g. during surgery)

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THE PATHOLOGIST

the pathologist a generalist physician

always works together with other disciplines / specialists :
this makes the work a lot of fun
namely working with a large variety of other people, professions

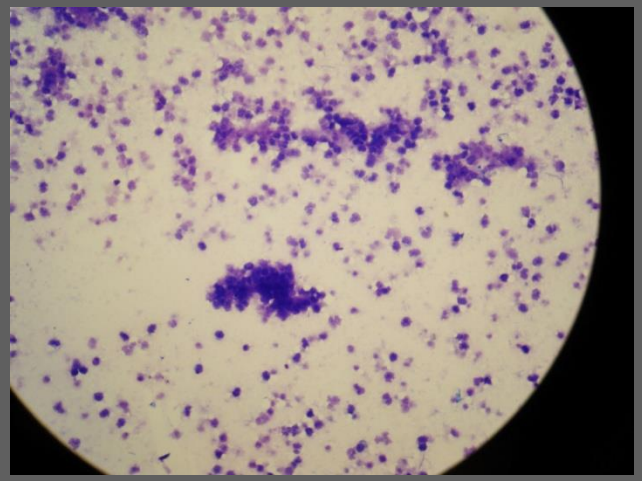
the pleasure of sharing

(note Herve This)

PATHOLOGY and LABORATORY MEDICINE

clinical and *ante mortem*

- needle aspirates, biopsies
- clinical pathology : haematology, blood chemistry
- intra-operative surgical pathology



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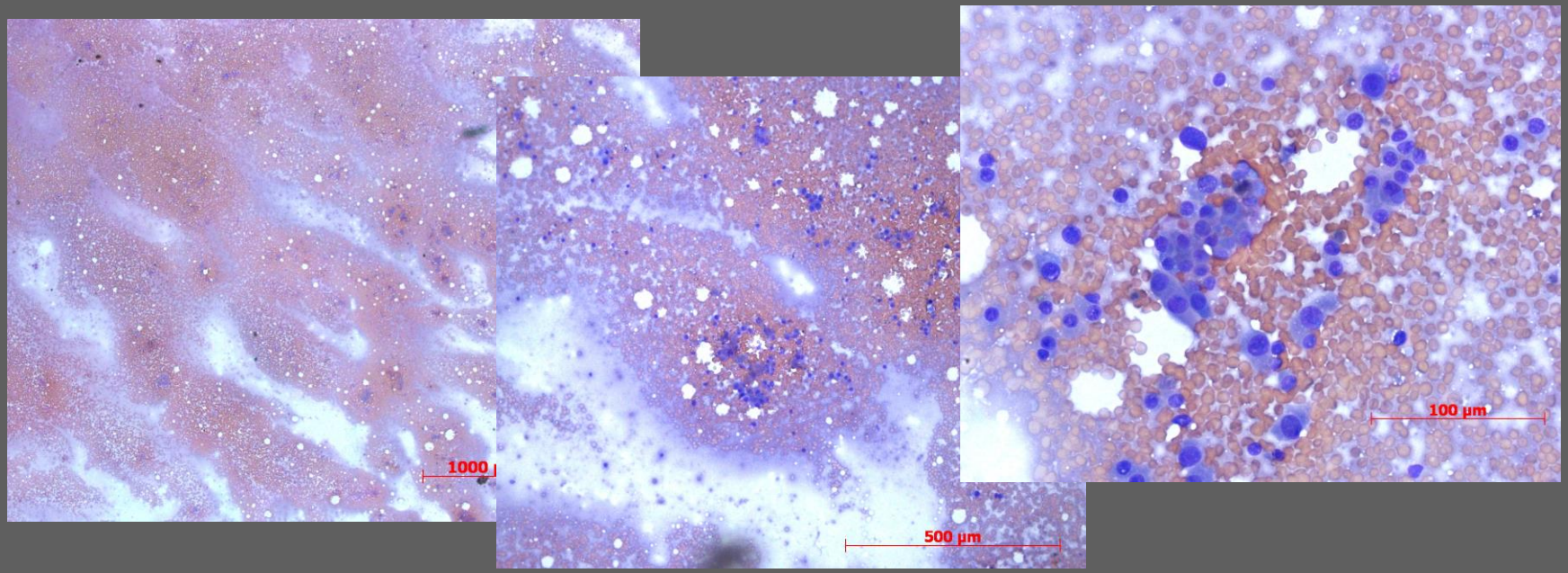

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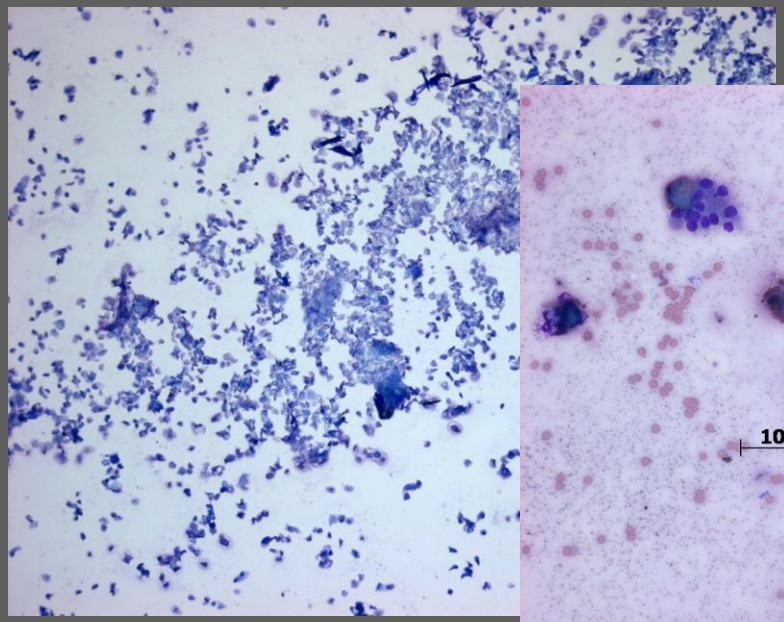

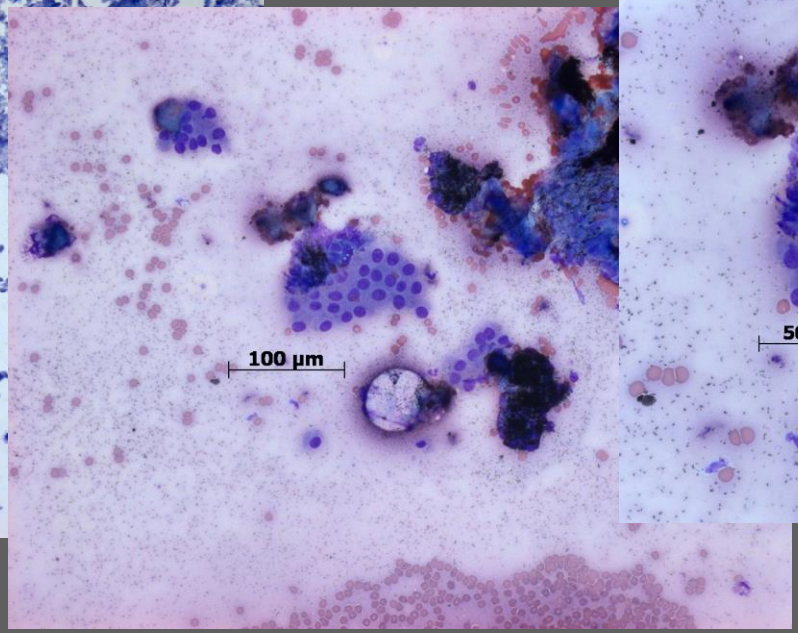

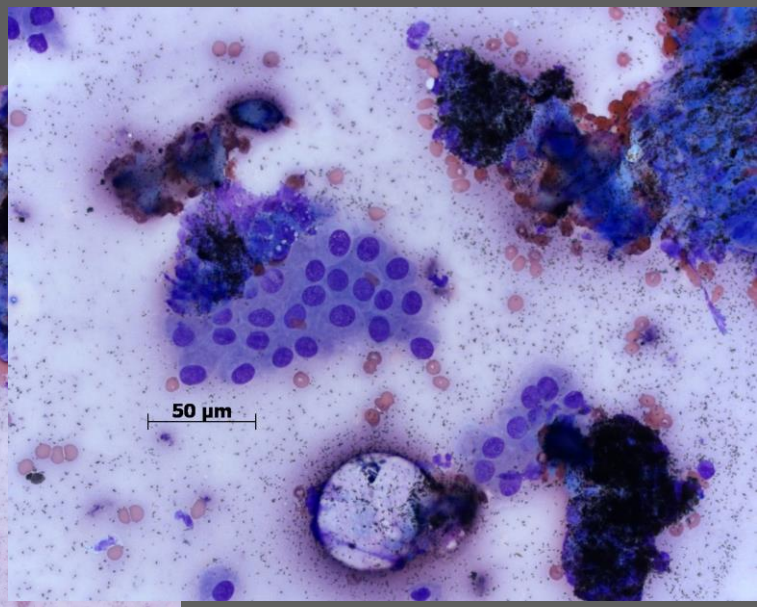

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THE PATHOLOGIST

A medical pathologist is a physician with a specialty degree in the scientific study of the body and its parts. This always includes several years learning to do autopsies and ancillary investigations, and to work in Laboratory Medicine in combination with Clinical Medicine.

The pathologist is a very good example of a generalist physician, working with specialists

the one who puts the puzzle together
if only sometimes at the end

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THE PATHOLOGIST

A pathologist can also be a veterinarian with a specialty degree in the scientific study of the body and its parts in many different animal species.

This always includes several years learning to do autopsies, learning anatomy / physiology of various species, ancillary investigations, and to work in Laboratory Medicine.

The veterinary pathologist will be working with specialists, biologists, zoologists
trying to put the puzzle together

PATHOLOGIST … STORY TELLER

If there is no story to be put together at the end……

where is the fun ?

Pathology reporting is most satisfying when the conclusions make sense

Pathologist are by nature very curious, never quite satisfied with the answers, often distracted by serendipity

(Some are said to have started doing autopsies on their Teddy Bears.. Finding the source of the noise)

PATHOLOGIST … STORY TELLER

Stories need to be put together at the end……

Pathologist are also working with Paleontologists trying to piece together the living history of specimens found for instance in excavations etc.

can have influence on history (e.g. Napoleon)

can describe diseases in mummies and skeletons

PATHOLOGIST … STORY TELLER

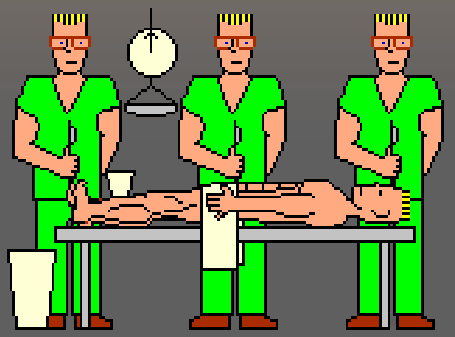
This perfectly preserved baby from Peru was born with a heart defect. NAT GEO

Pathologist are also working with Paleontologists trying to piece together the living history of specimens found for instance in excavations etc.

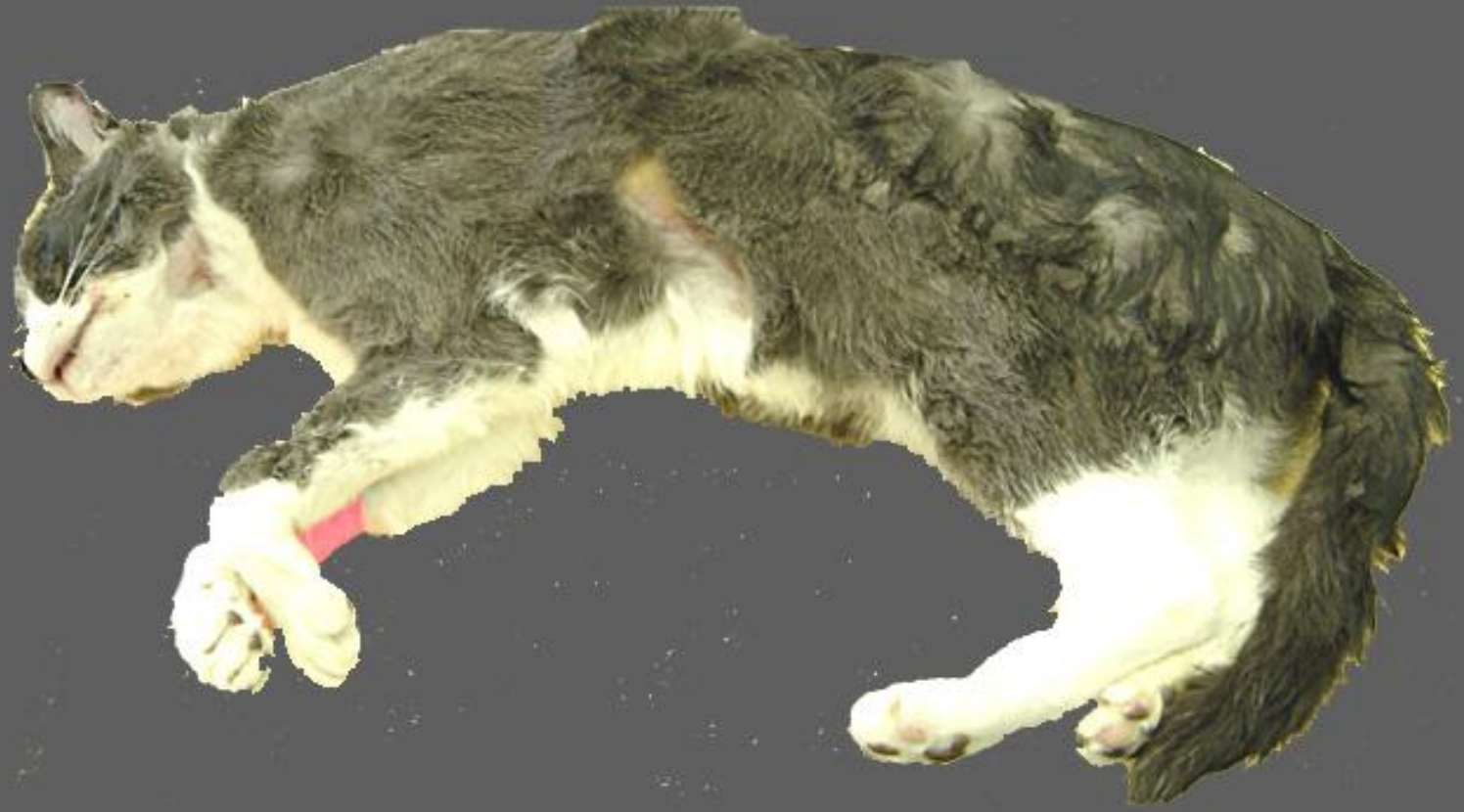
can describe diseases in mummies and skeletons

A 2011 study of 52 mummies in the Egyptian Museum in Cairo showed that almost half had clogged arteries, the kind of condition that can lead to a heart attack or stroke.

EXAMPLE OF AN AUTOPSY



a dead cat
(In case of a human corpse the body would have already been identified.)
Lawful consent needs to be obtained for an autopsy or necropsy to get started.



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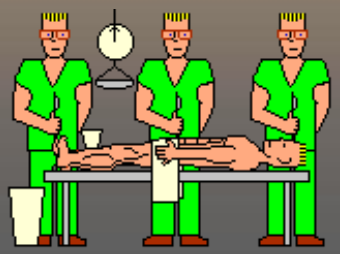

AUTOPSY

the actual procedure

The procedure is done with respect and seriousness. The prevailing mood in the autopsy room is curiosity, scientific interest, and pleasure at being able to find the truth and share it.
Most pathologists choose their specialty, at least in part, because they like finding answers and like to share their acquired knowledge, which might be useful to the living (e.g. side effects of therapies, exposure to dangerous workplaces, sports).

"hic locus est ubi mors gaudet succurrere vitae"

this is the place where death rejoices to teach those who live

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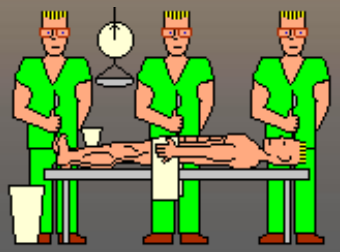

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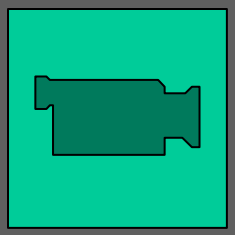

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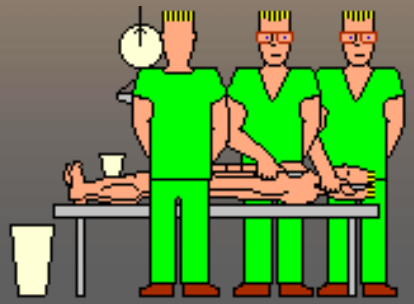
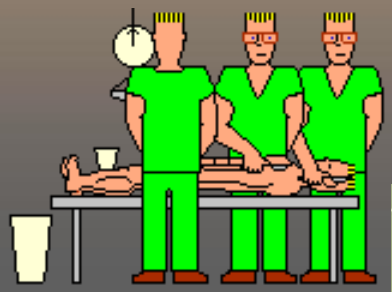


AUTOPSY

The pathologist first examines the outside of the body. A great deal can be learned in this way about the general health for instance

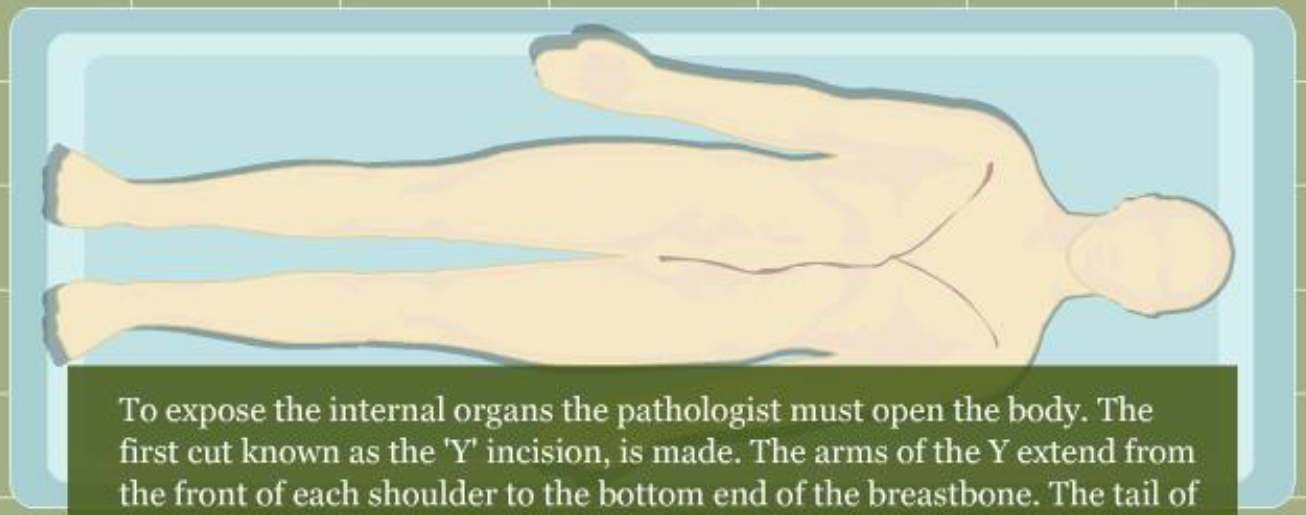
dead dog

Observations
Measuring
Recording
Describing



AUTOPSY

technique



To expose the internal organs the pathologist must open the body. The first cut known as the 'Y' incision, is made. The arms of the Y extend from the front of each shoulder to the bottom end of the breastbone. The tail of the Y extends from the sternum to the pubic bone and typically deviates to avoid the navel.

The incision is very deep, extending to the rib cage on the chest, and completely through the abdominal wall below that. The skin from this cut is peeled back, with the top flap pulled over the face.

Observation
Measuring
Recording

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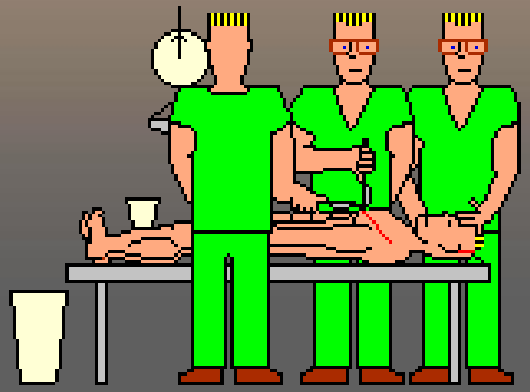

AUTOPSY

STANDARD PROCEDURES

The body is opened using a Y-shaped incision from shoulders to mid-chest and down to the pubic region. If the head is to be opened, the pathologist makes a second incision across the head, joining the bony prominences just below and behind the ears. When this is sewed back up, it will be concealed by the pillow on which the dead person's head rests.

The pathologist uses a scalpel for these incisions. There is almost no bleeding, since a dead body has no blood pressure except that produced by gravity.

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AUTOPSY

sometimes pathologists have to deal with curious bystanders who might not be respectful

L'image du martyr

Le 10 octobre 1967, le corps du Che est exposé à Vallegrande. Enterrée en secret, sa dépouille ne sera rapatriée et inhumée à Cuba qu'en 1997.

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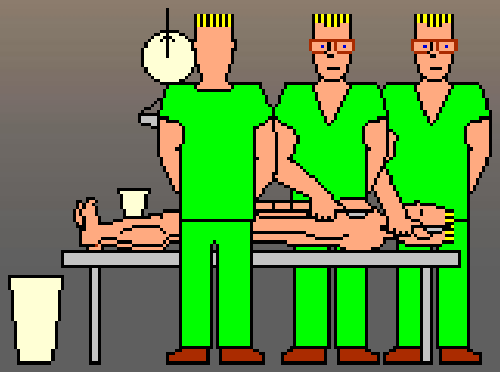
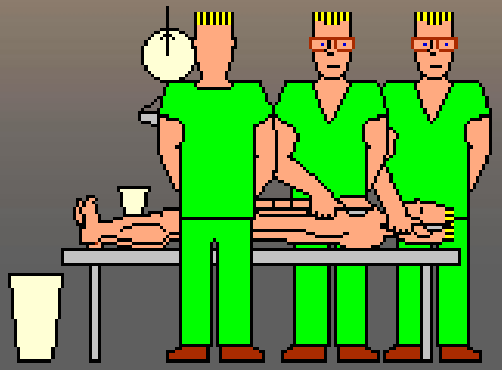


AUTOPSY / NECROPSY

The pathologist first examines the outside of the body. A great deal can be learned in this way.

Observations
Measuring
Recording

on location there would be additional information available



AUTOPSY

Observations
Measuring
Recording
sometimes there is clear evidence

rarely

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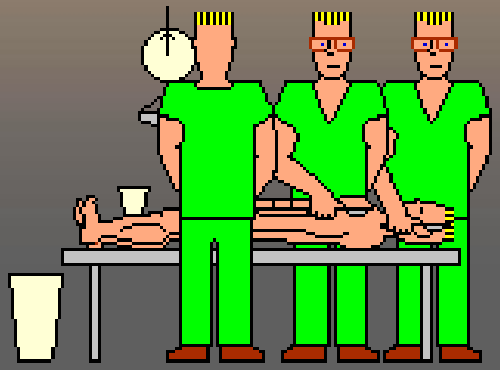

AUTOPSY

The pathologist first examines the outside of the body. A great deal can be learned in this way.

Observations
Measuring
Recording

clear evidence for the cause of death

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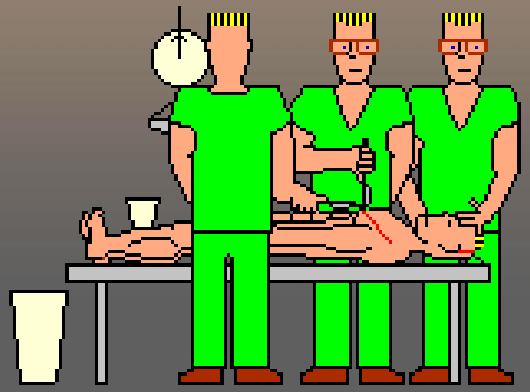
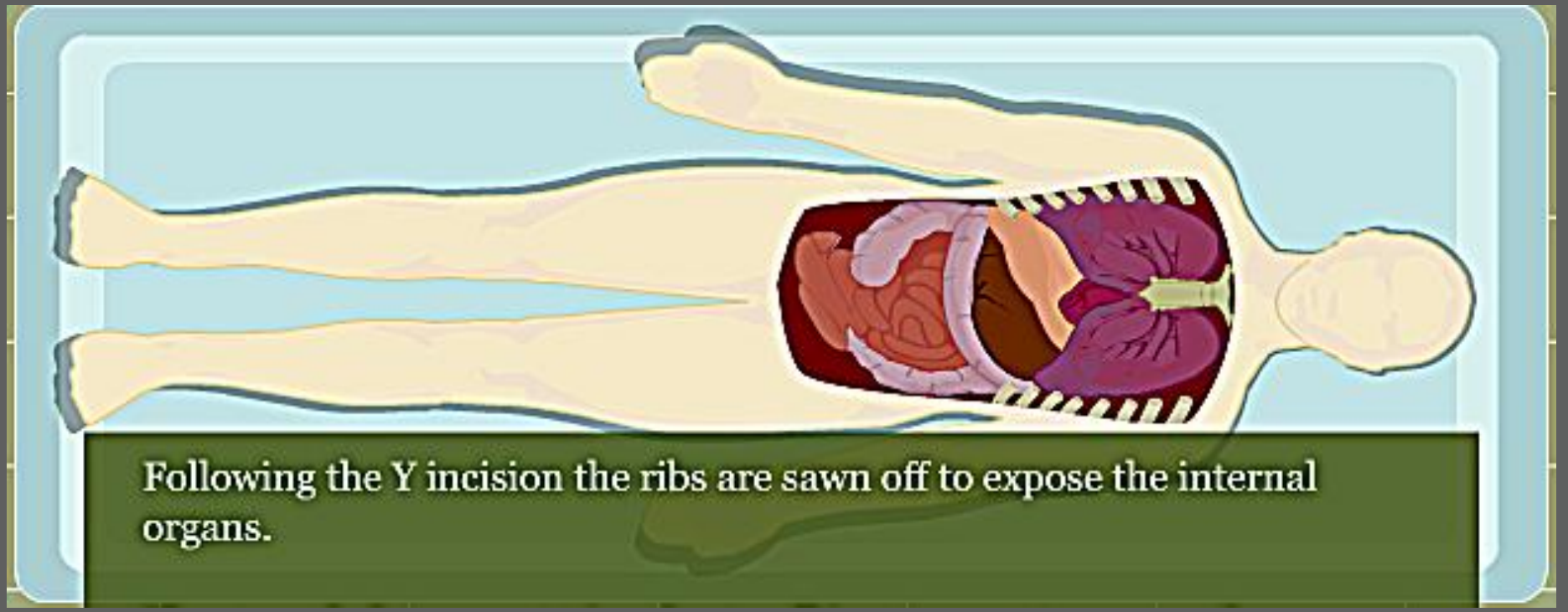
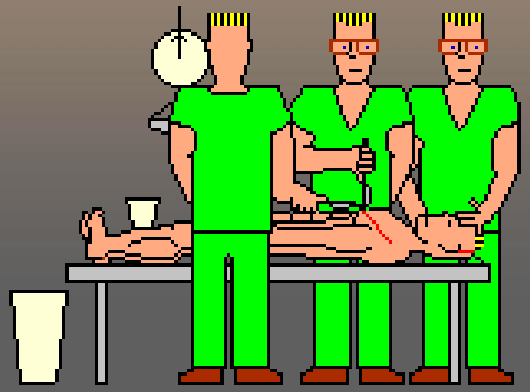


AUTOPSY


Following the Y incision the ribs are sawn off to expose the internal organs.



AUTOPSY

Each pathology service has its own autopsy technique. The most common way to remove the organs is known as the Rokitansky method - removing the body organs all at once. That is, the heart, lungs, liver, kidneys and spleen etc are removed in one block and then dissected on the autopsy table.

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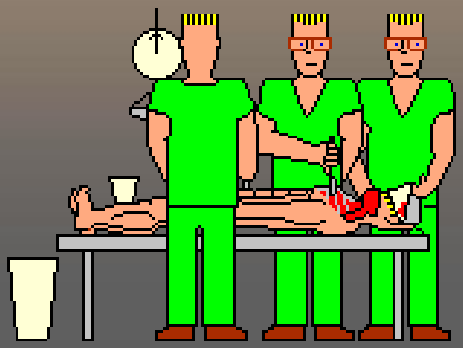
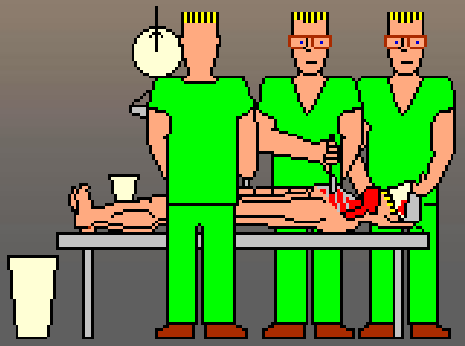


AUTOPSY

The incisions are carried down to the rib cage and breastbone, and the cavity which contains the organs of the abdomen. The soft tissues in front of the chest are then reflected back. Again, the pathologist looks around for any abnormalities.

There is a great deal to be learned from touch also



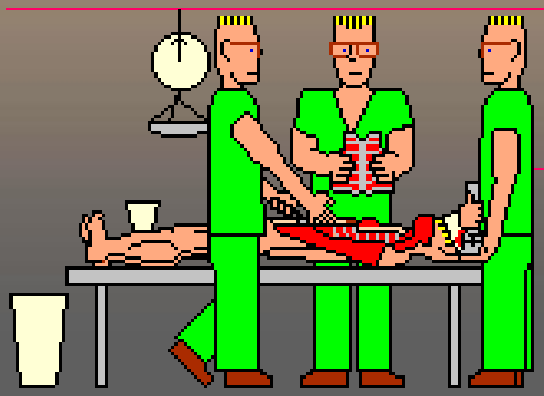
AUTOPSY

The soft tissues, skin in front of the chest are then reflected back. Again, the pathologist looks around for any abnormalities.

COLOR is important

discoloration of fat in subcutaneous tissue

GP



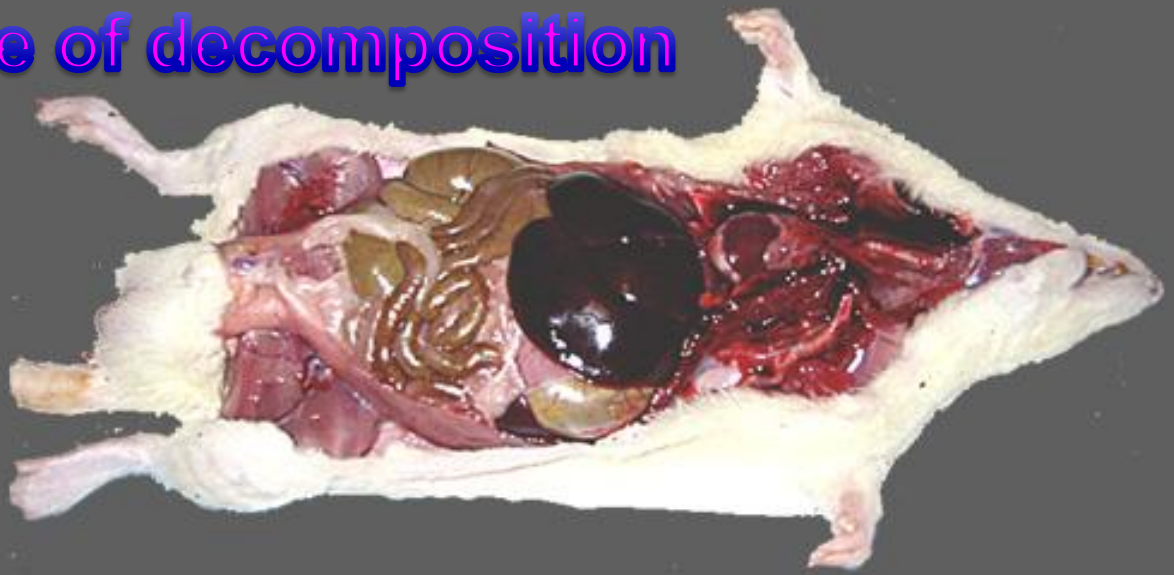
AUTOPSY

When the breastbone and attached rib cartilages are removed, they are examined (sometimes they are fractured during cardiopulmonary resuscitation)

Freeing up the intestine takes some time.

smell

stage of decomposition



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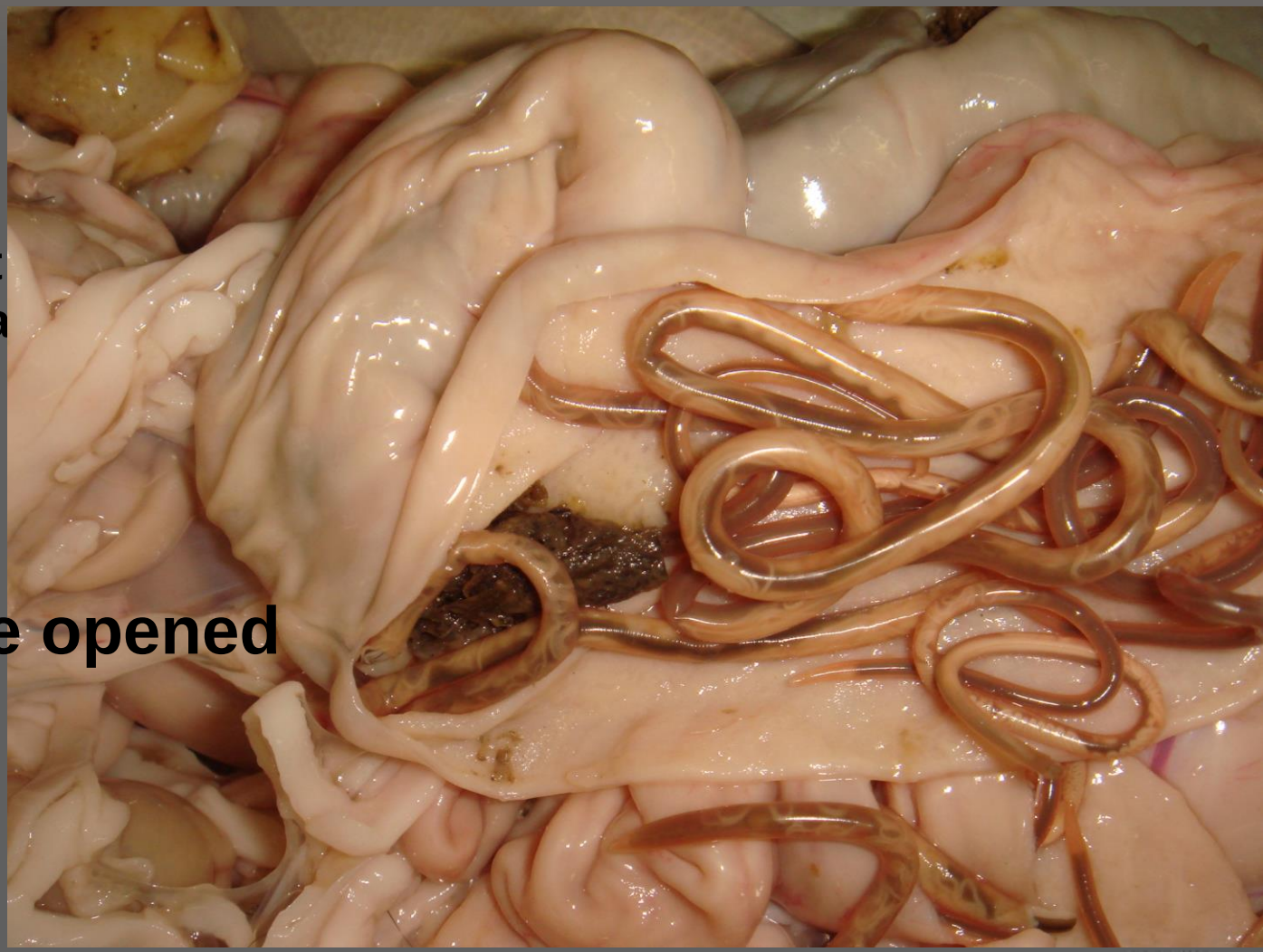
opening the abdomen reveals not only organs but also fluids, colored or not

AUTOPSY

organs are laid out
for further examina

intestines are opened



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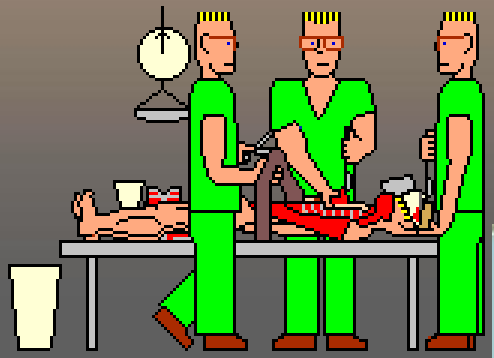
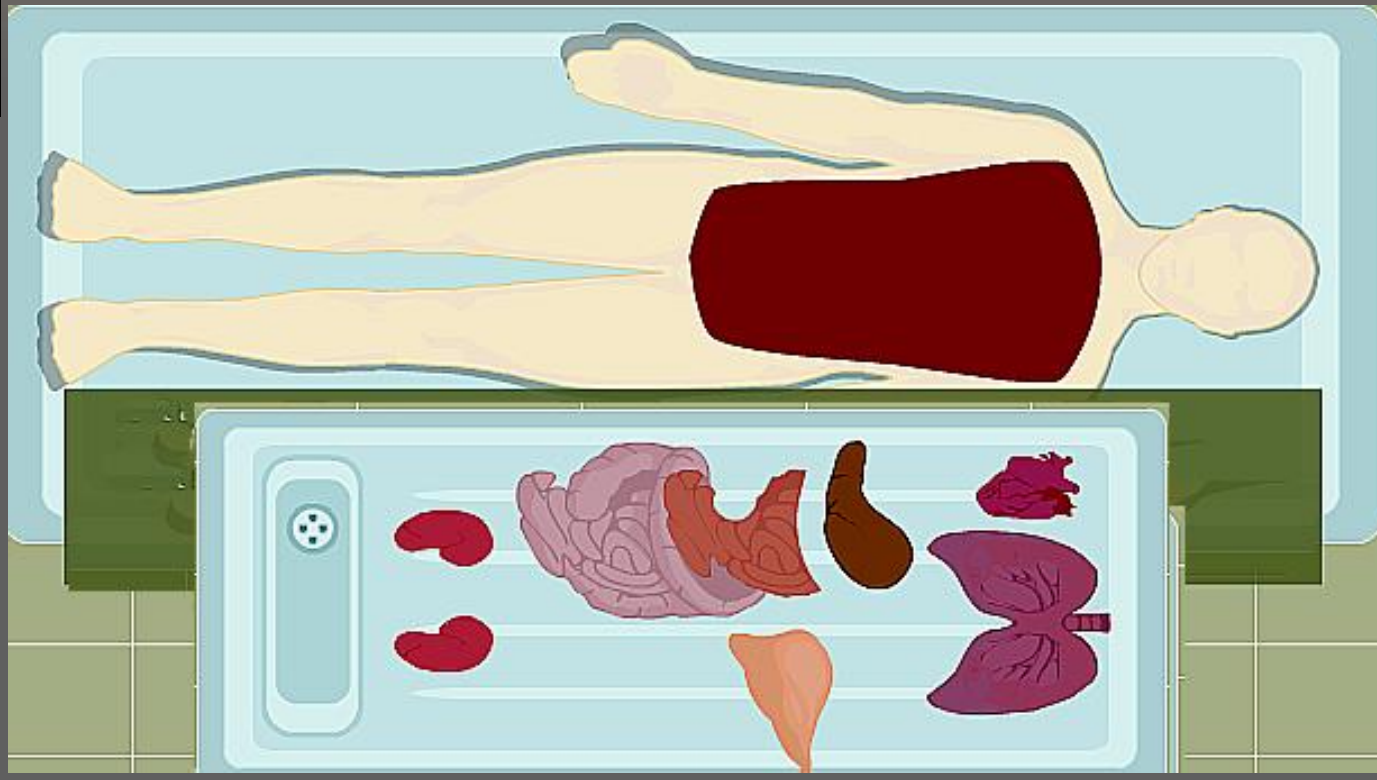


AUTOPSY

organs are laid out
for further examination



The chest organs, including the heart and lungs, are inspected. Sometimes the pathologist takes blood from the heart to check for bacteria, toxins etc. in the blood. Even the fluid in the eye can be analysed.

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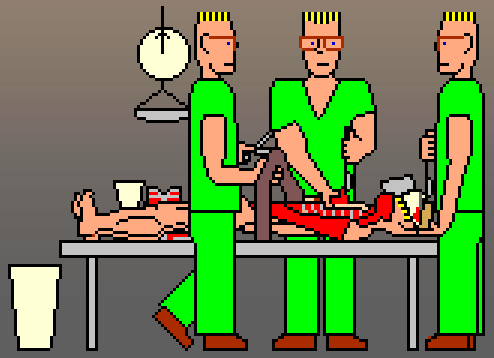

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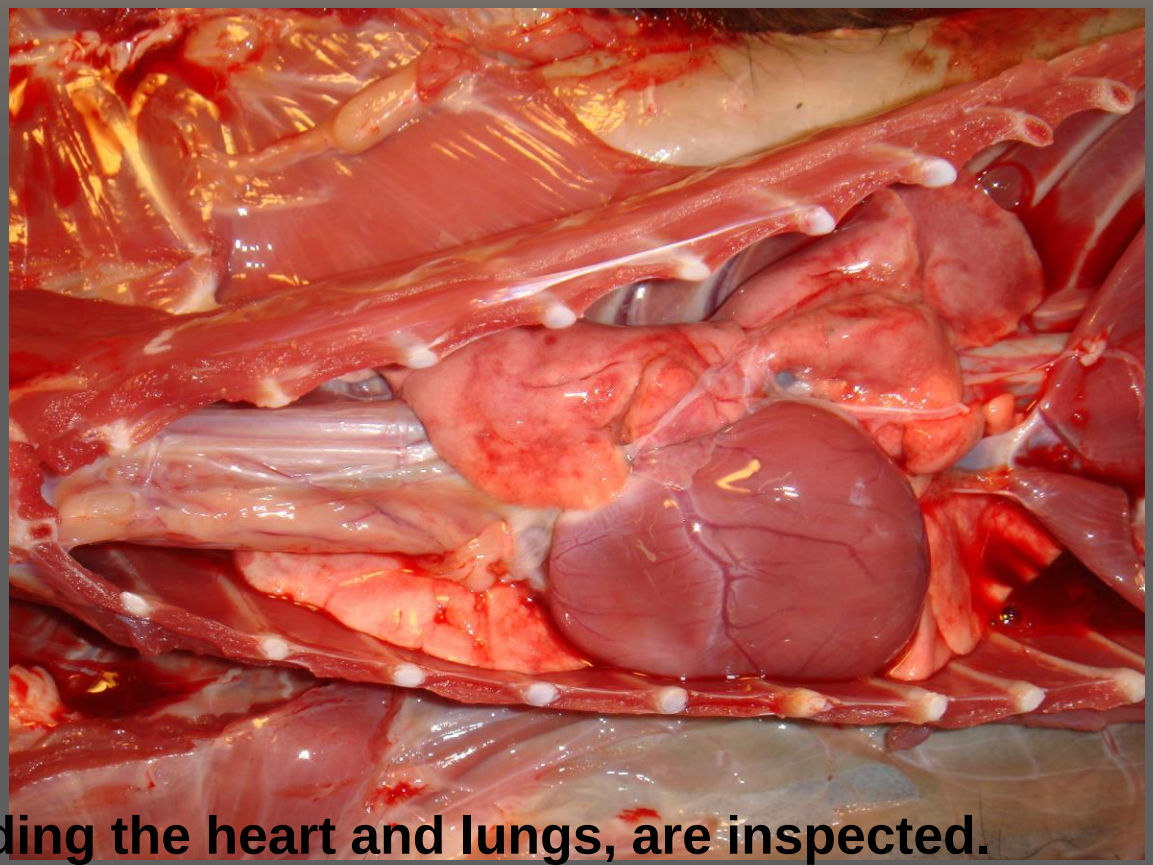

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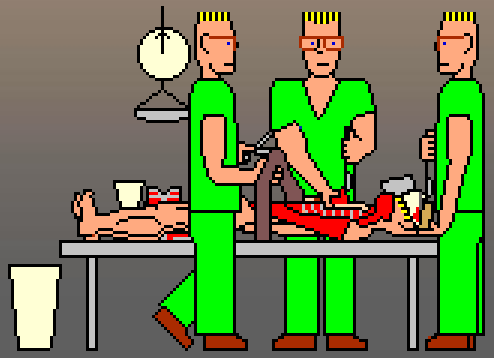

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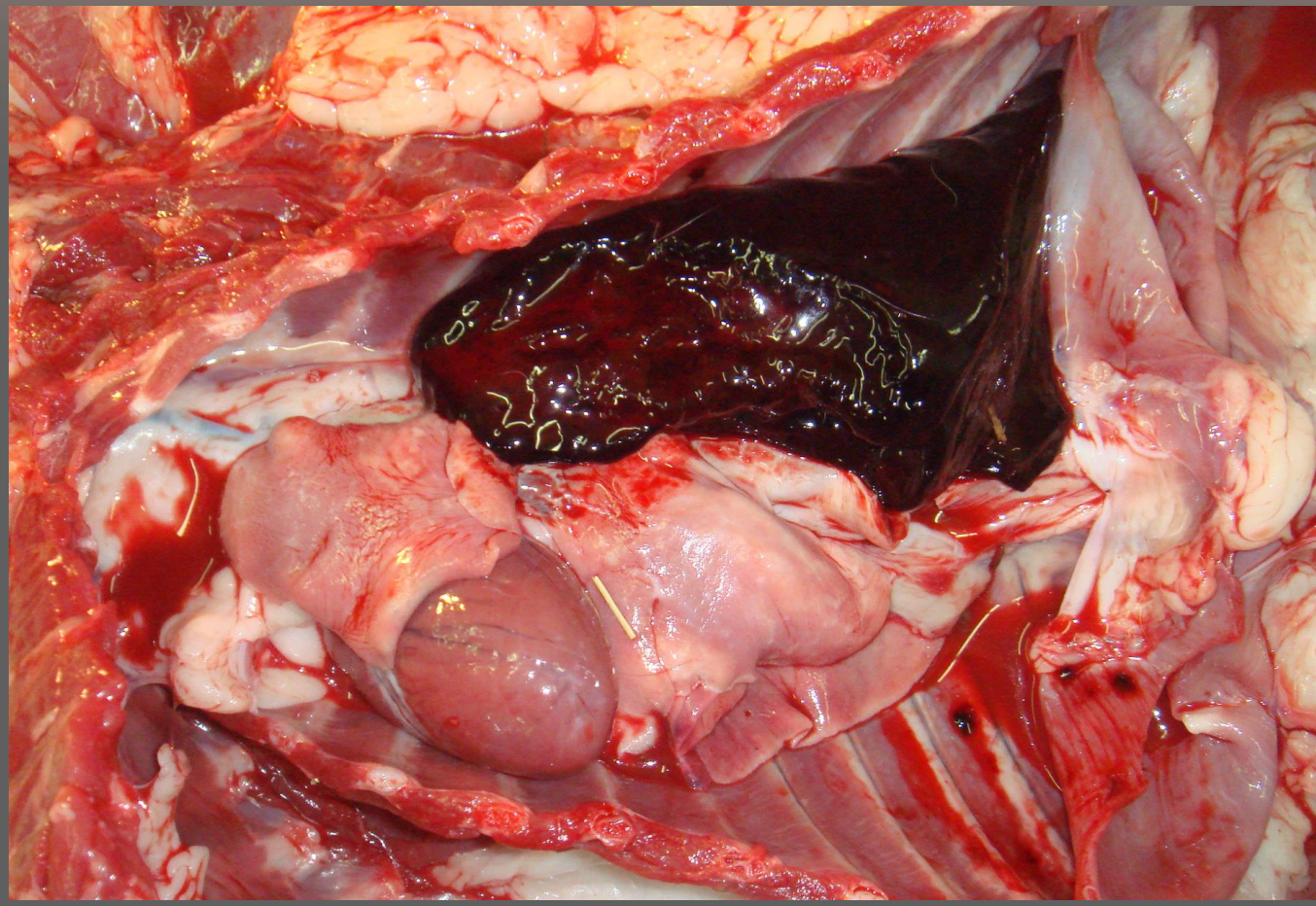

The chest organs, including the heart and lungs, and chest fluid are inspected.

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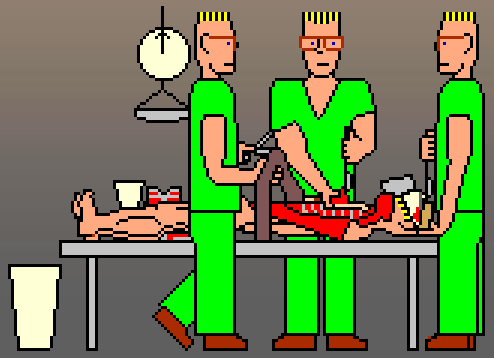
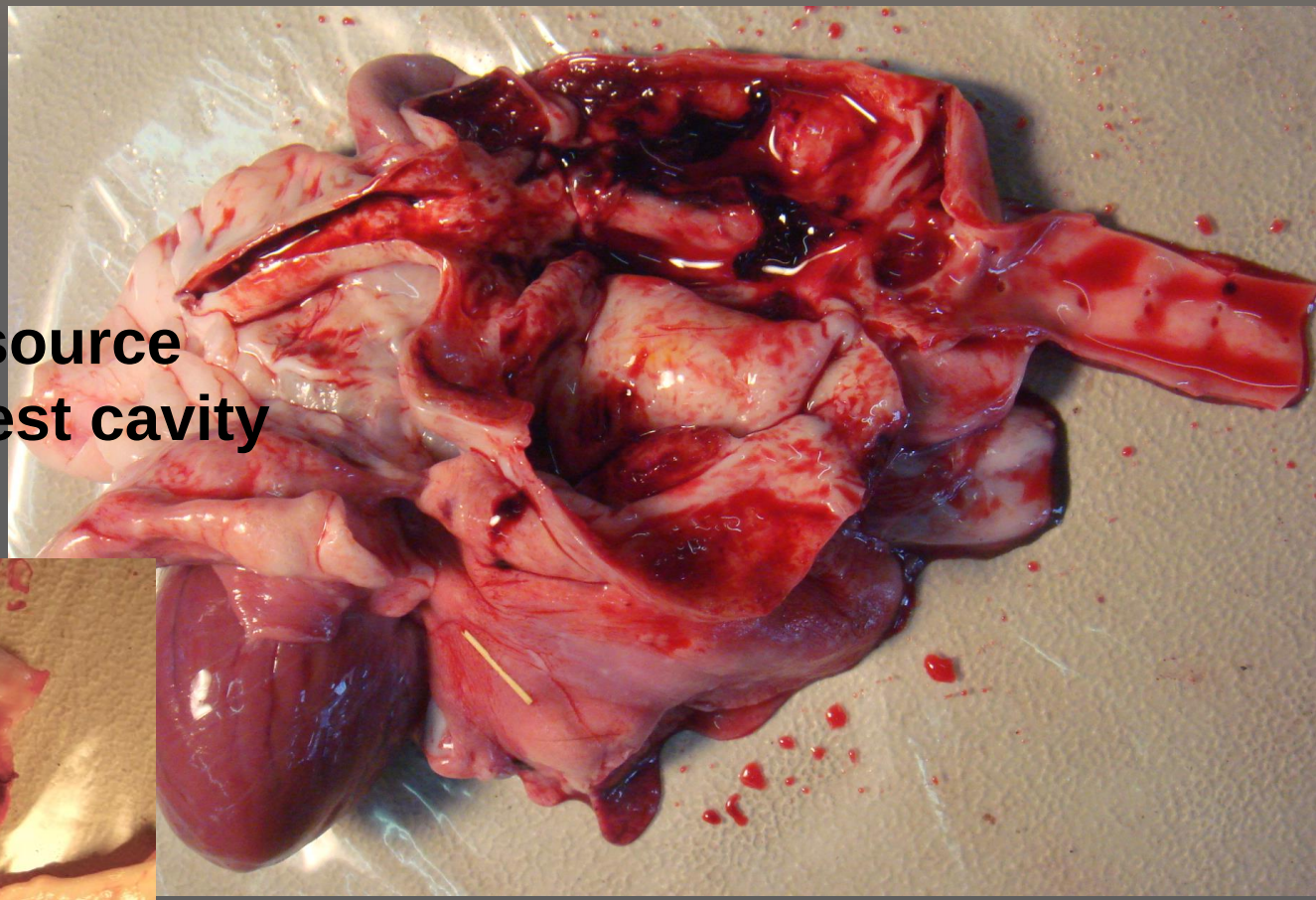
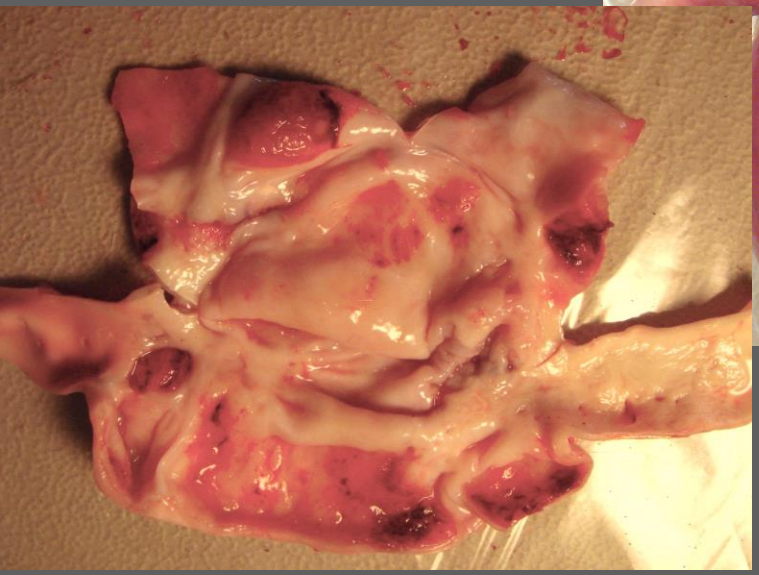


AUTOPSY

investigating the source of blood in the chest cavity





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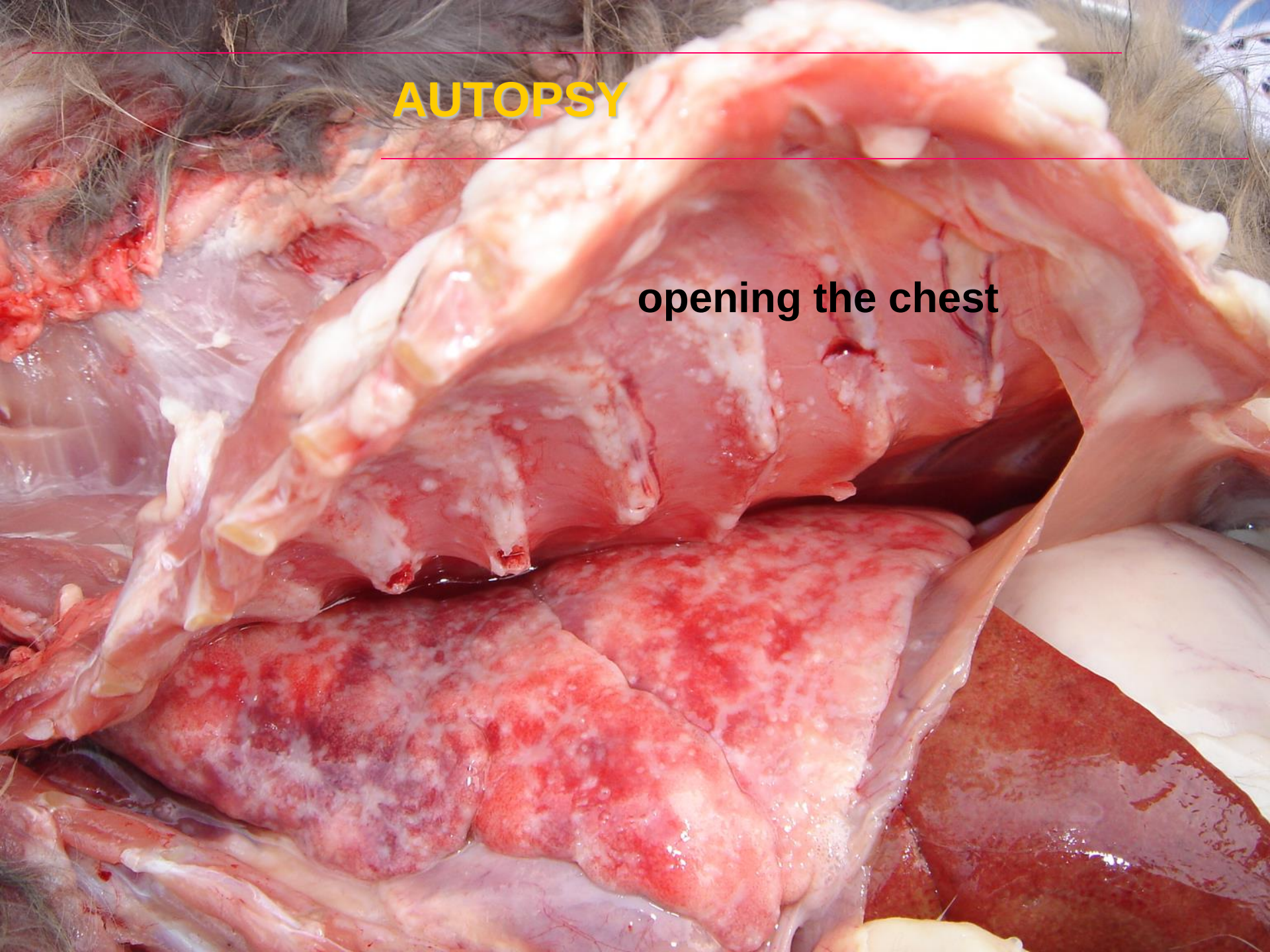
AUTOPSY



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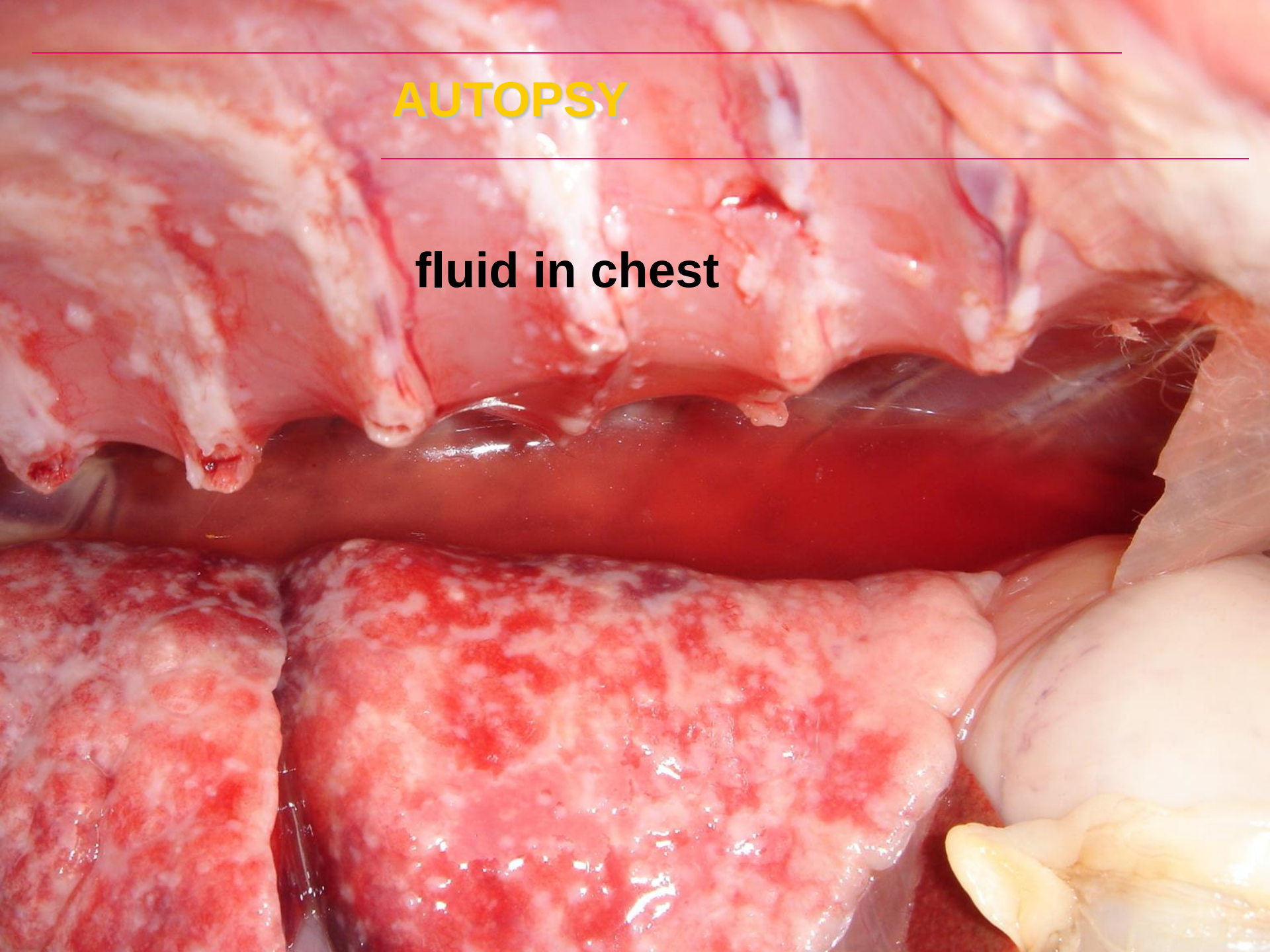
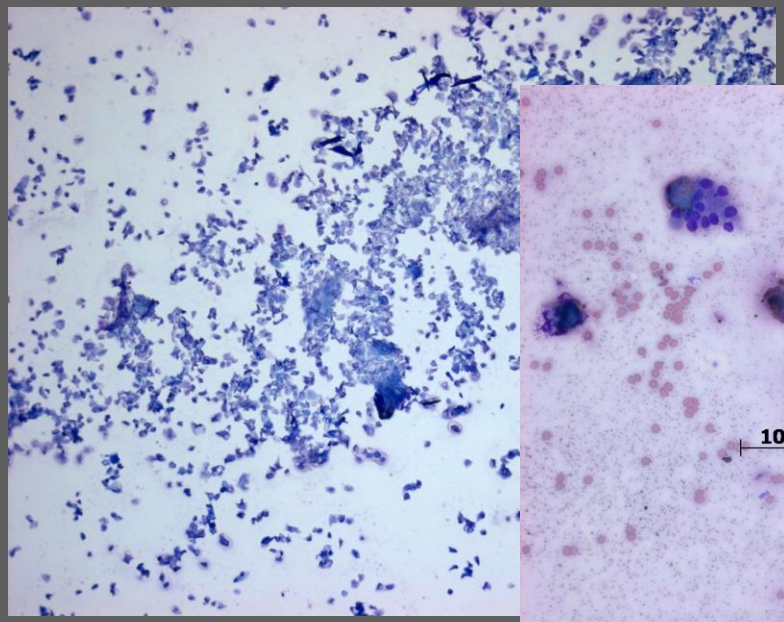
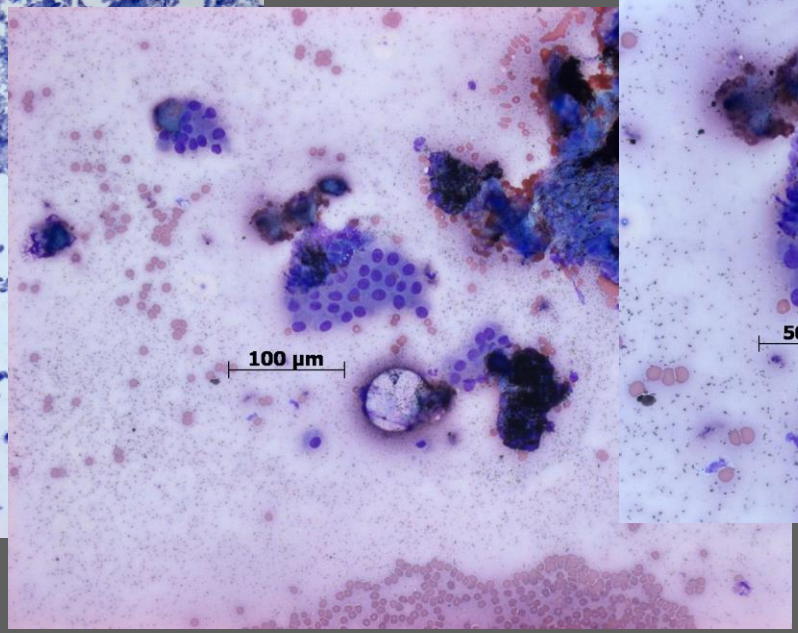


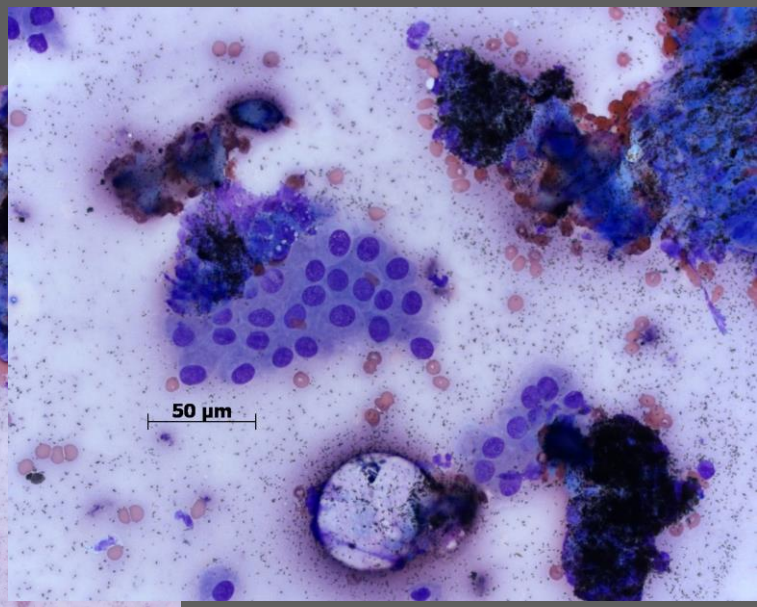
PATHOLOGY and LABORATORY MEDICINE

clinical and *ante mortem post mortem*

- needle aspirates, biopsies
- clinical pathology : haematology, blood chemistry
- intra-operative surgical pathology







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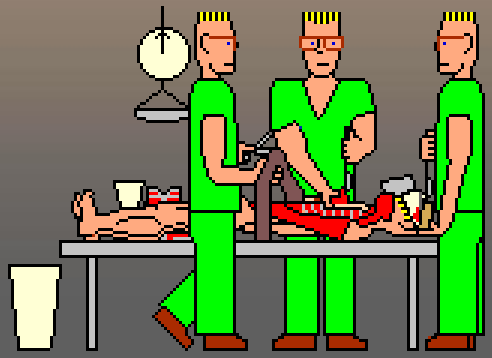
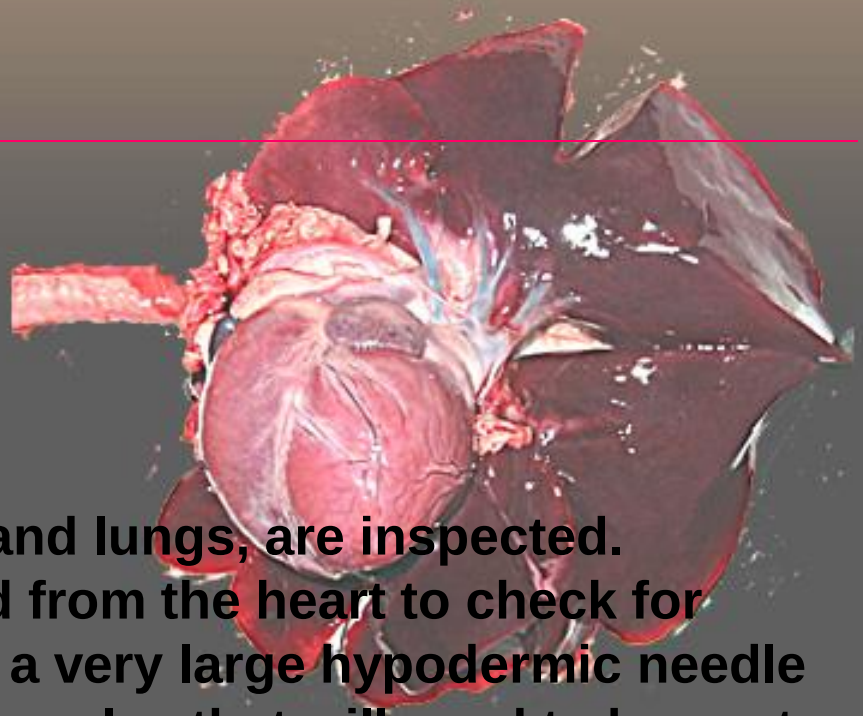


AUTOPSY



The chest organs, including the heart and lungs, are inspected. Sometimes the pathologist takes blood from the heart to check for bacteria in the blood. For this, he uses a very large hypodermic needle and syringe. He may also find something else that will need to be sent to the microbiology lab to search for infection. Sometimes the pathologist will send blood, urine, bile, or even the fluid of the eye for chemical study and to look for medicine, street drugs, alcohols, and/or poisons.

Then the pathologist must decide in what order to perform the rest of the autopsy. The choice will be based on a variety of considerations.

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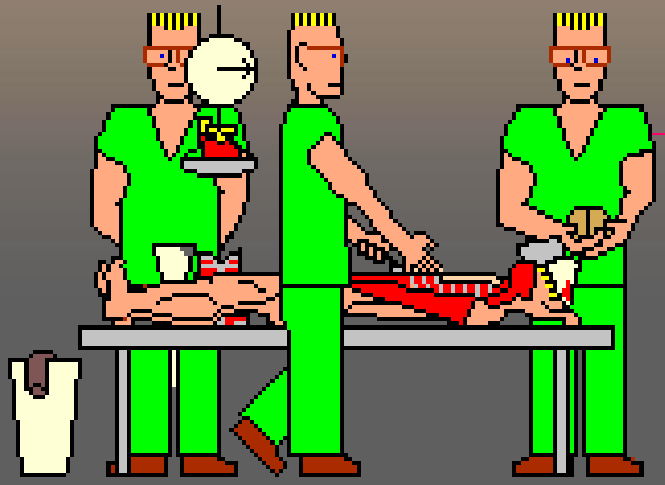
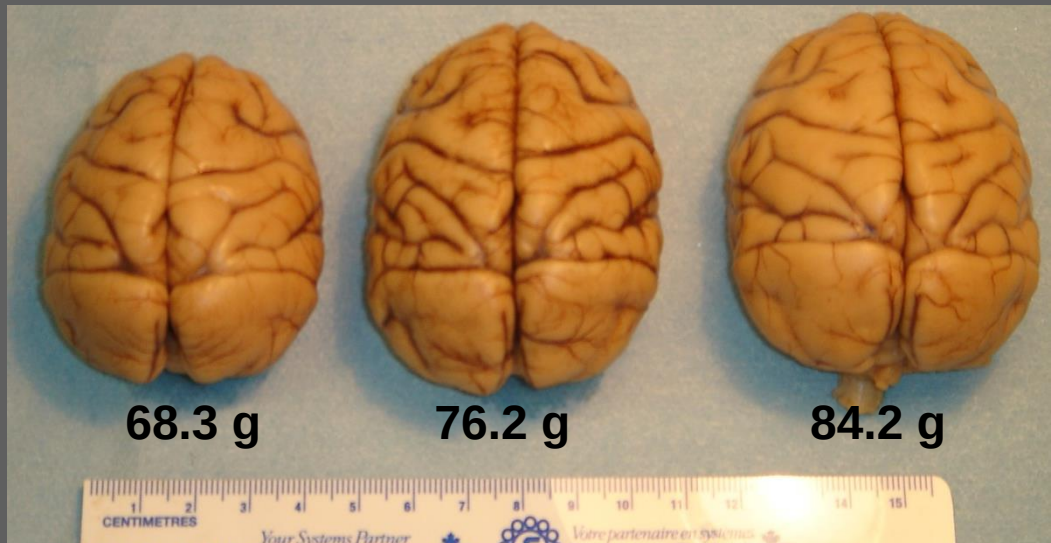


AUTOPSY

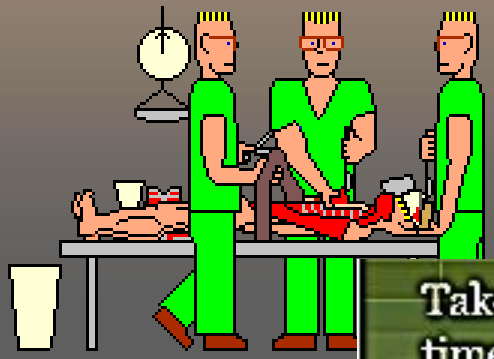
The pathologist weighs the major solid organs (heart, lung, brain, kidney, liver, spleen, sometimes others) on a grocer's scale. The smaller organs (thyroid, adrenals) get weighed on a chemist's triple-beam balance. The next step in this abdominal dissection will be exploring the bile ducts and then freeing up the liver.

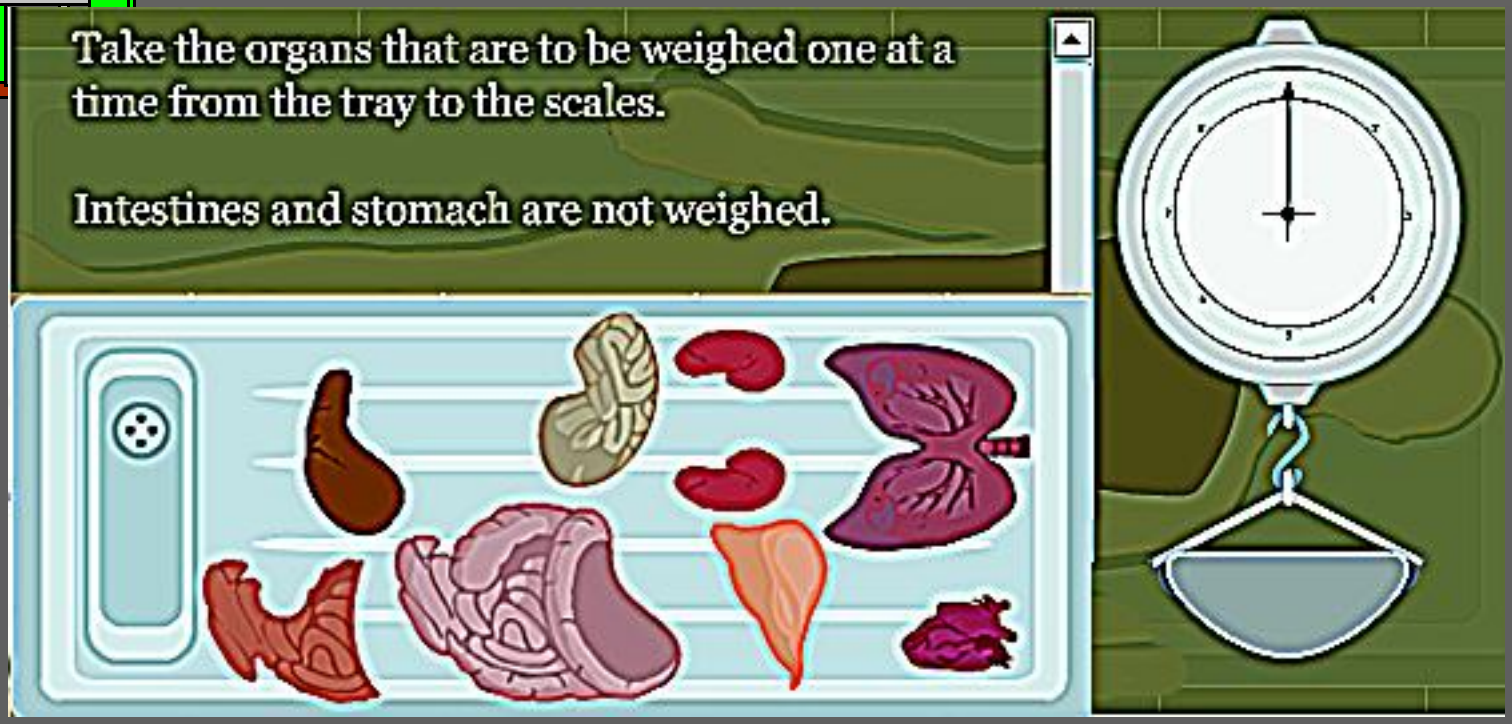
for humans
there are tables with average weights of organs according to age, sex etc.

there are some difficulties to find tables for animals



AUTOPSY





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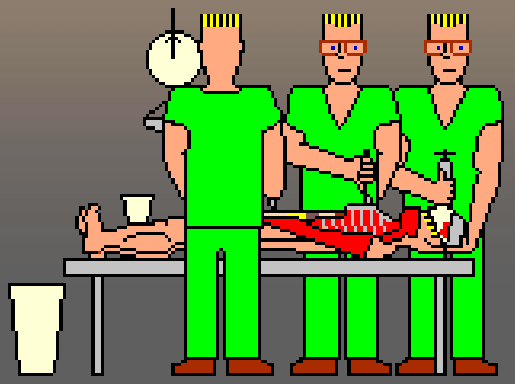
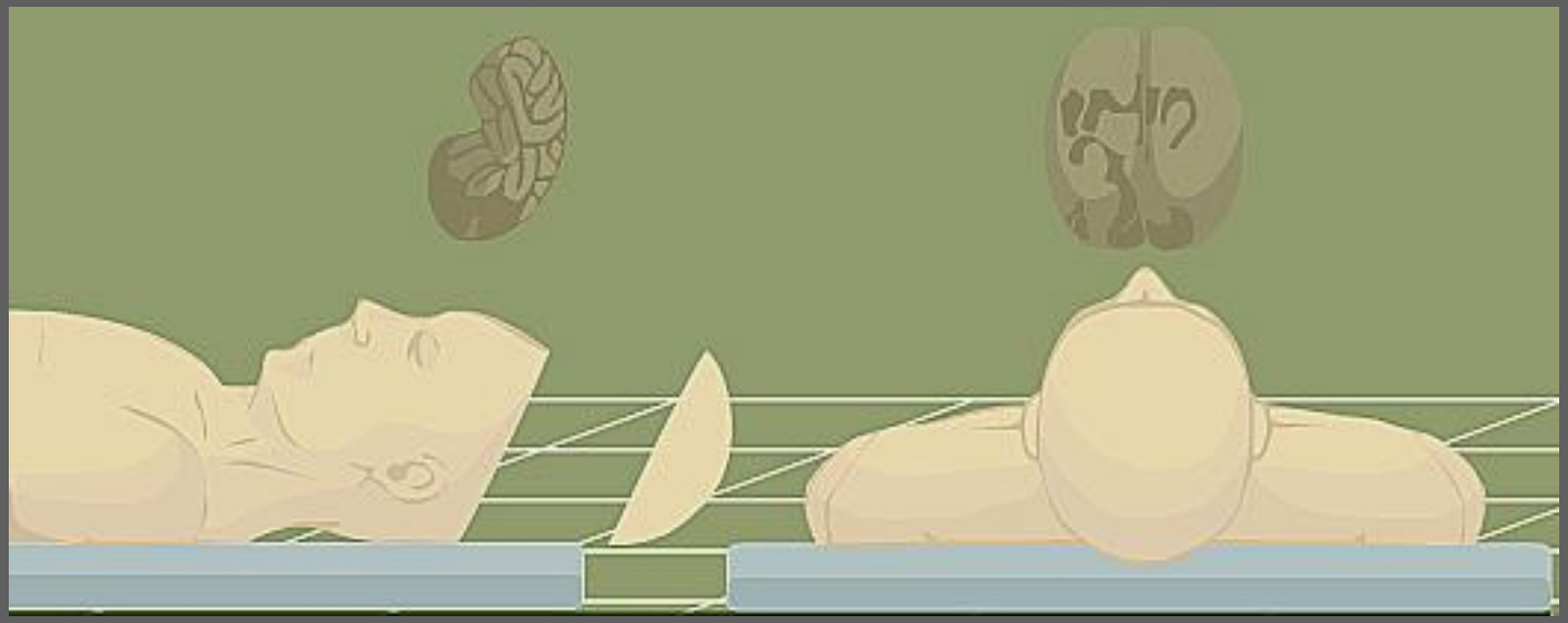


AUTOPSY

To open the skull a special vibrating saw is used that cuts bone but not soft tissue. This is an important safety feature.



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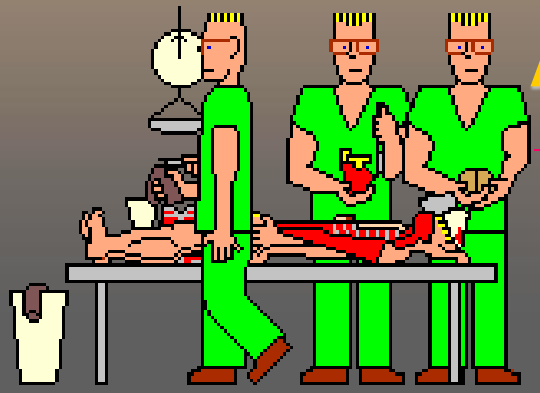
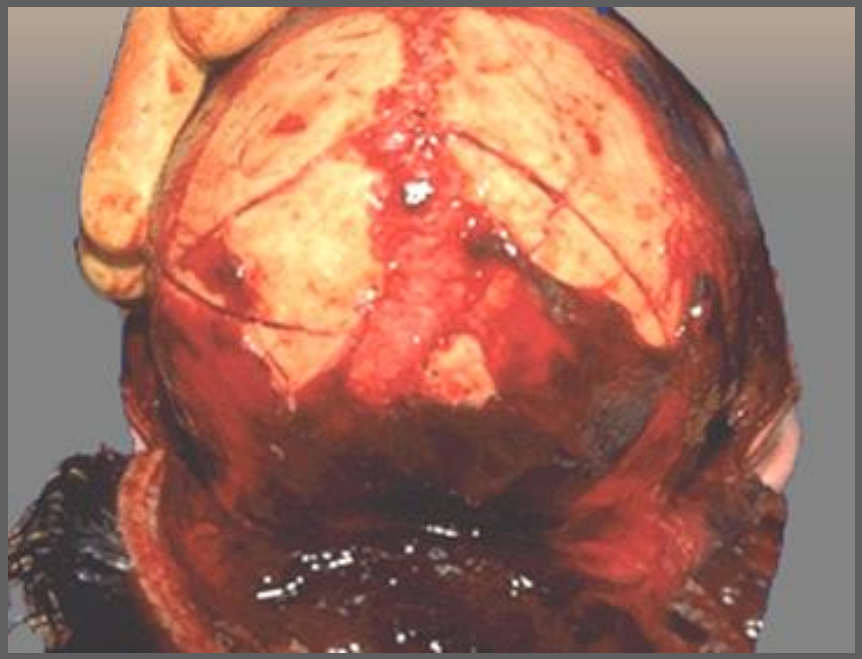
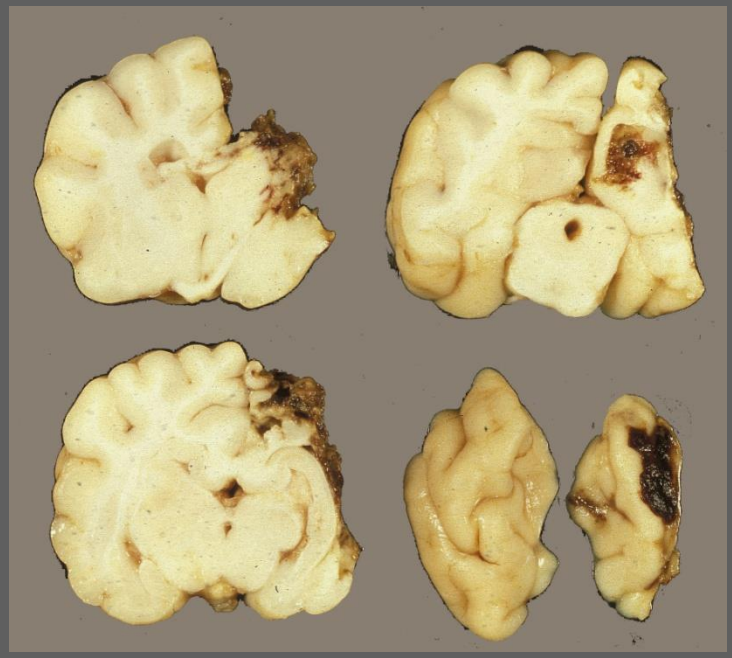


AUTOPSY

Inspecting the brain often reveals surprises. A good pathologist takes some time to do this.





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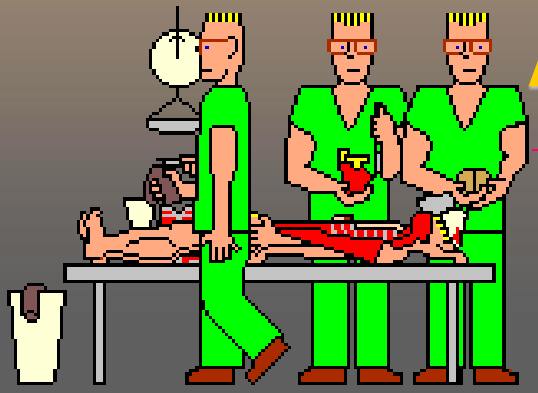
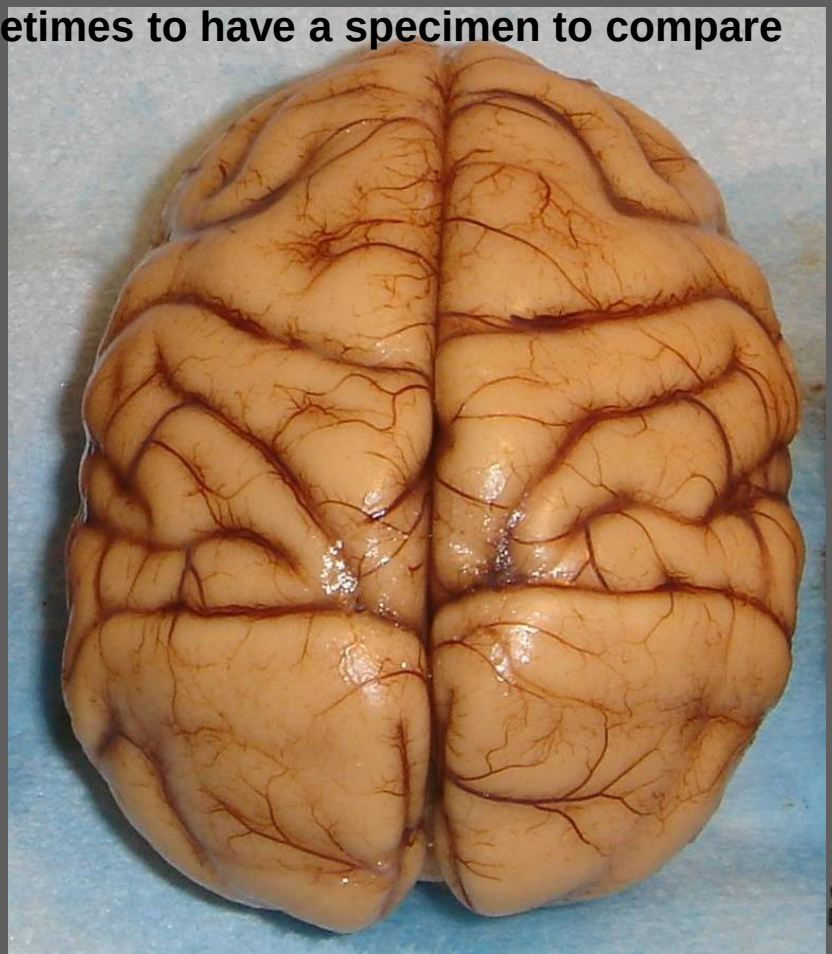


AUTOPSY

Inspecting the brain often reveals surprises. A good pathologist takes some time to do this.

it is good sometimes to have a specimen to compare



GP

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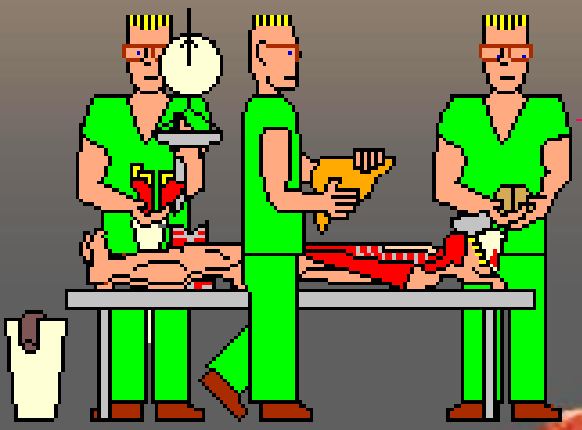

AUTOPSY

The liver has been removed. The pathologist has found something important. It appears that this man had a fatty liver. It is too light, too orange, and a bit too big. Perhaps this man had been drinking heavily for a while.

Check notes / clinical observations / patient history

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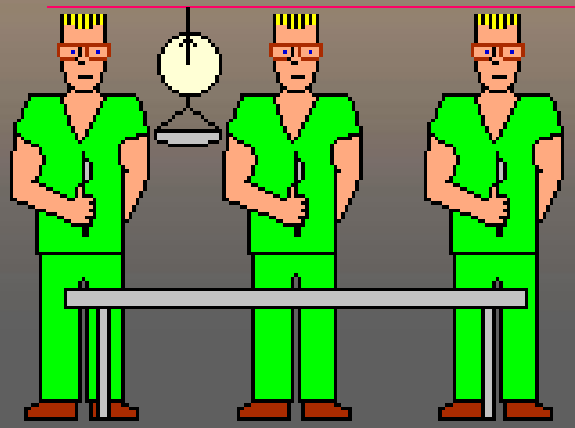

AUTOPSY

if the only finding in this imaginary autopsy was fatty liver.

There are several ways in which heavy drinking, without any other disease, can kill a person. The pathologists will rule each of these in or out, and will probably be able to give a single answer to the police or family.

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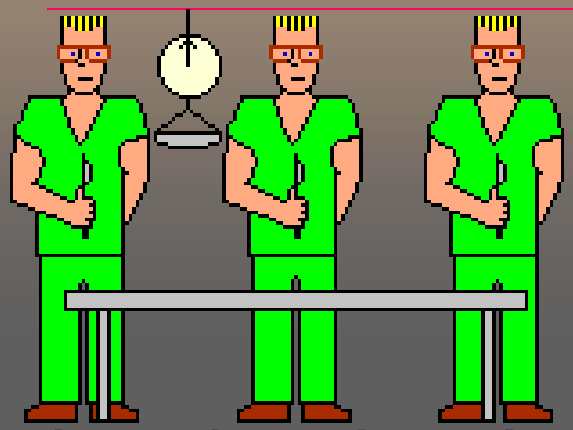
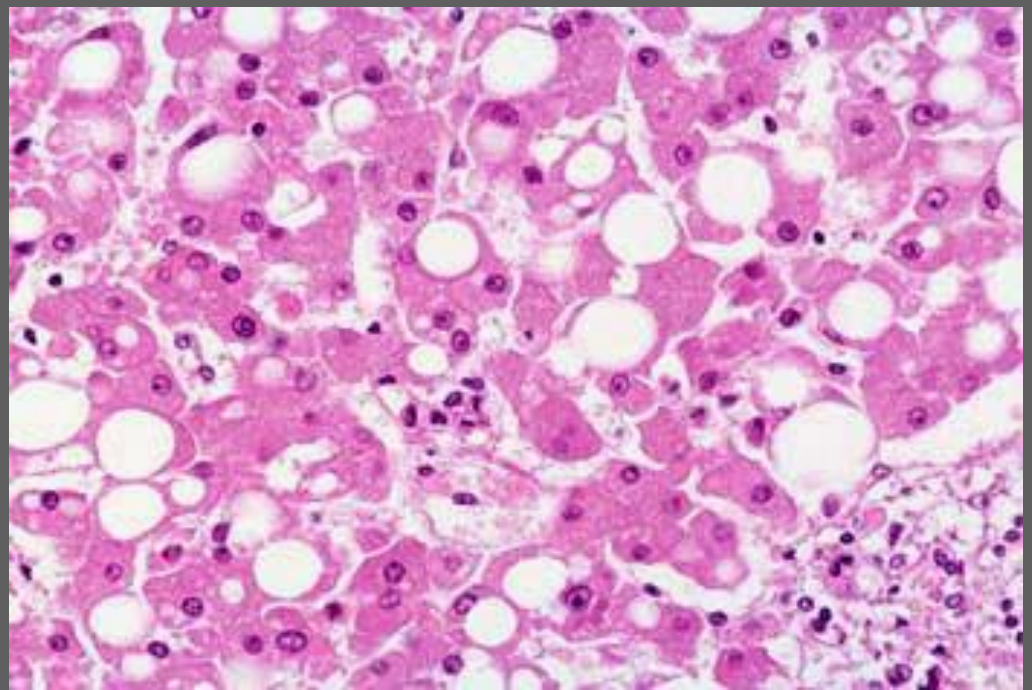


AUTOPSY

These sketches do not show all the steps of an autopsy, but will give you the general idea.

The pathologists will submit the tissue they saved to the histology lab tomorrow (after fixation), to be made into microscopic slides (within days). When these are ready, they will examine the sections (under the microscope), look at the results of any lab work, and draw their final conclusions.



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AUTOPSY

The lungs are almost never normal at autopsy. The pathologist will inspect and feel them for areas of pneumonia and other abnormalities.

The pathologist weighs both sides of the lungs together, then each one separately. Afterwards, the lungs may get inflated with fixative.

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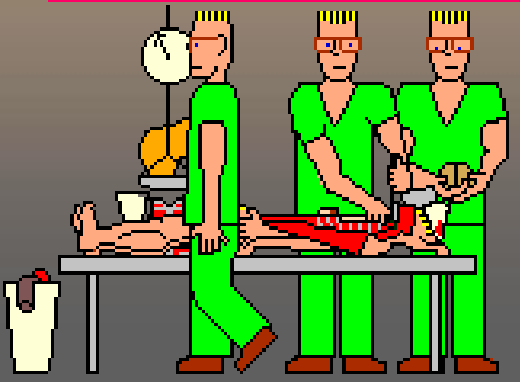
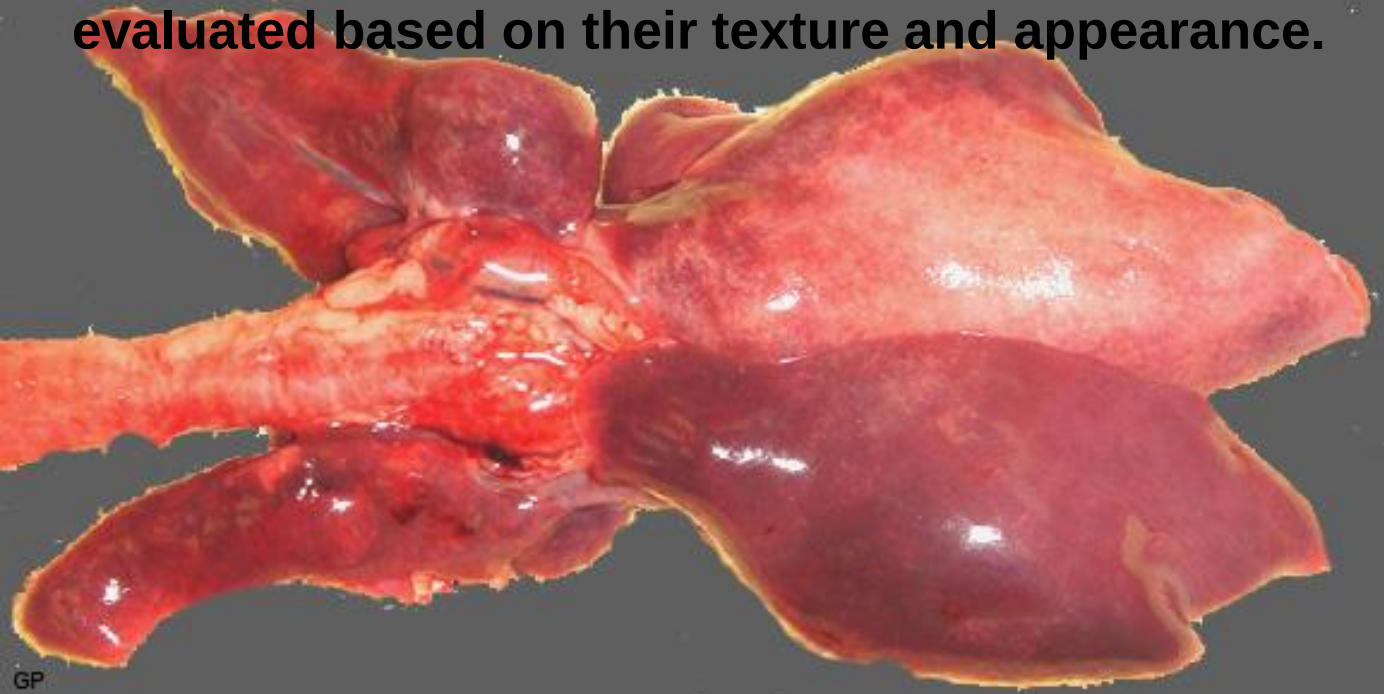


AUTOPSY

Dissecting the lungs can be done in any of several ways. All methods reveal the surfaces of the large airways, and the great arteries of the lungs. Most pathologists use the long knife again while studying the lungs. The air spaces of the lungs will be evaluated based on their texture and appearance.



GP

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AUTOPSY

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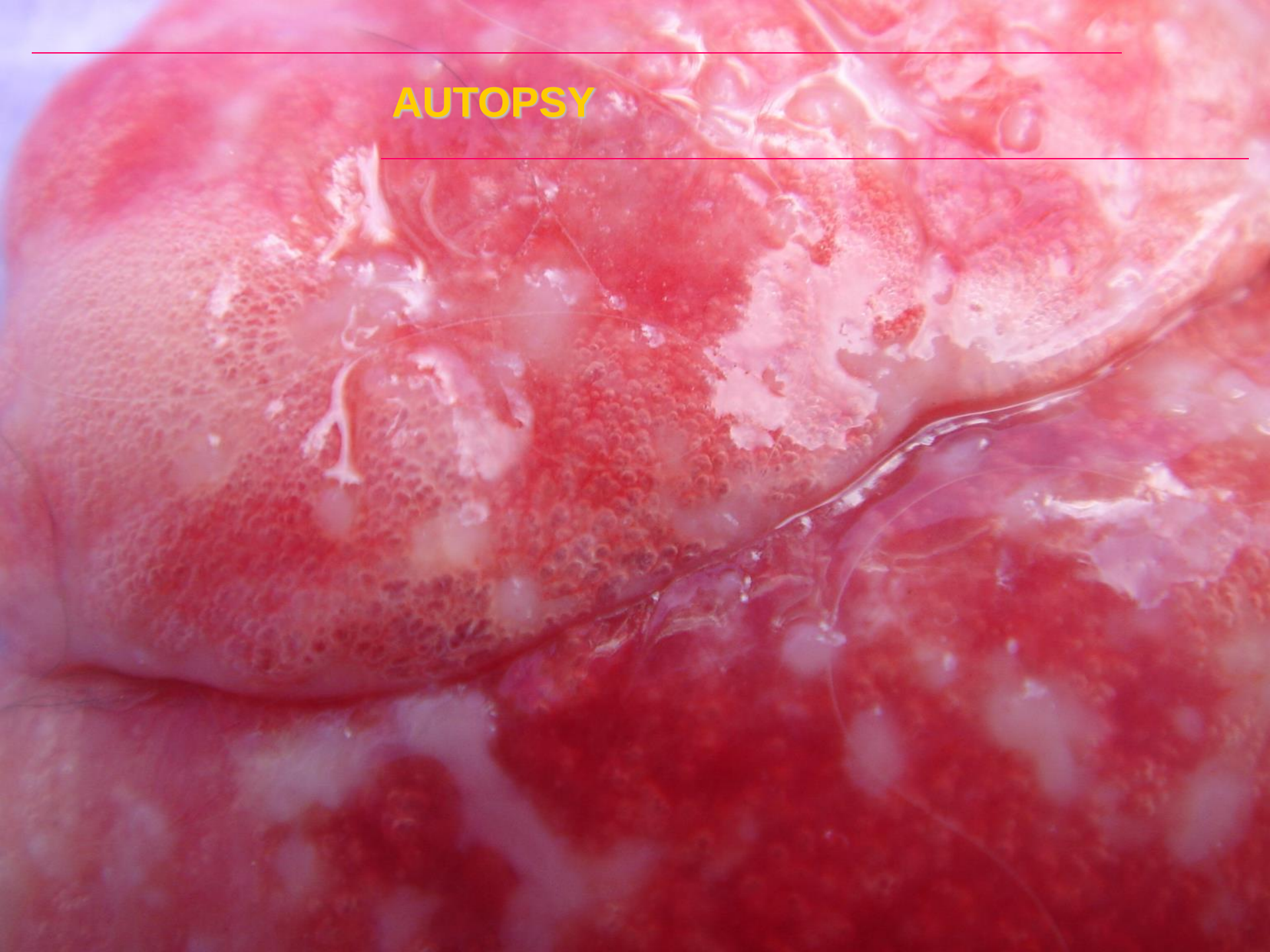
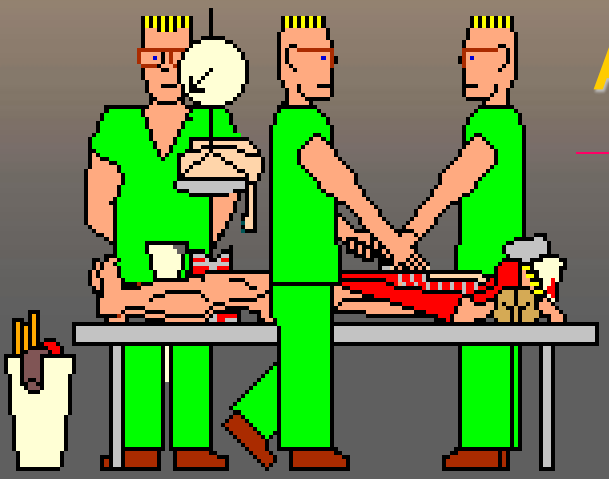
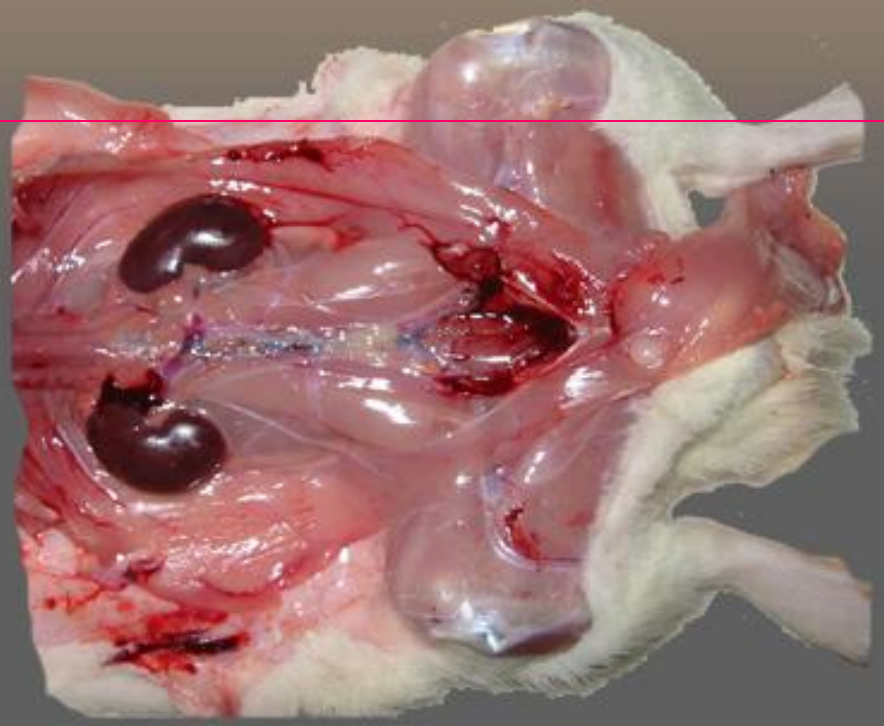
AUTOPSY





AUTOPSY



The rest of the team is continuing with the removal of the other organs. They have decided to take the urinary system as one piece, and the digestive system down to the small intestine as another single piece. This will require careful dissection.

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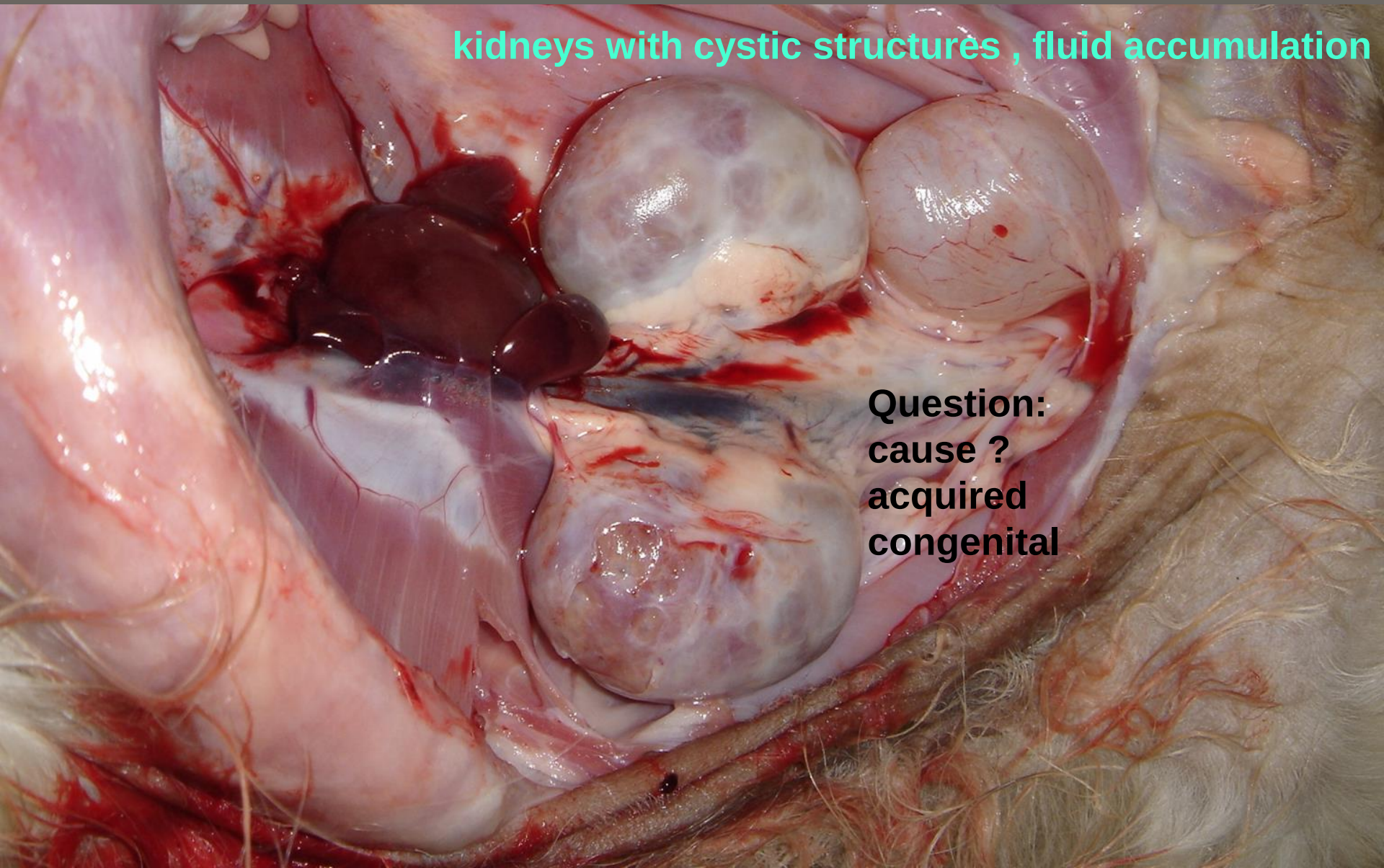
AUTOPSY


kidneys with cystic structures , fluid accumulation
Question:
cause ?
acquired
congenital

AUTOPSY

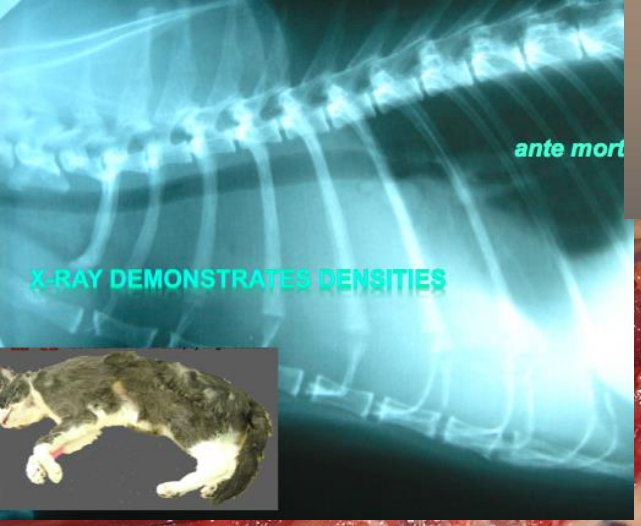
ante mortem X-Ray

X-RAY DEMONSTRATES DENSITIES

AUTOPSY

entire body laid out for study

AUTOPSY



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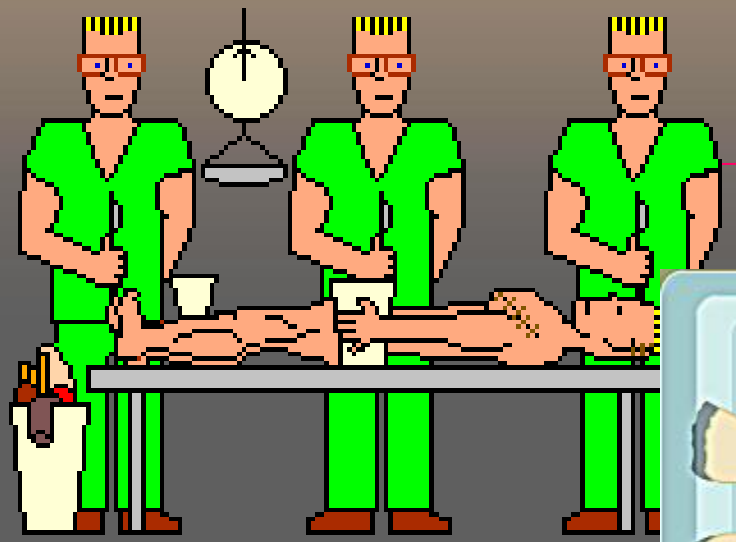

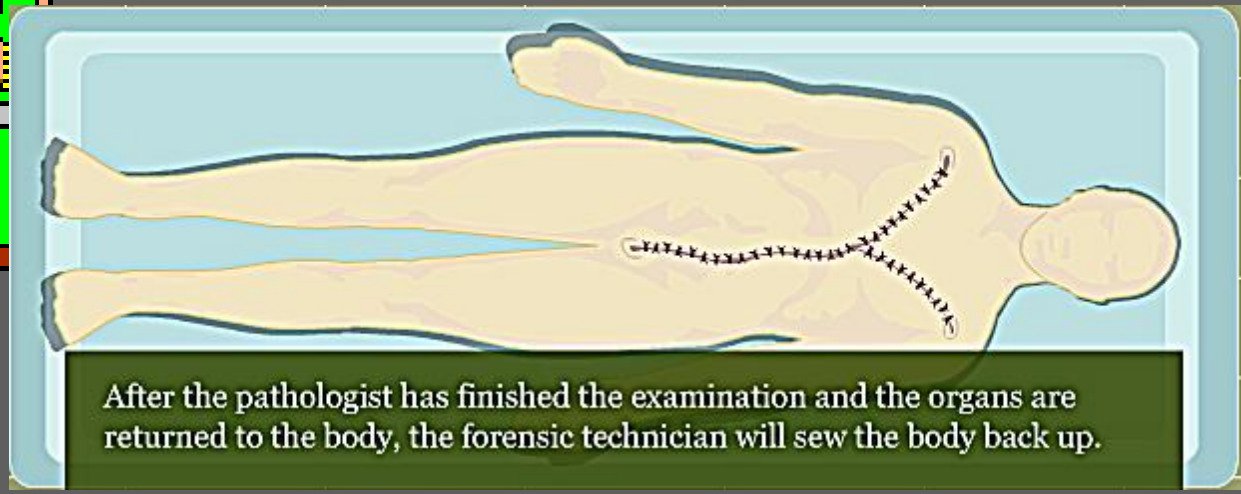

When the internal organs, have been examined, the pathologist may return all but the portions they have saved to the body cavity. Or the organs may be cremated without being returned. The appropriate laws, and the wishes of the family, are obeyed. The breastbone and ribs are usually replaced in the body. The skull and trunk incisions are sewed shut ("baseball stitch"). The body is washed and is then ready to go to the funeral director

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AUTOPSY

A final report of a study pathologist is usually reviewed by other pathologists.
Often this is called a peer review.
Samples are kept to allow other pathologists to go back and look at specimens again

Importance of review
Importance of good recording
Documentation
Justification of diagnosis (differential diagnosis)

Discussion with colleagues

this shows you the importance of being connected and not working alone

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AUTOPSY

importance of critical differential diagnosis

pathologist should not work in isolation

always look for second opinion

and
do they ever have opinions !

here is an example for illustration

AUTOPSY

Man's 'nightmare' ends after Crown finds pathologist erred

Charges dropped; wife wasn't strangled, she drowned in pool

BY JAKE RUPERT

An Ottawa man's 2½-year "nightmare" ended yesterday when the Crown abruptly halted its prosecution of him on charges of killing his wife.

New evidence showed that [redacted], 52, had accidentally drowned, and had not been strangled, as a pathologist had first declared. The move left [redacted], 57, who has always maintained his innocence, emotional and speechless.

"He can't talk right now," said Mr. [redacted]'s lawyer, Michael Edelson. "It's been horrific for him and his family. It's really been a nightmare."

On Aug. 13, 2003, at about 9 p.m., Mr. [redacted] found his wife face down in the pool in the backyard of their Gloucester home. Police initially said they thought Mrs [redacted] drowned. But two days later, Mr [redacted], a bar manager, was arrested and charged with second-degree murder. The forensic pathologist that conducted the autopsy, Dr. [redacted], decided Mrs. [redacted] had died of strangulation.

See DEATH on PAGE A2

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ARTS
ASTROLOG
BUSINESS
CELEBRAT

AUTOPSY

SATURDAY, DECEMBER 3, 2005

NEWS

Death: 'A rush to judgment'

Continued from PAGE A1

The development shocked the family, and Mr. Edelson retained another pathologist to do a second autopsy on Mrs. body. That pathologist determined the cause of death was drowning.

A month later, Mr. , who had no previous criminal record, was released on bail to live with his daughter.

At a preliminary hearing, evidence showed Mrs. had been drinking heavily that night and was taking painkillers. She was outside, by the pool, speaking to a friend on the telephone, while her husband was inside eating, and a boarder was in the basement.

The woman she was talking to told police Mrs. said she needed to put down the phone to fix something in the pool, and she never came back on the line. The woman said she heard no struggle and no sounds indicating what happened.

The tenant said during that time, he didn't hear Mr. leave the house.

At roughly 9 p.m., Mr. called 911 saying he'd gone into the backyard and found his wife in the pool. He started CPR and emergency crews took over when they arrived.

While trying to revive Mrs. , paramedics made several attempts to insert a breathing tube in her wind pipe.

Mrs. was declared dead on arrival at the Montfort Hospital a short time later.

To the media, police said they were investigating the death, and it looked like a drowning. However, there were some nagging questions. For instance, Mrs. had an injury on her head.

At the preliminary hearing, under questioning by assistant Crown attorney Donna Eastwood, Dr. testified the cause of death was neck compression. She said that although there were no injuries on the outside of Mrs. neck, the injuries on the inside of her throat showed she'd been strangled.

However, under cross-examination by Mr. Edelson, it was shown the injuries on the inside of her throat could have been caused by paramedics trying to insert the breathing tube.

Classic pathological signs of strangulation, such as burst blood vessels in the face and eyes, weren't present. And there was evidence to suggest cause of death was drowning after she fell, hit her head, and ended up in the pool.

Despite being shown studies suggesting her findings could be wrong, and evidence suggesting Mrs. death was consistent with an accidental fall and drowning, Dr. refused to consider anything but strangulation as the cause of death.

Indeed, transcripts of the preliminary hearing show she became combative when it was suggested she'd made a mistake.

"It became obvious that there were significant problems with the pathology," Mr. Edelson said. "She became an advocate for her opinion in the face of the evidence."

Dr. didn't return a message for comment on this story yesterday.

In a statement to Ontario Court Justice Bernard Ryan yesterday, Ms. Eastwood said the new information caused her concern "about the pathology evidence as to the cause of death." She sought a second opinion from one of Ontario's leading forensic pathologists.

"The critical issue in this case is the cause of death," Ms. Eastwood told the court. "The original, unequivocal opinion was that the cause of death was due to neck compression.

"The opinion of the second pathologist retained by the Crown is that the absence of petechial hemorrhages and a lack of injuries to the front of the neck do not support neck compression as the cause of death. But that the presence of wet and heavy lungs and fluid in the airway support the diagnosis of drowning."

Ms. Eastwood said this, coupled with the defence pathologist's opinion that Mrs. accidentally drowned, show "there is no longer a reasonable prospect of conviction in this case.

"The Crown is not asking for a committal to trial."

Immediately after this, Judge Ryan discharged Mr. . "I would agree with Ms. Eastwood," he said. "I had some concerns, too, after hearing the evidence on this issue."

Afterwards, Mr. Edelson said his client's plight was the result of a "rush to judgment."

"If the police had done a proper investigation, they would have had a very different body of evidence to look at than when they made the decision to lay charges," he said.

"I think (Dr. work was one of the biggest problems in this case. It was also a rush to judgment."

FRIDAY'S LOTTERIES

Last night's winning numbers were drawn too late to make this edition of the Citizen. They will be printed tomorrow. To check your numbers, you can go online to www.olgclotteries.ca or phone the toll free line at 1-800-387-0098

AUTOPSY

ONGOING ORDEAL

FROM PAGE A1
II PATHOLOGIST

Innocent woman felt compelled to accept jail term, her lawyer says

Mother suffered baby-killer label

pathologist should not work in isolation

always look for second opinion

and

do they ever have opinions !

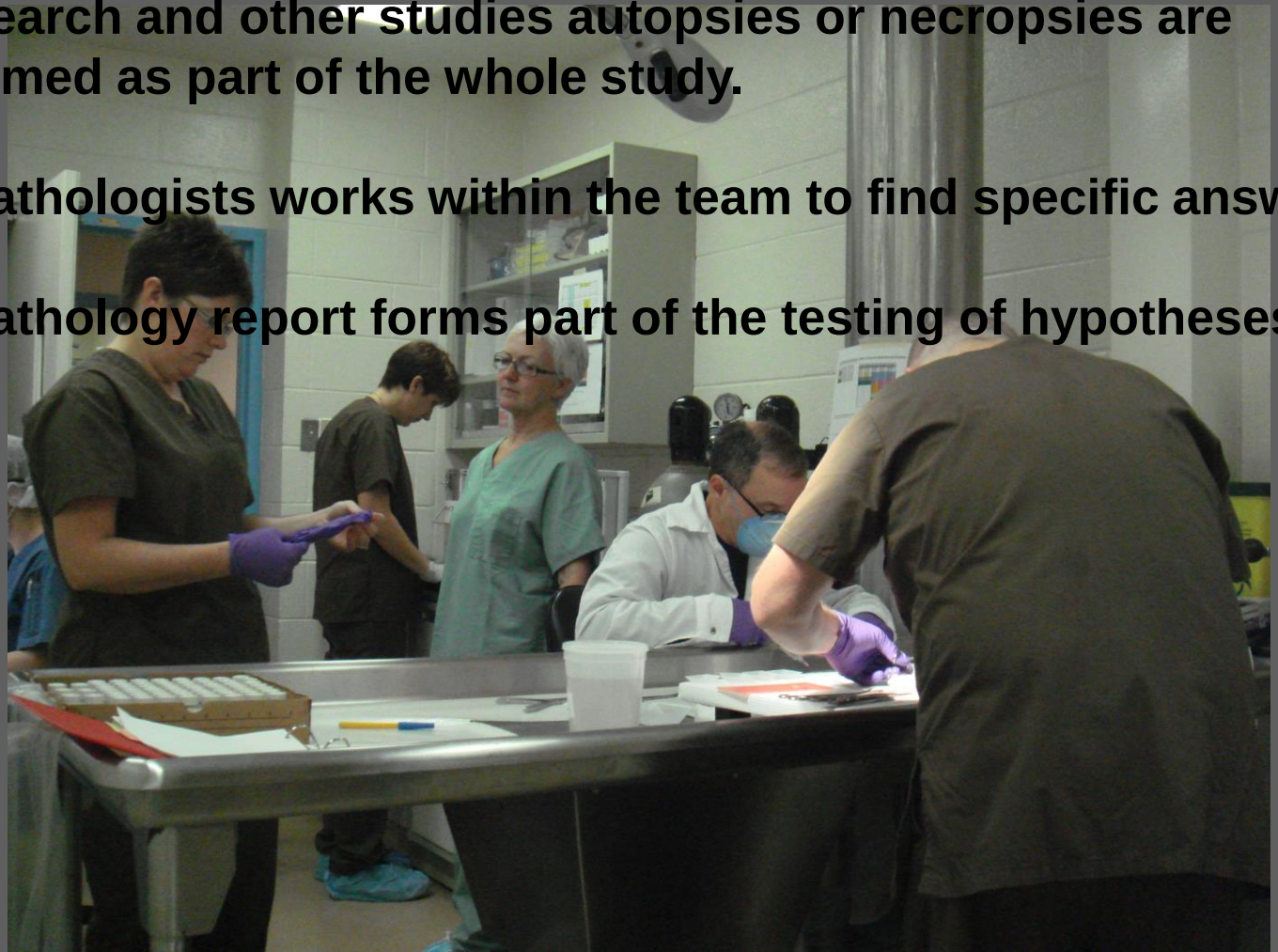
here is an example for illustration

other reasons for AUTOPSY

In research and other studies autopsies or necropsies are performed as part of the whole study.

The pathologists works within the team to find specific answers

The pathology report forms part of the testing of hypotheses



other reasons for AUTOPSY / NECROPSY

versatility of veterinary pathologist

advantage of comparative / biological view of pathology

field work together with other professionals :

e.g. biologists, traditional hunters, trappers in research on wildlife diseases

sometimes on other continents

AUTOPSY

importance of recording, documentation

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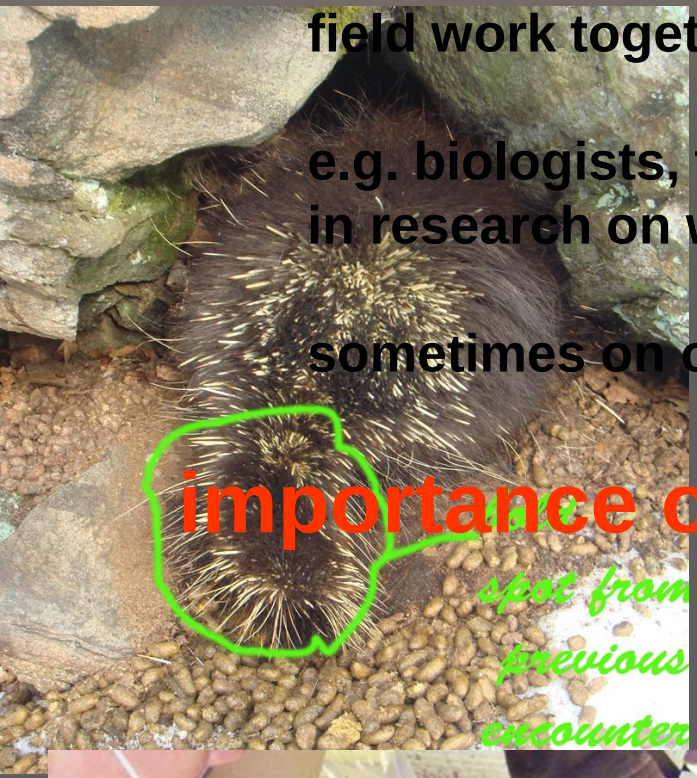
AUTOPSY



field work together with other professionals :

e.g. biologists, traditional hunters, trappers
in research on wildlife diseases

sometimes on other continents

importance of recording, documentation

spot from previous encounter

AUTOPSY

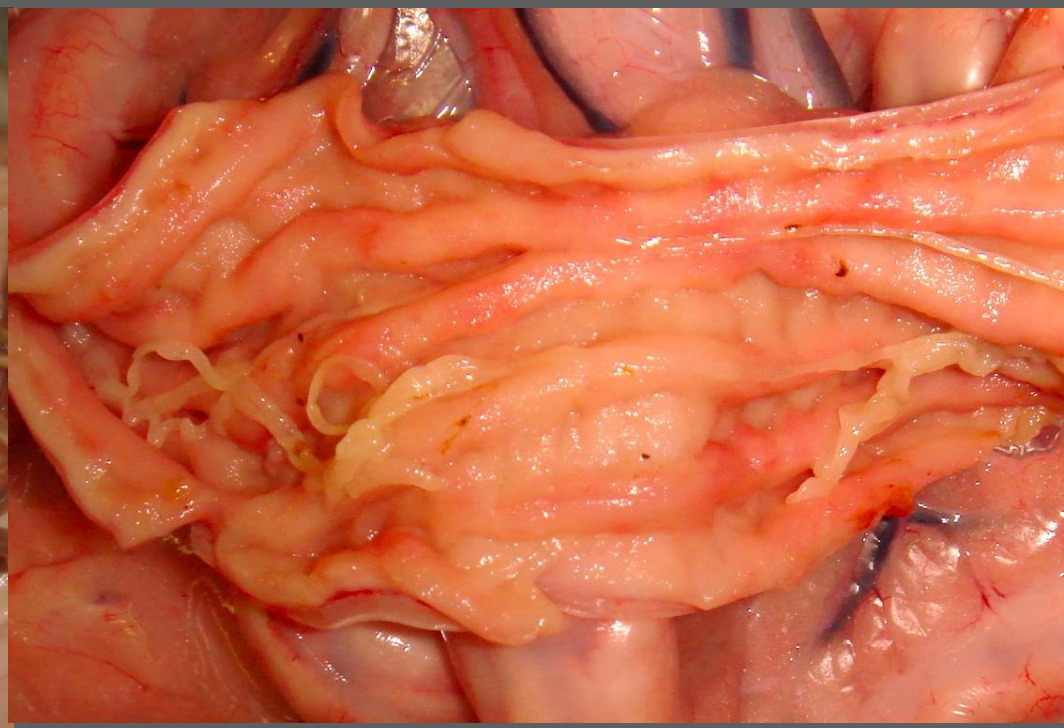
field work together with other professionals :

e.g. biologists, traditional hunters, trappers in research on wildlife diseases

AUTOPSY

field work together with other professionals :

e.g. biologists, traditional hunters, trappers in research on wildlife diseases

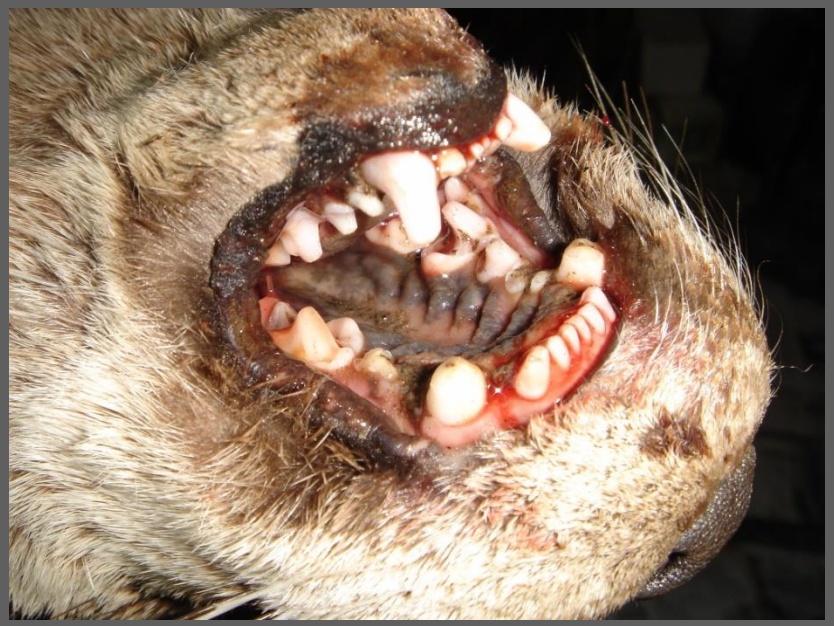


ENVIRONMENTAL RESEARCH

role of pathologist:

between organism and environment

starvation in wildlife



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ENVIRONMENTAL RESEARCH

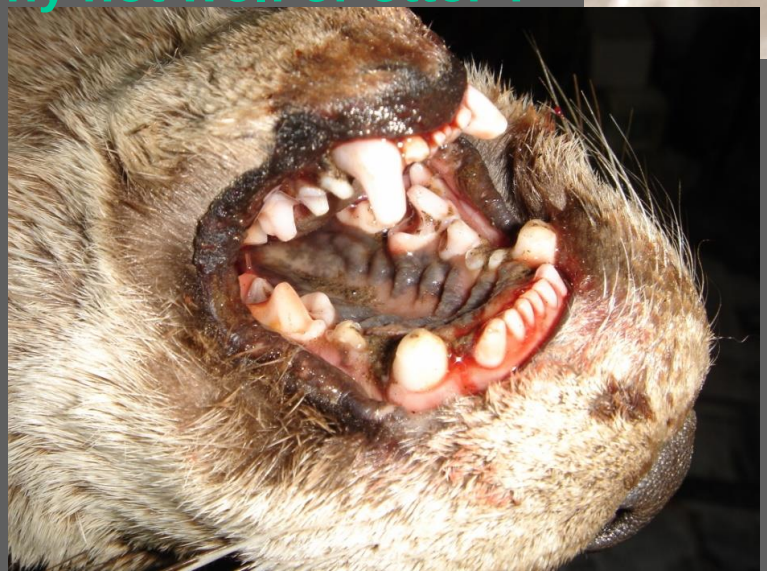
role of pathologist:

Interaction between organism and environment

starvation in wildlife :

(the case of the starving Lynx)

why not wolf or otter ?



other reasons for AUTOPSY / NECROPSY

some times veterinary pathologists have to compete with others

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ENVIRONMENTAL RESEARCH

role of pathologist:

between organism and environment

turtles get run over on road
sometimes just flipped over

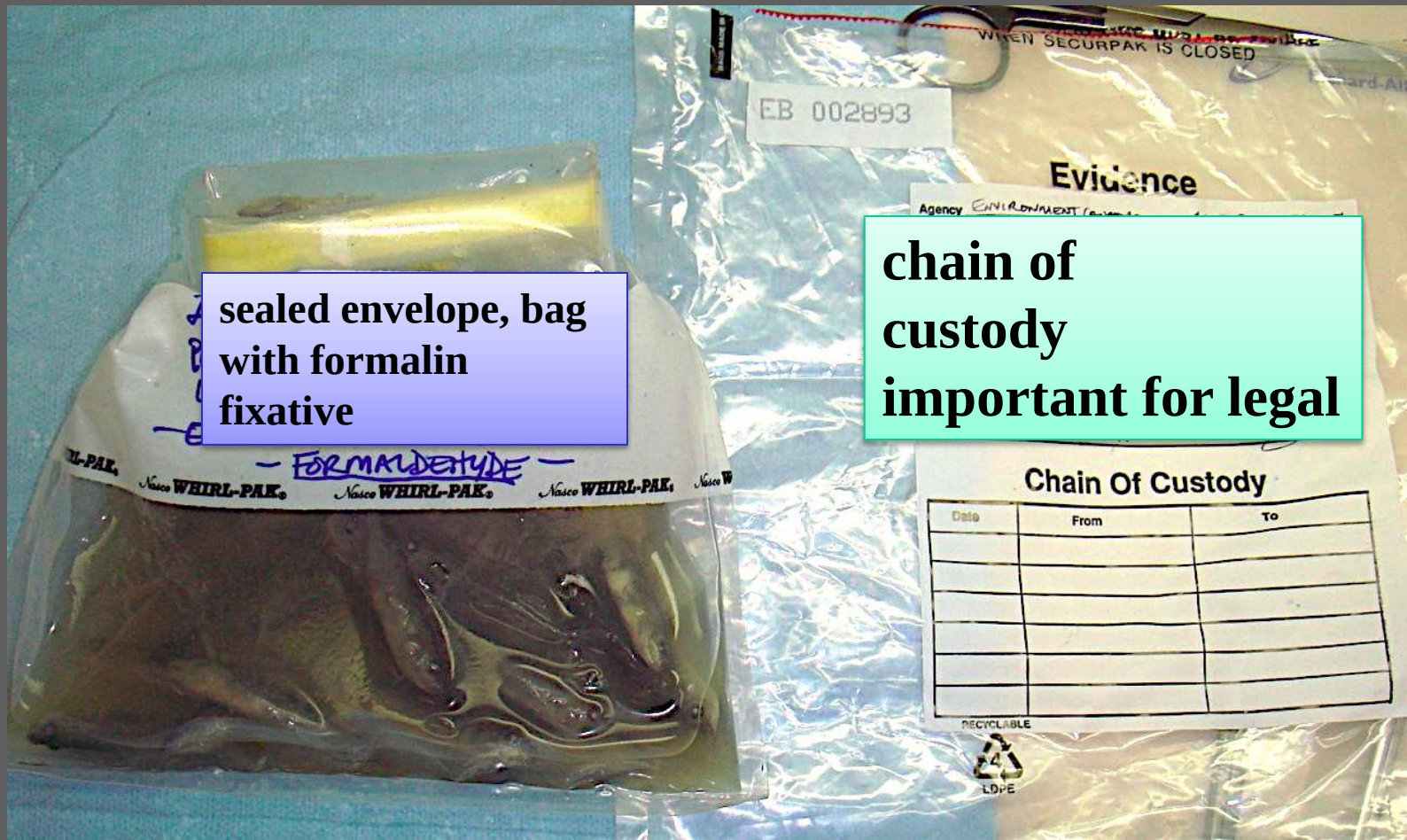
how do they get up ?

GP

ENVIRONMENTAL RESEARCH

role of pathologist:

between organism and environment



ENVIRONMENTAL RESEARCH

role of pathologist:

between organism and environment

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ENVIRONMENTAL RESEARCH

role of pathologist:

between organism and environment

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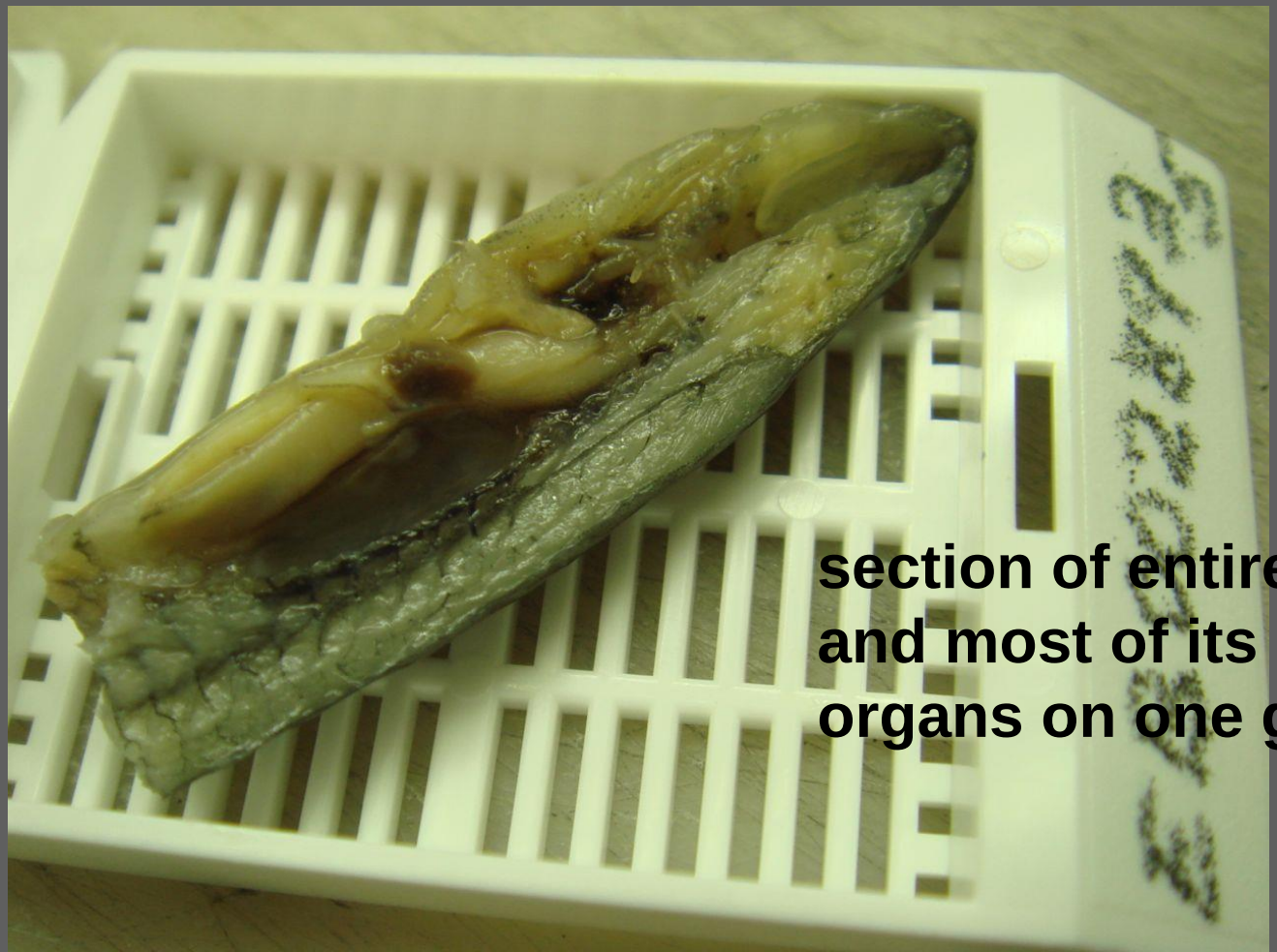
ENVIRONMENTAL RESEARCH

role of pathologist:

between organism and environment



section of entire organism and most of its organs on one glass slide

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EXPERIMENTAL RESEARCH

Research with hypotheses, which we can prove or disprove

where do such hypotheses come from ?

observations : **case reports**

epidemiology

biological research

EXPERIMENTAL RESEARCH

role of pathologist: **to establish link between cellular and molecular**

between cellular and organ

between organ and whole body

between organism and environment

EXPERIMENTAL RESEARCH

role of pathologist: **respect the interaction**
between organism and environment
between organism and chemicals etc.
behavior intrinsic or extrinsic

animals serve as models, ultimately they serve us
we think in analogies
after all the living beings on this earth have basically similar building blocks
at least from an anatomical point of view

typical situation in the development of pharmaceuticals:

we choose a model to test products before we use them ourselves

the biased view : if results are promising we have a good model and are confident

if results are questionable ? perhaps it is just that what happens in the rat is not necessarily indicative of what is going to happen to us

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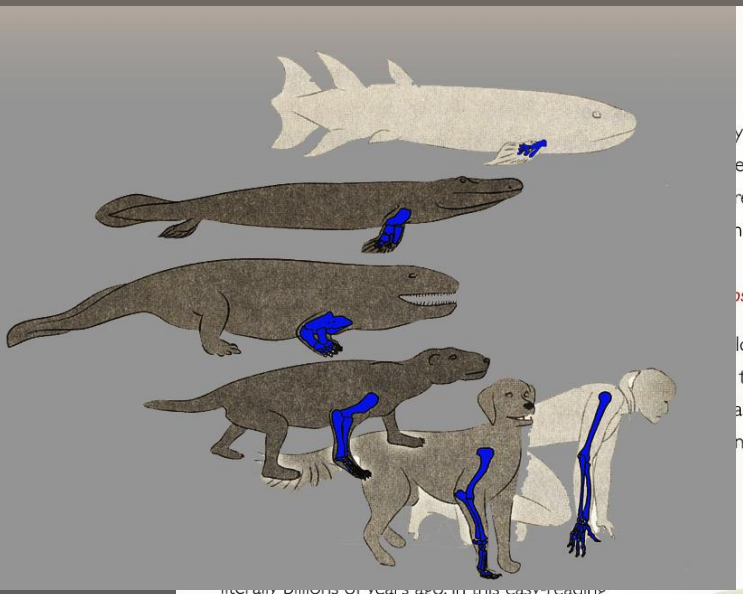
AUTOPSY / NECROPSY / ANALOGY



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literally billions of years ago. In this easy-reading volume, Shubin shows us how to discover that long and fascinating history in the structure of our own bodies while weaving in a charming account of his own scientific journey. This is the ideal book for anyone who wants to explore beyond the usual anthropocentric account of human origins."

—Ian Tattersall, curator, American Museum of Natural History

ISBN 978-0-375-42447-2 SCIENCE
52400
9 780375 424472

YOUR INNER FISH

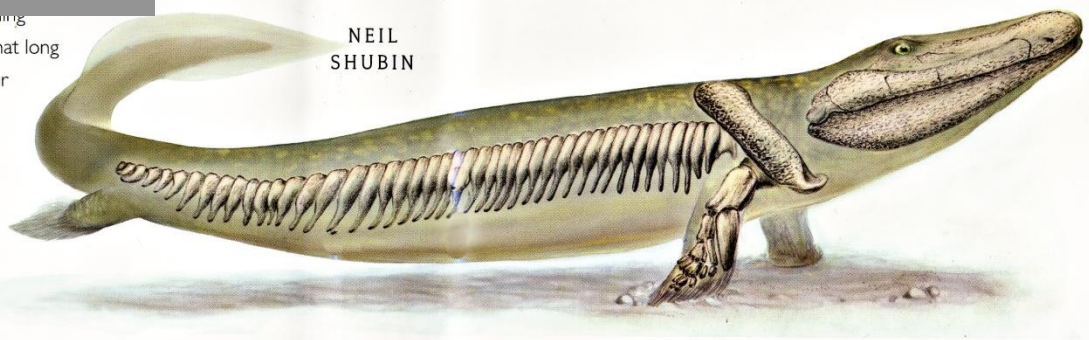
A JOURNEY INTO THE 3.5-BILLION-YEAR HISTORY OF THE HUMAN BODY

NEIL SHUBIN

PANTHEON

YOUR INNER FISH

A JOURNEY INTO THE 3.5-BILLION-YEAR HISTORY OF THE HUMAN BODY



NEIL SHUBIN

not alone

In the Flesh: The Monro Dynasty

Three hundred years ago, Scottish army surgeon John Monro (1670–1740) initiated a series of events that lead to the establishment of a dynasty which, beginning with his son Alexander Monro, changed the course of medical teaching and learning. Three men (father, son and grandson), each called Alexander Monro (*Primus, Secundus and Tertius*), consecutively held the Chair of Anatomy at the University of Edinburgh for 126 years.

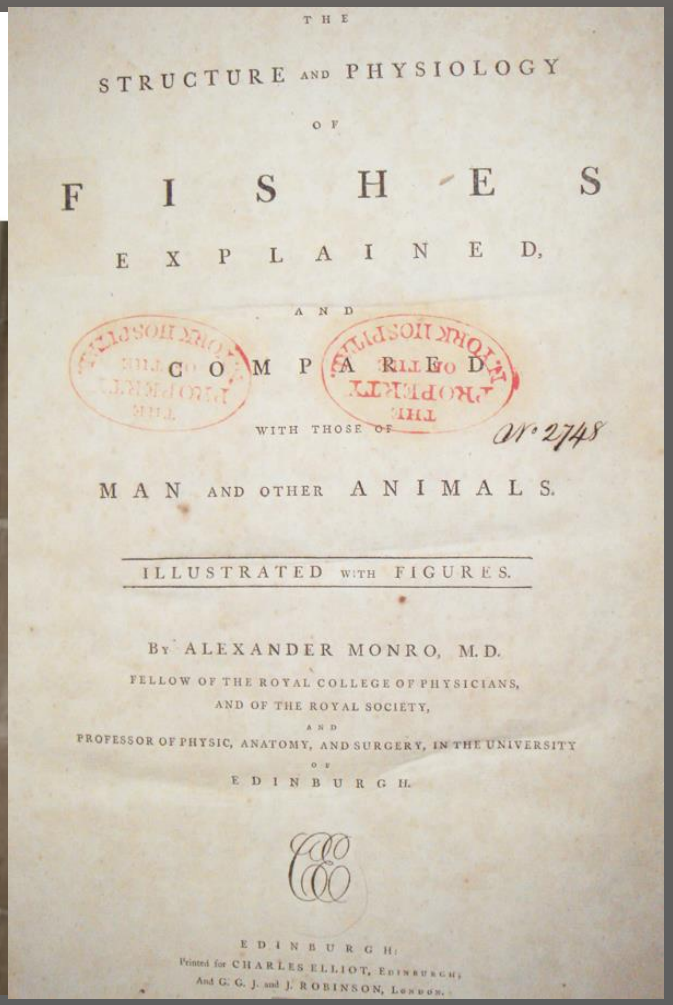
FUN with SERENDIPITY
Comparative Pathology

Alexander Monro (Secundus)

1733 - 1817

Anatomist. Monro succeeded his father, another Alexander (1697 - 1767), as Professor of Anatomy at the University of Edinburgh. He discovered the lymphatic systems, established the structure and function of the nervous system and noted the physiological effects of drugs.

Monro in turn was succeeded by his son, Alexander (1773 - 1859), the third to hold the Chair of Anatomy.



THE

STRUCTURE AND PHYSIOLOGY

OF

FISHES

EXPLAINED,

AND

COMPARED

WITH THOSE OF

MAN AND OTHER ANIMALS.

ILLUSTRATED WITH FIGURES.

By ALEXANDER MONRO, M.D.

FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS,

AND OF THE ROYAL SOCIETY,

AND

PROFESSOR OF PHYSIC, ANATOMY, AND SURGERY, IN THE UNIVERSITY

OF

EDINBURGH.

EDINBURGH:

Printed for CHARLES ELLIOT, EDINBURGH;

And G. G. J. and J. ROBINSON, LONDON.

NEW YORK HOSPITAL THE MEDICAL LIBRARY No. 2748

Comparative Pathology out of Necessity ?

Studying anatomy / pathology required dissection. Dissection required bodies.
A watch tower was built to guard the bodies

there was a dark side to this discipline

The first Alexander Monro worried in 1725 that "the requirements of anatomical teaching provided unscrupulous criminals with a particularly macabre opportunity for illicit gain.“

in 1828 with the notorious case of Burke and Hare. Having legally sold one dead person to the university, they went on to sell another sixteen. Unfortunately, all of those had been alive until they met the two murderers.

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EXPERIMENTAL RESEARCH

role of pathologist: respect the interaction
between organism and environment
behavior intrinsic or extrinsic

looking at
dead rat pups:

why is there no milk
In their stomach ?

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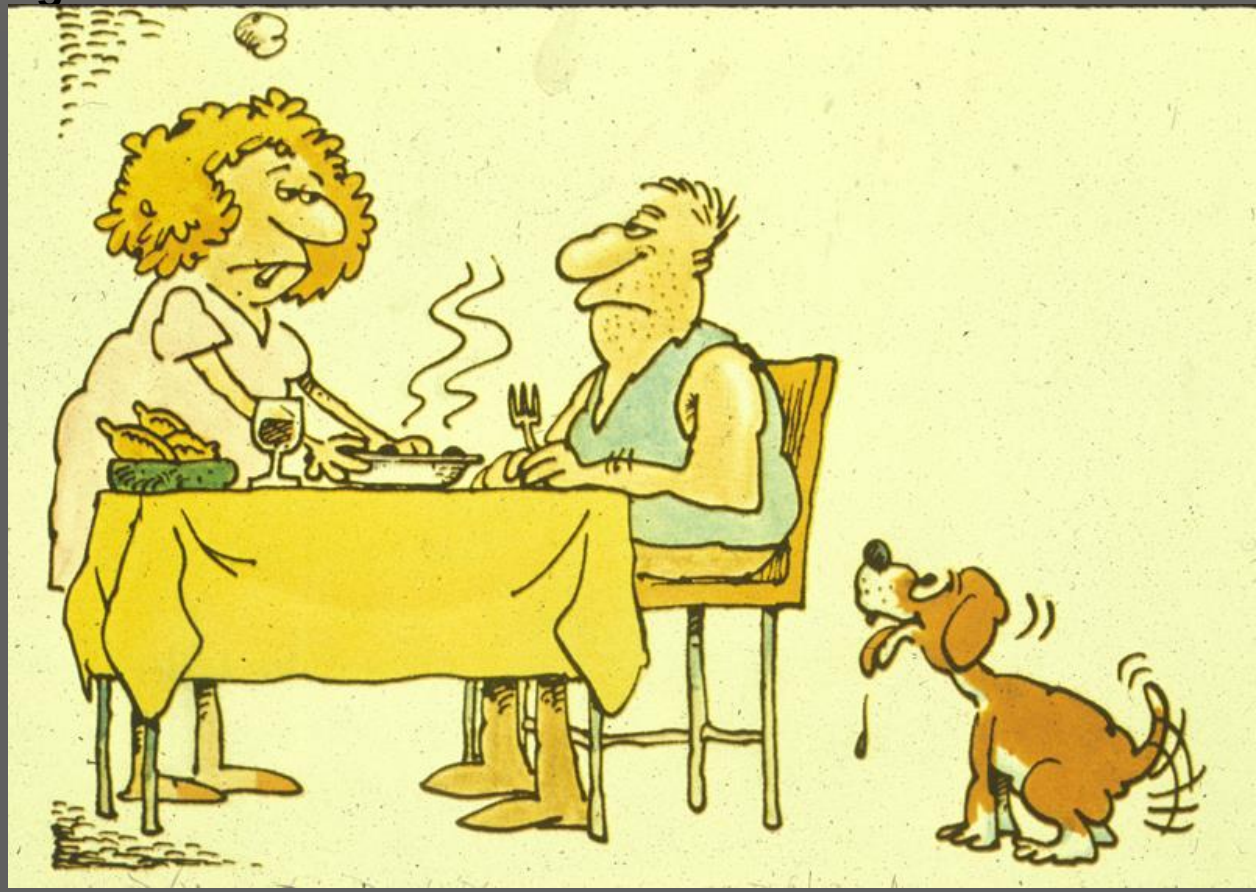
GENERAL OBSERVATIONS

Experimental PATHOGENESIS

sequence of events leading to the observations

- **stimulus**
- **injury**
- **etiologic agent**
- **etiologic event**
- **toxin**



the pathologist describes the pathogenesis
puts the whole story together

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GENERAL OBSERVATIONS

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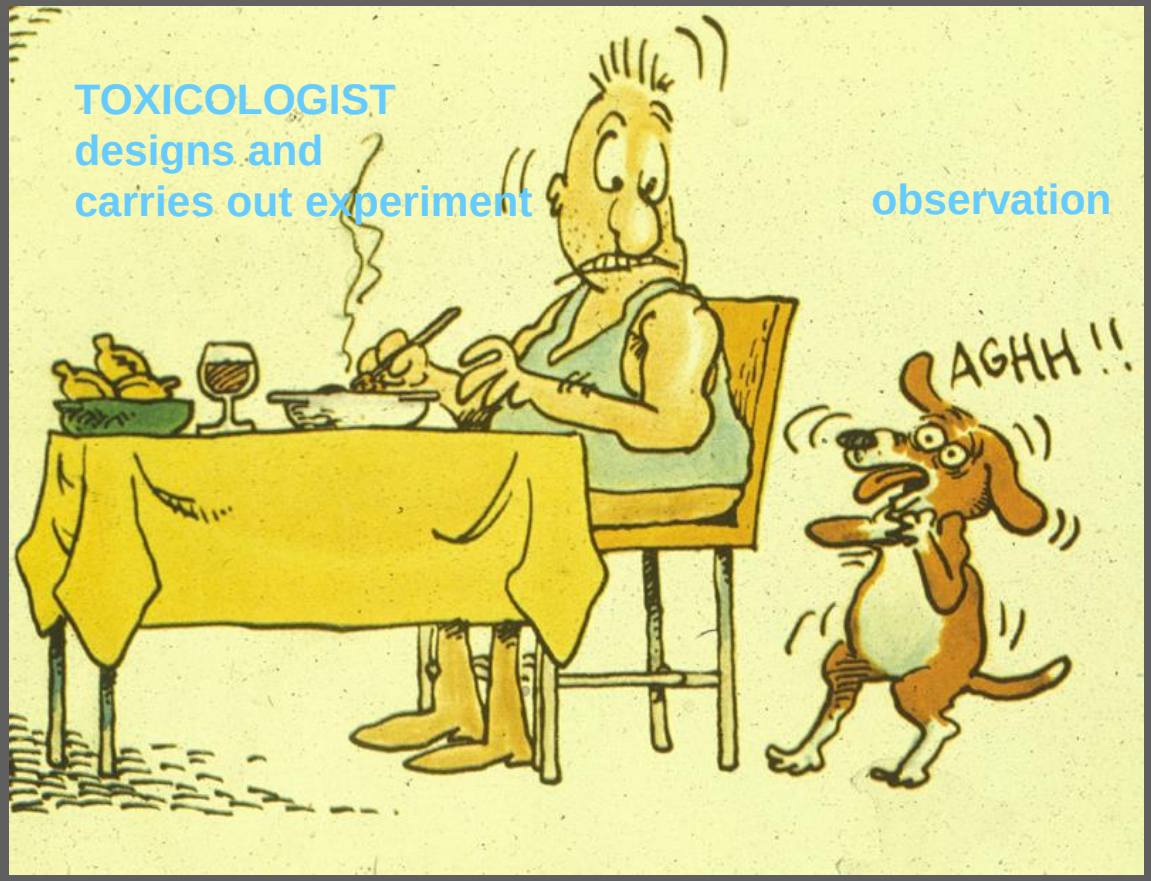

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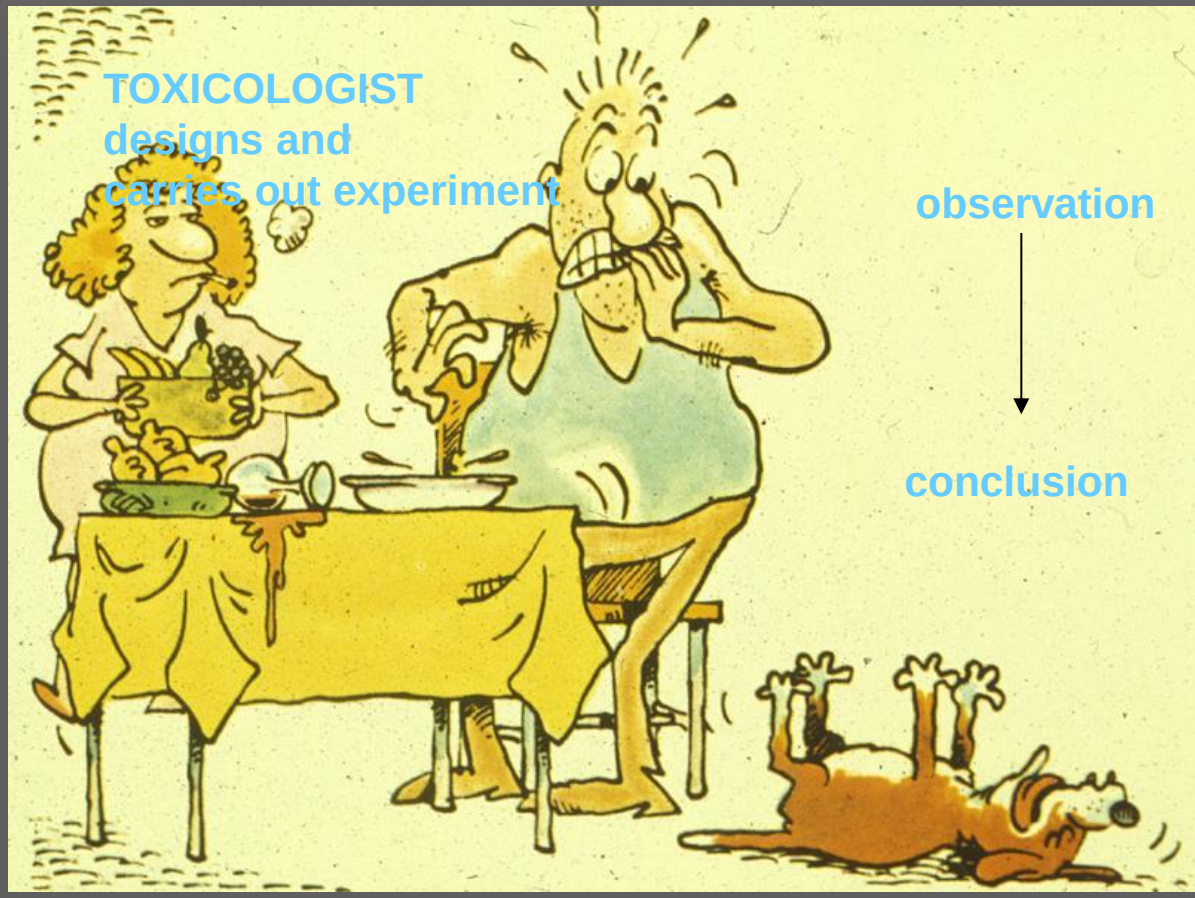

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GENERAL OBSERVATIONS

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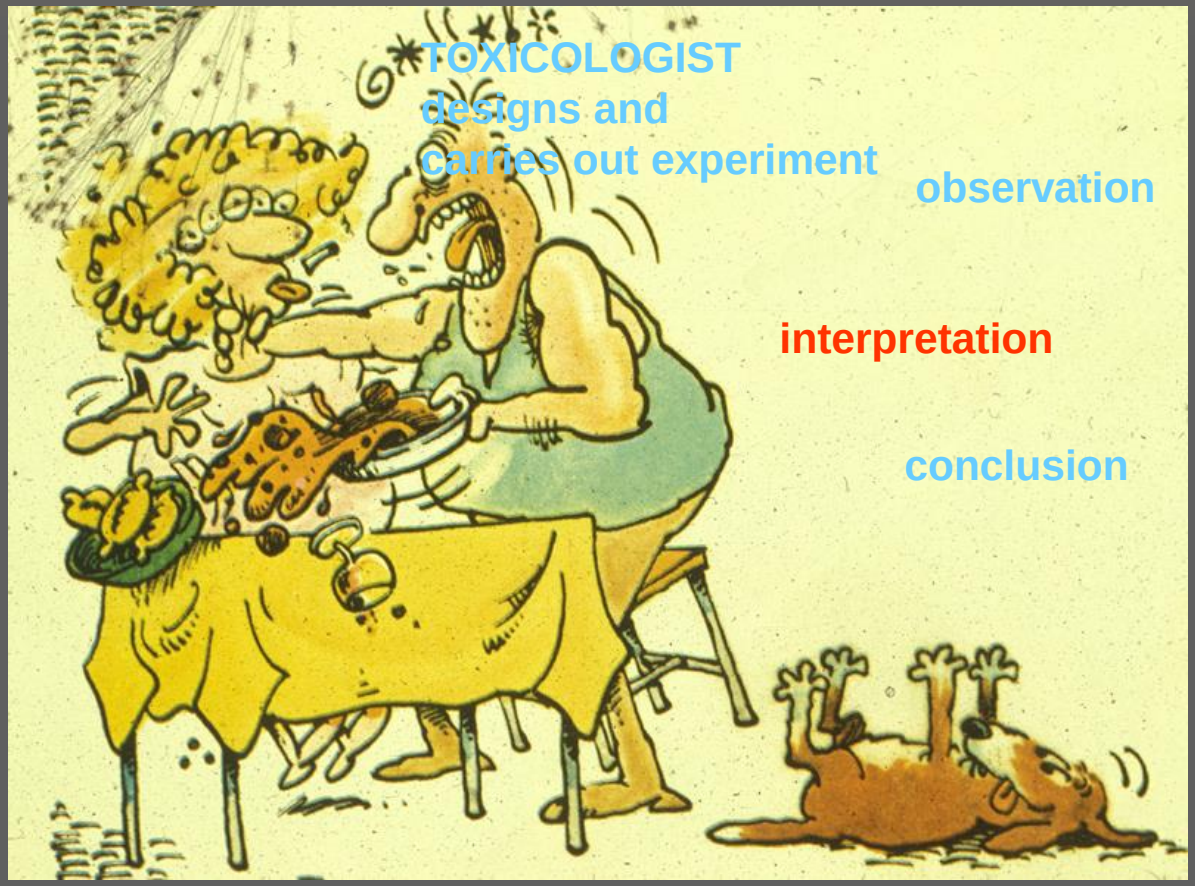

the pathologist describes the pathogenesis
puts the whole story together

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GENERAL OBSERVATIONS

Experimental PATHOGENESIS

sequence of events leading to the observations

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- **injury**
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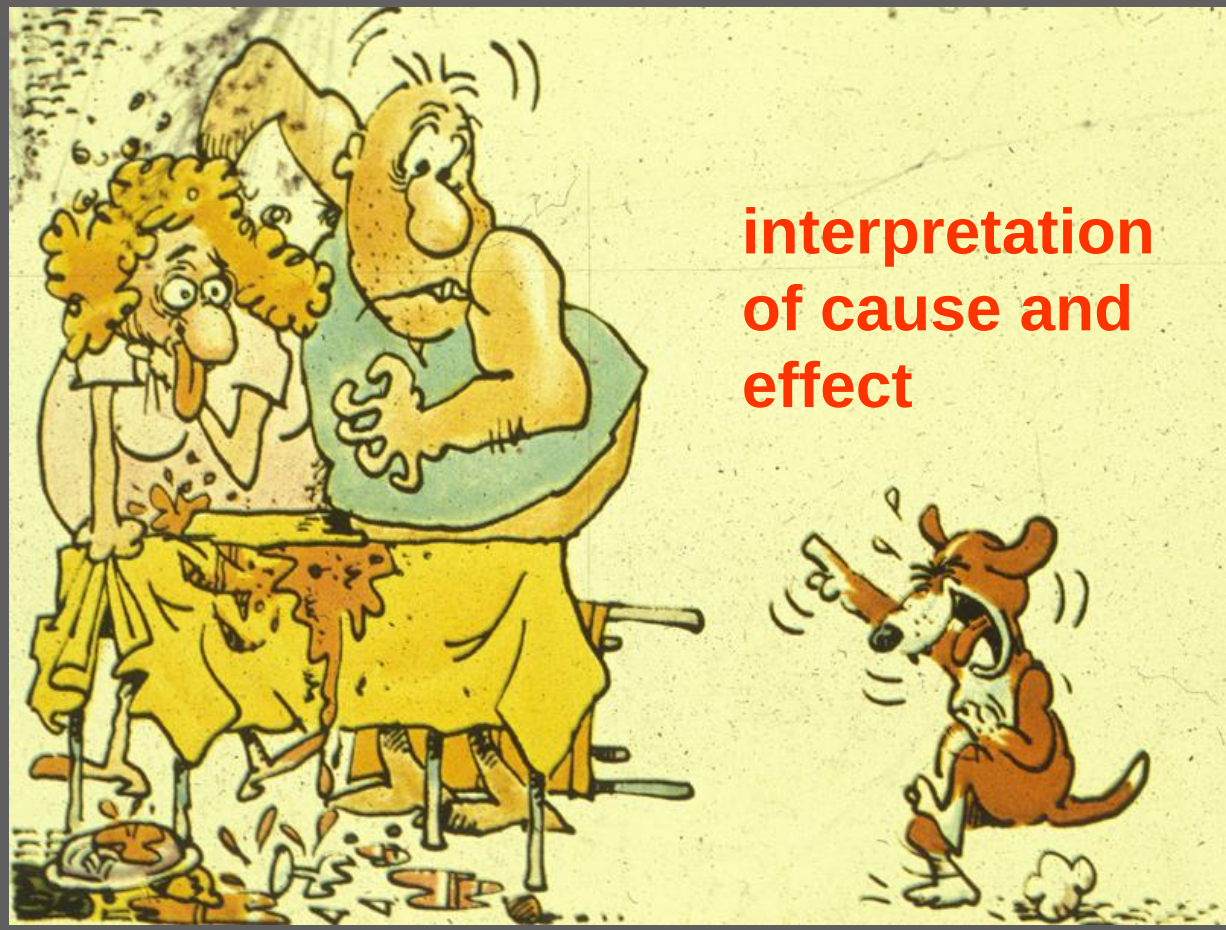
- **etiologic event**
- **toxin**

the pathologist describes the pathogenesis, puts the whole story together in a causal relationship



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other reasons for AUTOPSY / NECROPSY

versatility of veterinary pathologist

together with other professionals :

e.g. cardiac surgeons, mechanical engineers

development of implantable devices
e.g. devices to support the heart function:

Ventricular Assist Devices VAD's

planned AUTOPSY

experimental studies

Collecting data *in vivo*

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GP

AUTOPSY

collecting data

ante mortem

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AUTOPSY

step by step examination of targeted areas

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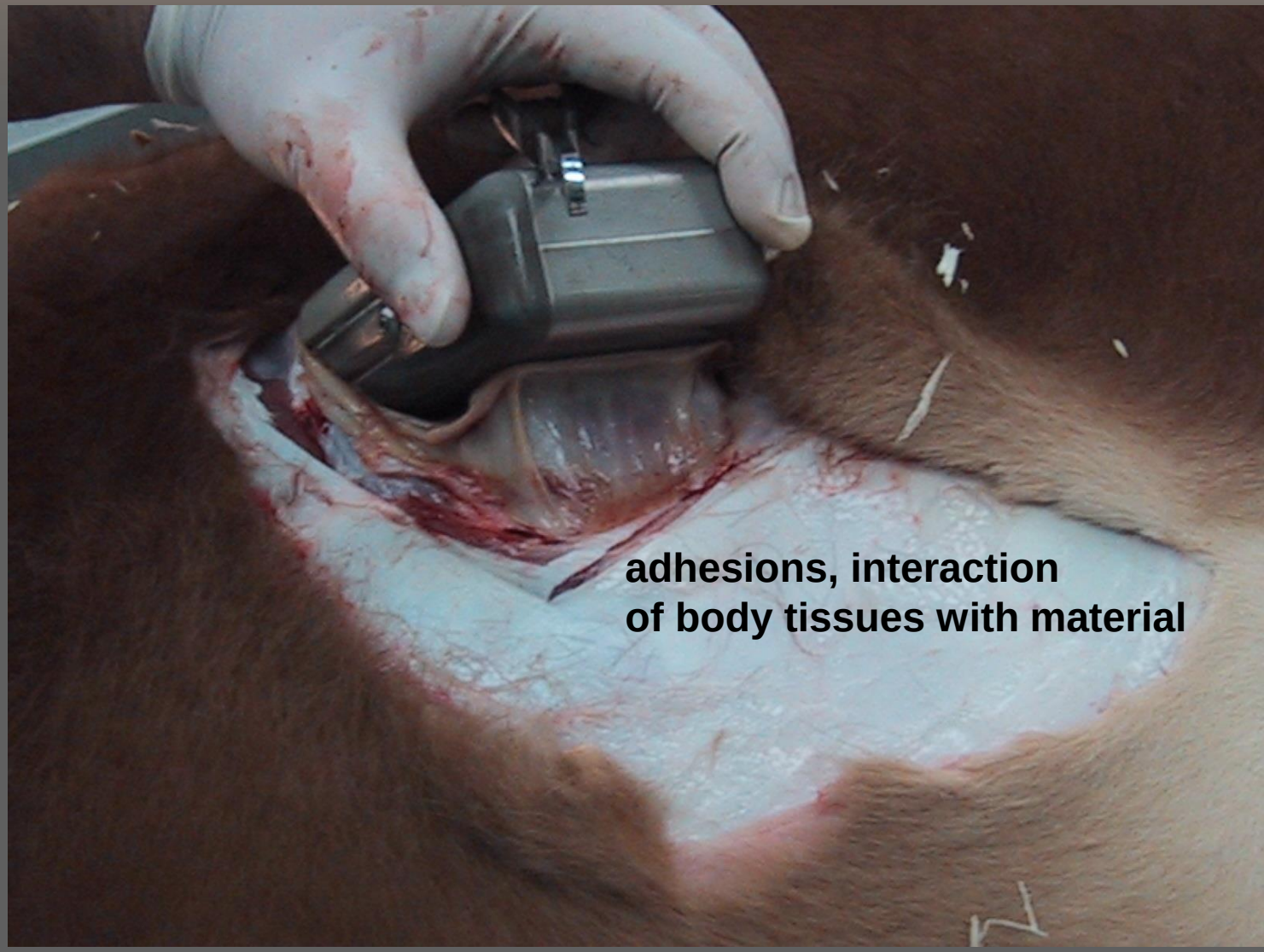
AUTOPSY



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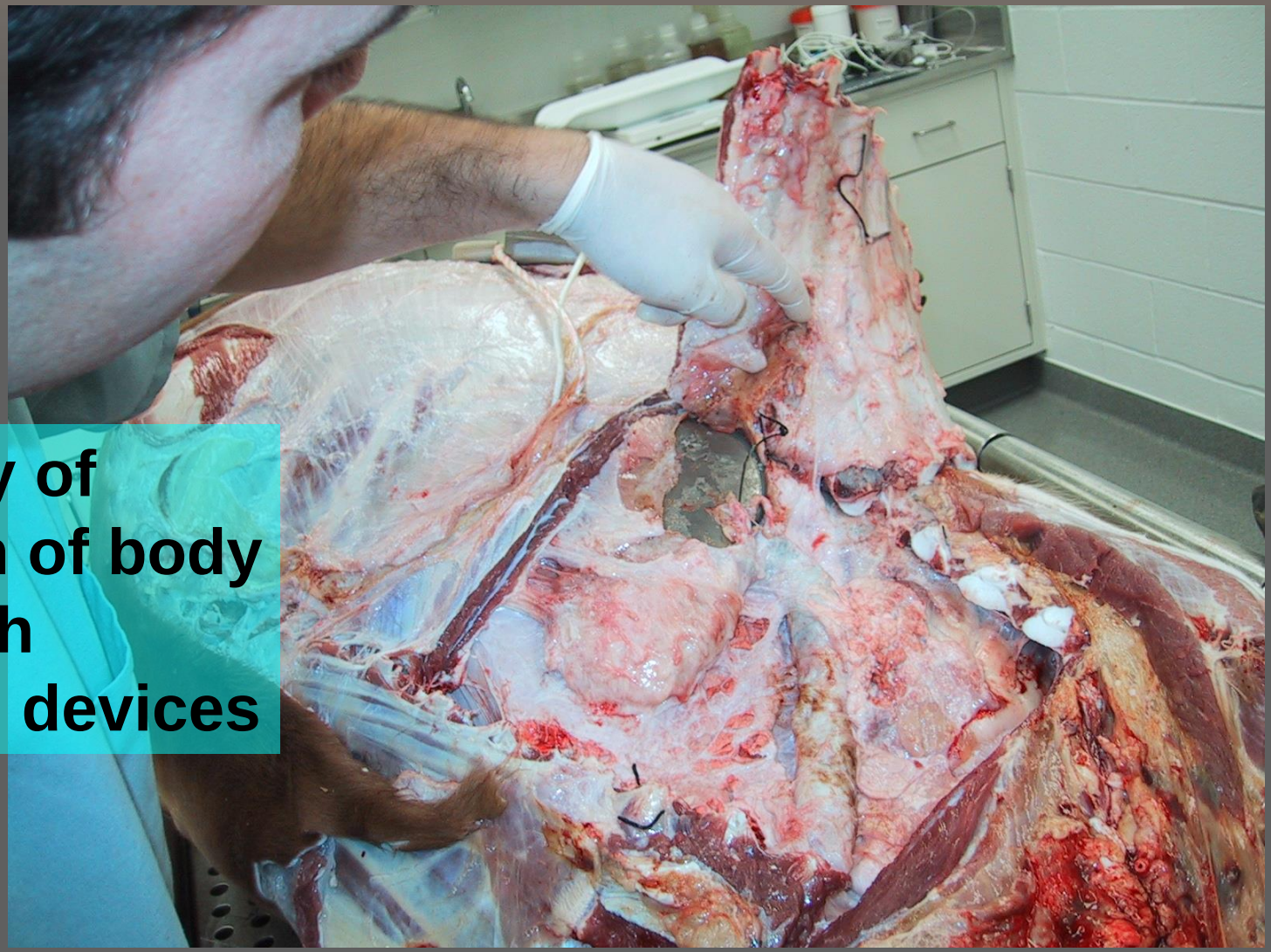
AUTOPSY



study of interaction of body with implanted devices

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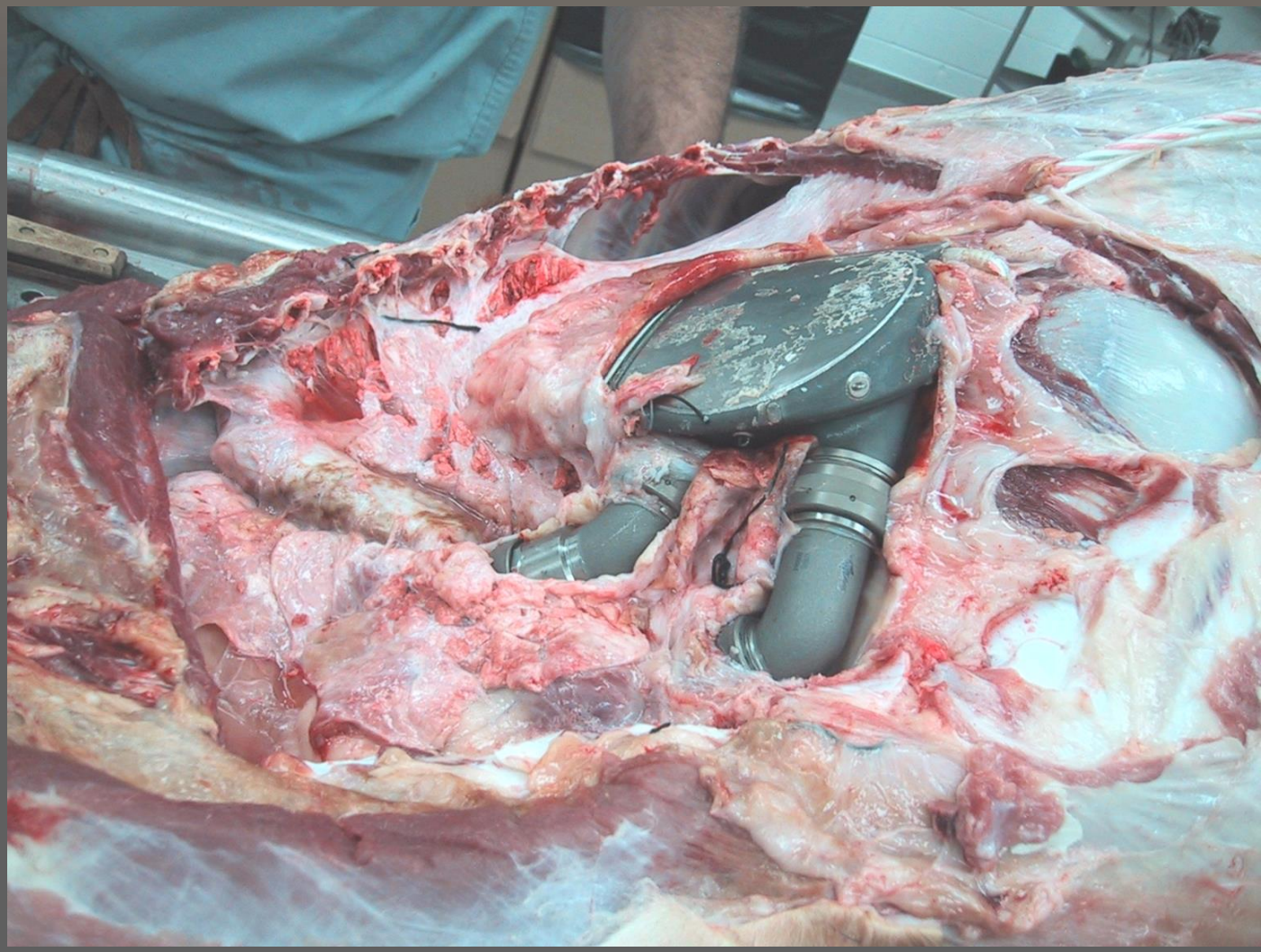
AUTOPSY

adhesions

adhesions !



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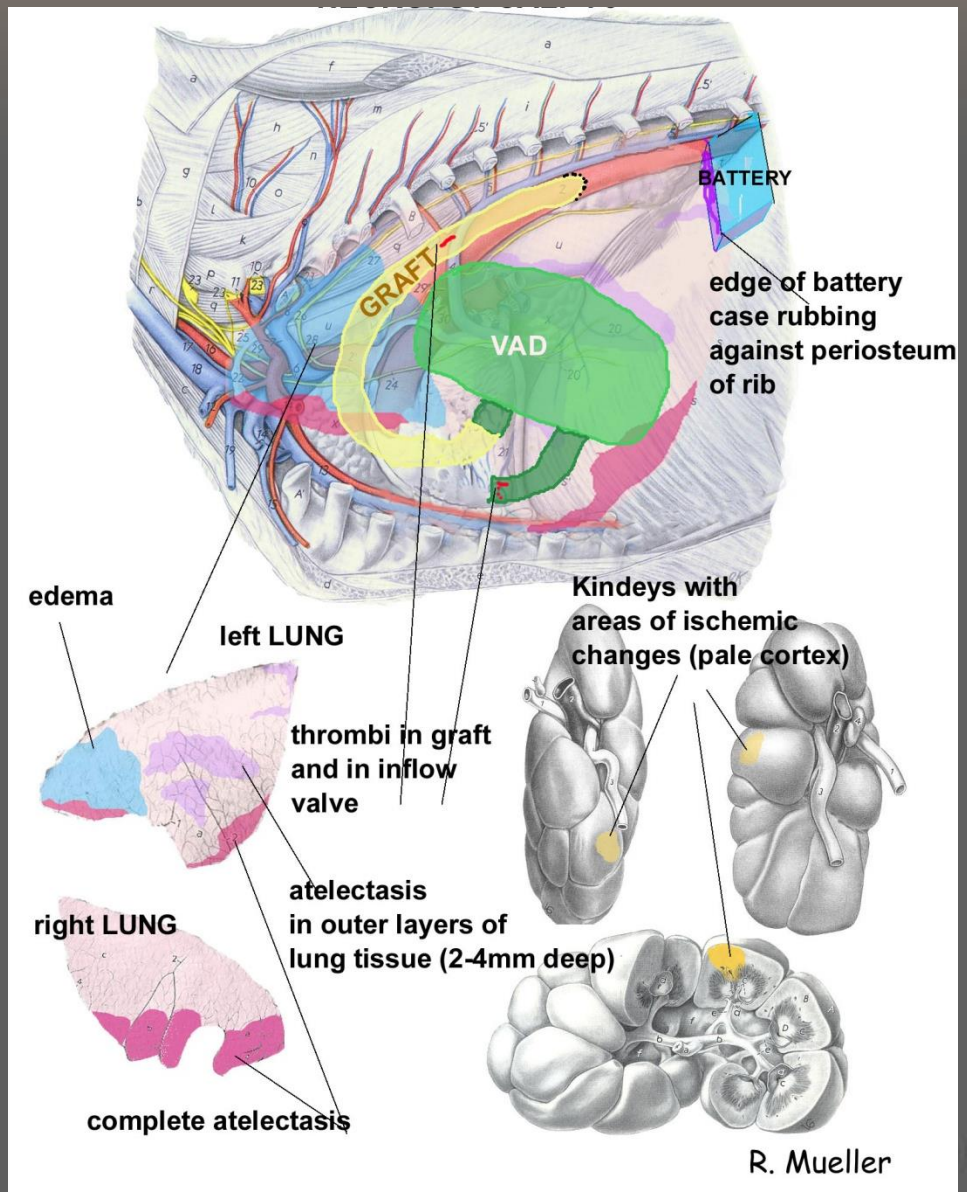
AUTOPSY

reporting with visual explanations

putting observation in context

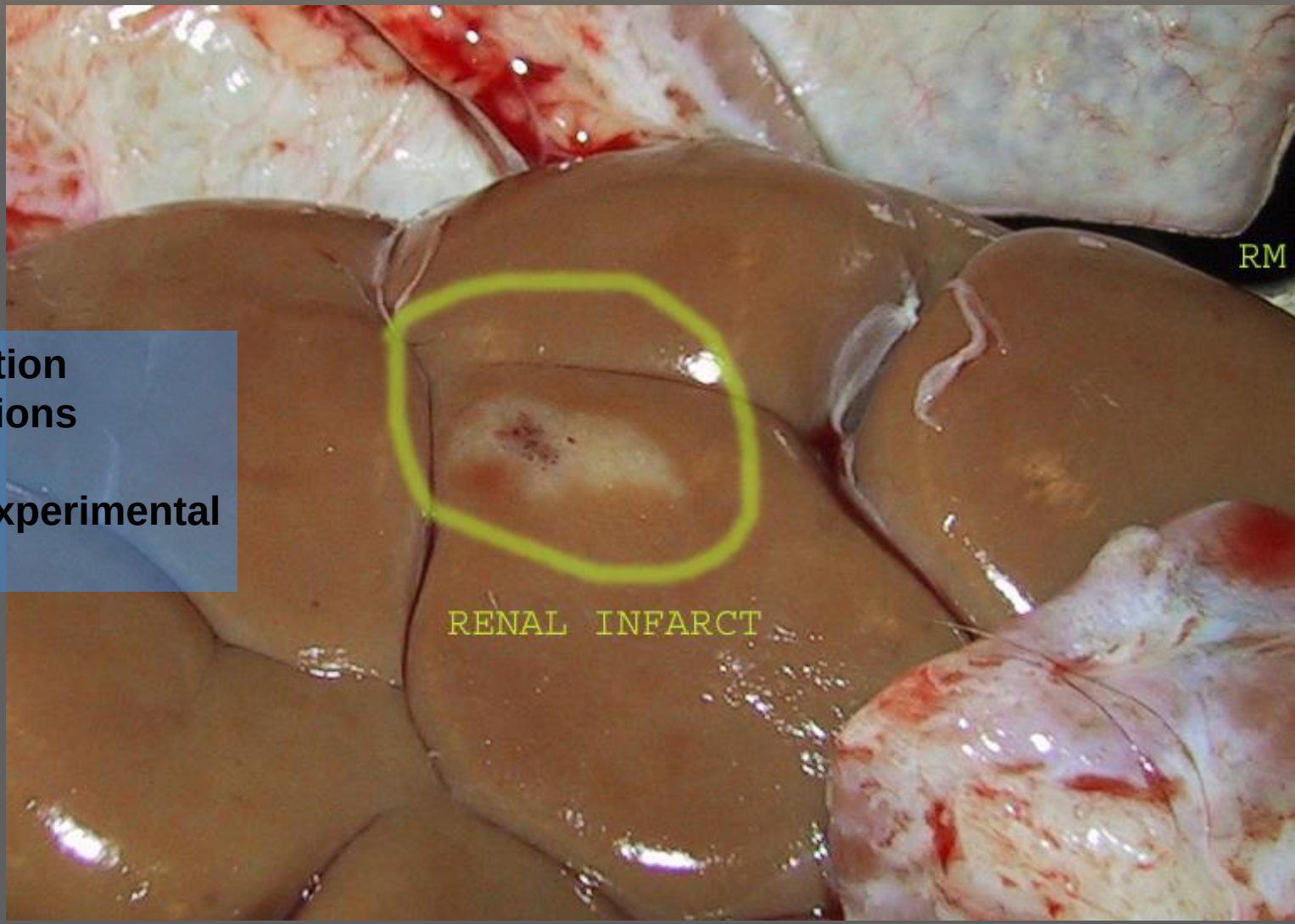
attribute relevancy



AUTOPSY

documentation of observations

results of experimental surgery



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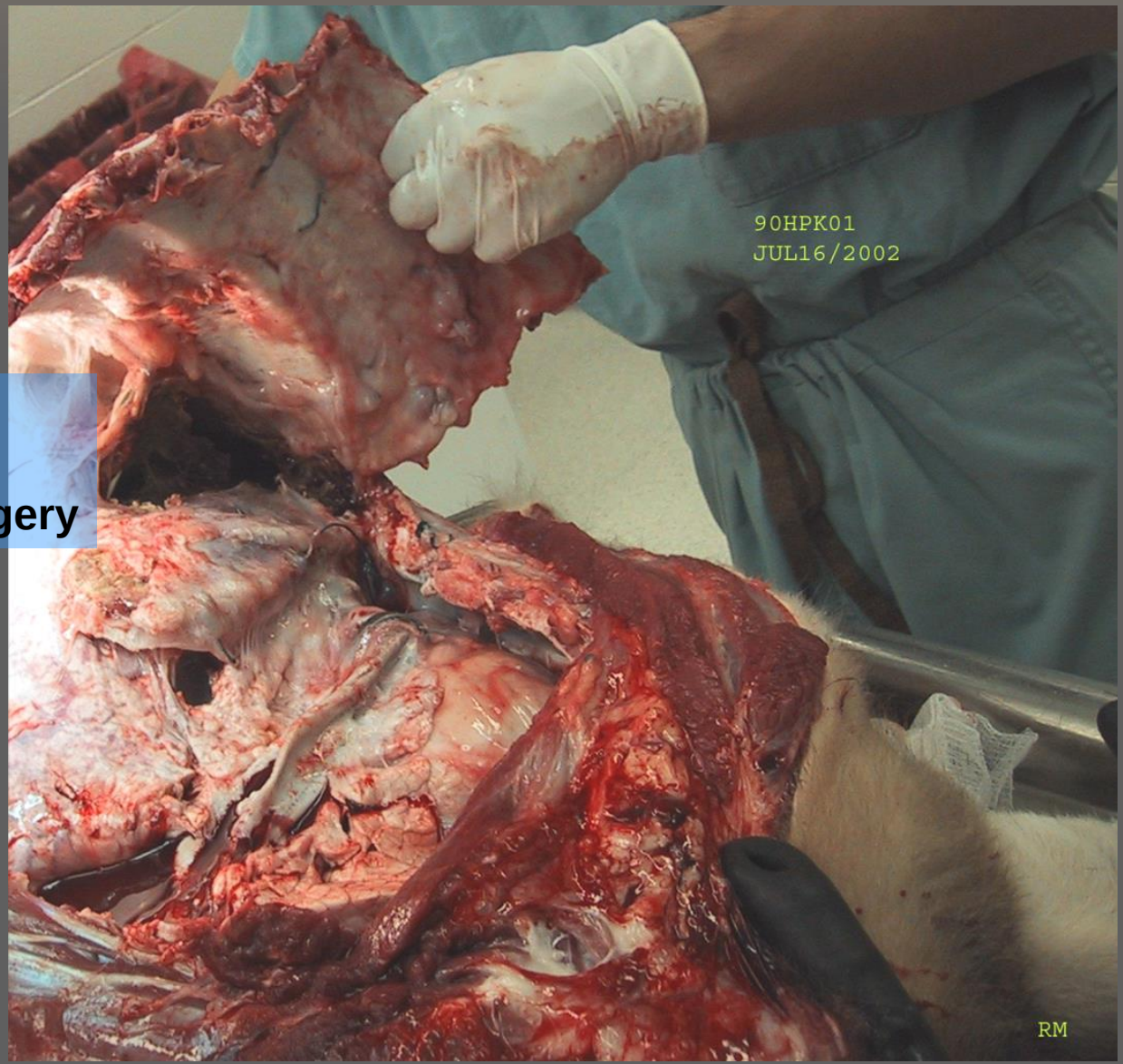
AUTOPSY

adhesions in chest
result of surgery



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GENERAL PATHOLOGY OBSERVATIONS

PATHOS - suffering **LOGOS - study**

Observation at Autopsy

- ***change of size***
- ***change of shape***
- ***change of color***
- ***change of smell***

deviation from what is considered normal

GENERAL PATHOLOGY OBSERVATIONS

the observations are based on the experience that causes of various origins are leading to changes in morphology

pathogenesis etiology — **morphology** — **clinical significance**

task of PATHOLOGIST

diagnosis synthesis → **STORY**

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GENERAL PATHOLOGY OBSERVATIONS

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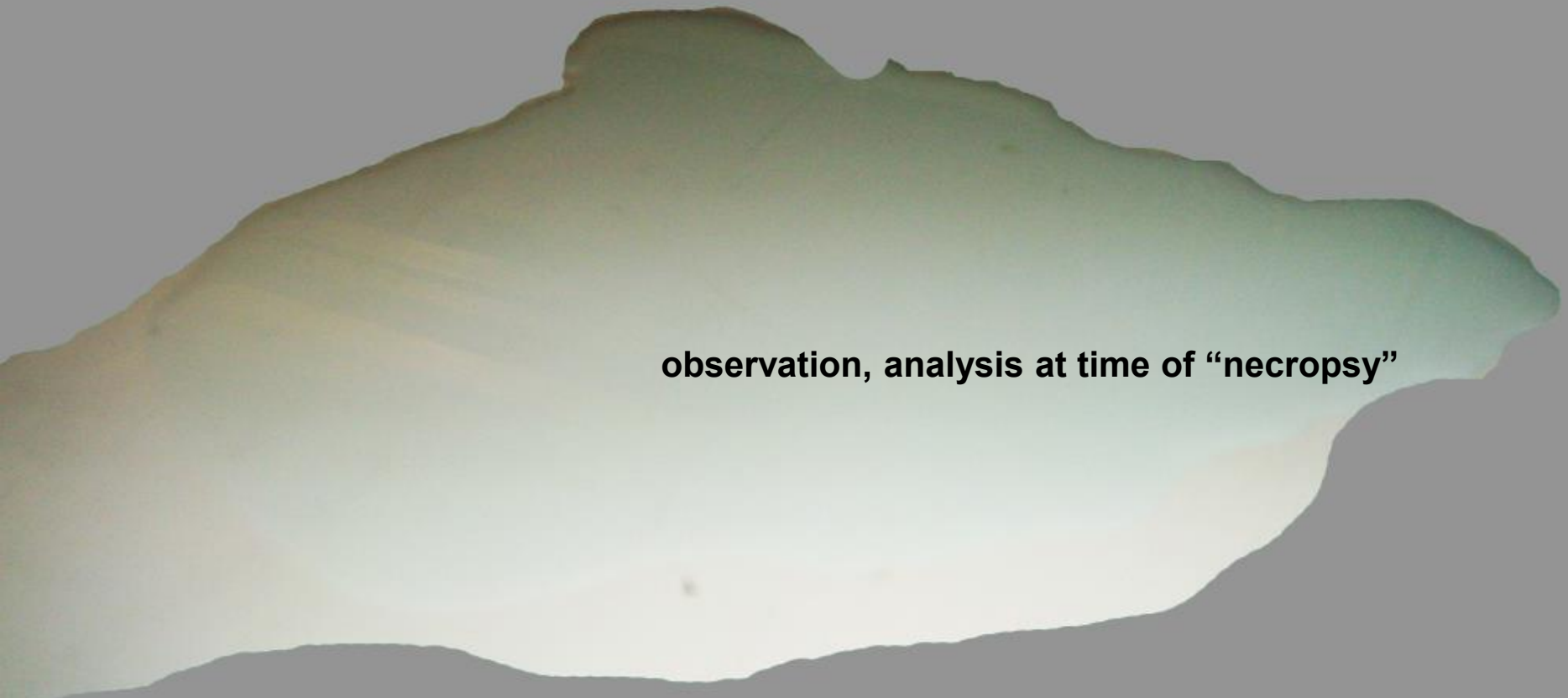

observation, analysis at time of “necropsy”

GENERAL PATHOLOGY OBSERVATIONS

70 % of body is water

75 % of muscle is water

50 % of fat is water
50 % of bone is water

Respiratory

Digestive **continuous new elements exchange etc .**

GENERAL PATHOLOGY OBSERVATIONS

GENERAL PATHOLOGY OBSERVATIONS

ETIOLOGY cause

finding the culprit (i.e. germ)
finding the primary cause → therapy
prevention

factors to consider

intrinsic (i.e. genetic)
extrinsic (i.e. acquired)

discovery and knowledge of primary disease → diagnosis

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GENERAL PATHOLOGY OBSERVATIONS

PATHOGENESIS

sequence of events leading to the observations

- **stimulus**
- **injury**
- **etiologic agent**
- **etiologic event**

response →

expression of disease

the pathologist describes the pathogenesis
puts the whole story together

GENERAL PATHOLOGY OBSERVATIONS

the study of pathogenesis today is more exciting than ever as new tools become available

the new tools allow for increased scientific relevance in exercising the craft of medicine

medicine is the art of combining science and intuition with patient care thus really helping the patient

GENERAL PATHOLOGY OBSERVATIONS

morphologic changes are the basis of diagnostic pathology

changes can be structural
physical

→ **cells, tissues, organs show characteristics to etiologic processes**

often pathologic observations infer causality

similar observations
variety of causes !

GENERAL PATHOLOGY OBSERVATIONS

diagnostic pathology

based on observation, defined by the nature and progression of disease

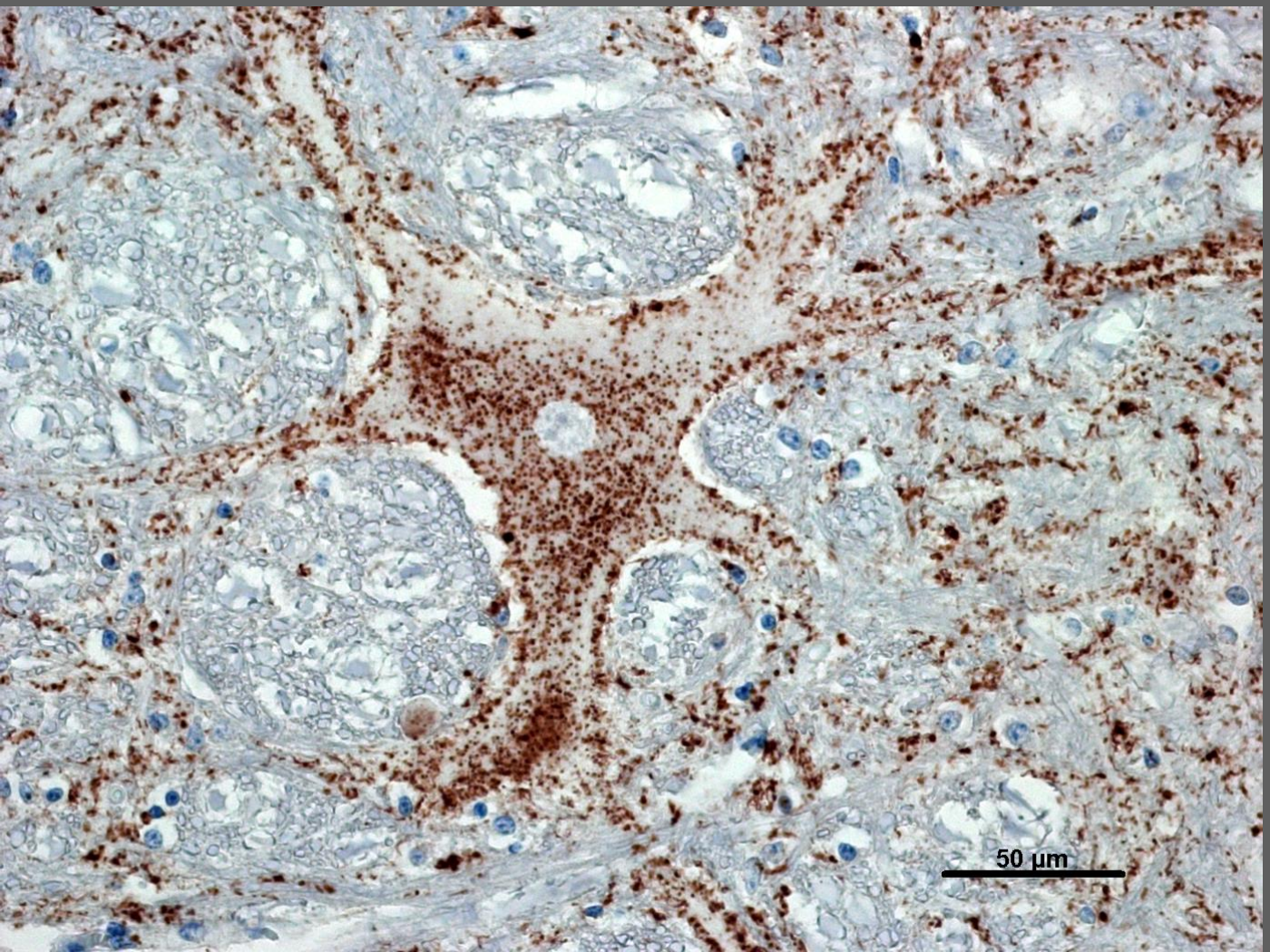
limitation of the traditional morphology

leads to inclusion of additional investigative methods

examples

- **molecular biology**
- **immunology**
- **immunohistochemistry**
- **genetics**

Immuno Histochemistry



demonstration of prions in neurons

mad cow disease

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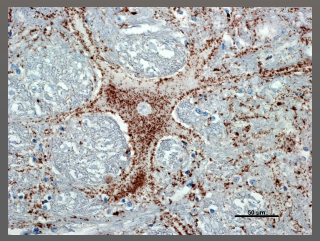
Immuno Histochemistry

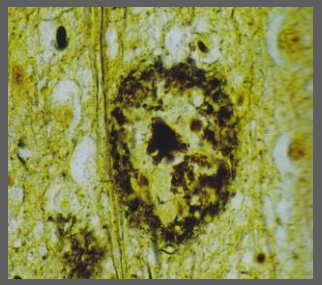
demonstration of prions in neurons

mad cow disease



demonstration of plaques

Alzheimer's disease



causal relationship ?

if we find scars in the skin (our largest organ)

do we conclude the patient has a skin disease with the scars being the cause ?

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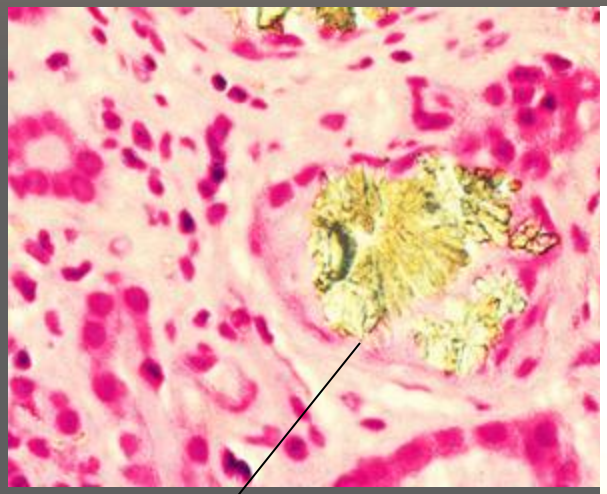
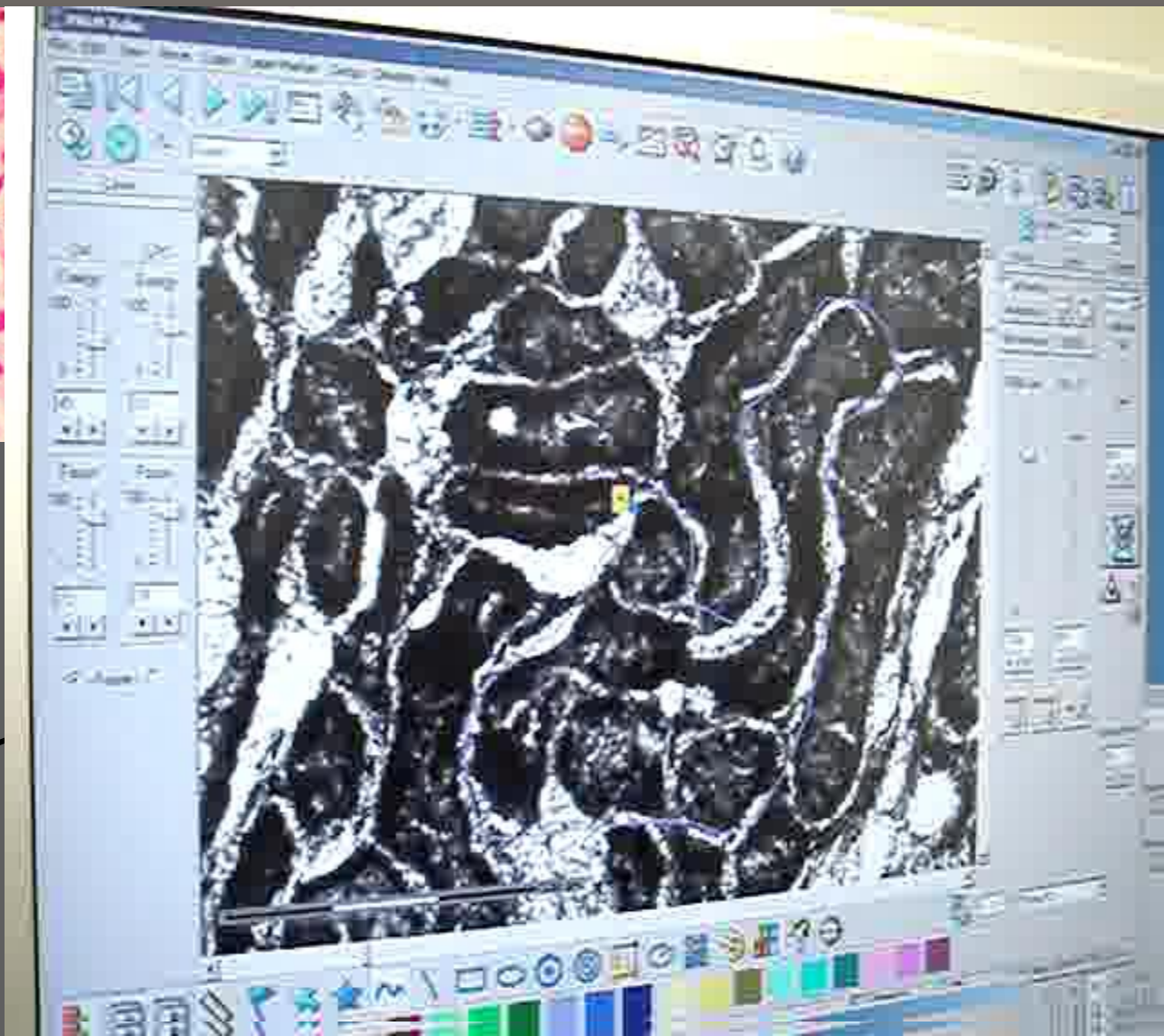
Microscope
Laser Dissection / Capture



removal of specific structures or cells for further analysis

using laser dissection to cut out structure and flipping it into a small container



GENERAL PATHOLOGY OBSERVATIONS

diagnostic pathology

based on observation, defined by the nature and progression of disease

most important in biopsy pathology – clinical pathology

in vivo **sampling of tissues:**

- **bone marrow**
- **tumor biopsies (during and after surgery)**

establish prospective behavior of disease (i.e. tumor)

GENERAL PATHOLOGY OBSERVATIONS

there is a future in pathology

morphology alone is not enough

future sequence of events:

1) DIAGNOSIS of DISEASE
2) DIAGNOSIS of ETIOLOGY **including new techniques that apply genetic factors**

3) SPECIFIC THERAPY **etiology / individual / family**

4) Designer THERAPY **drug metabolism / genetic profile**

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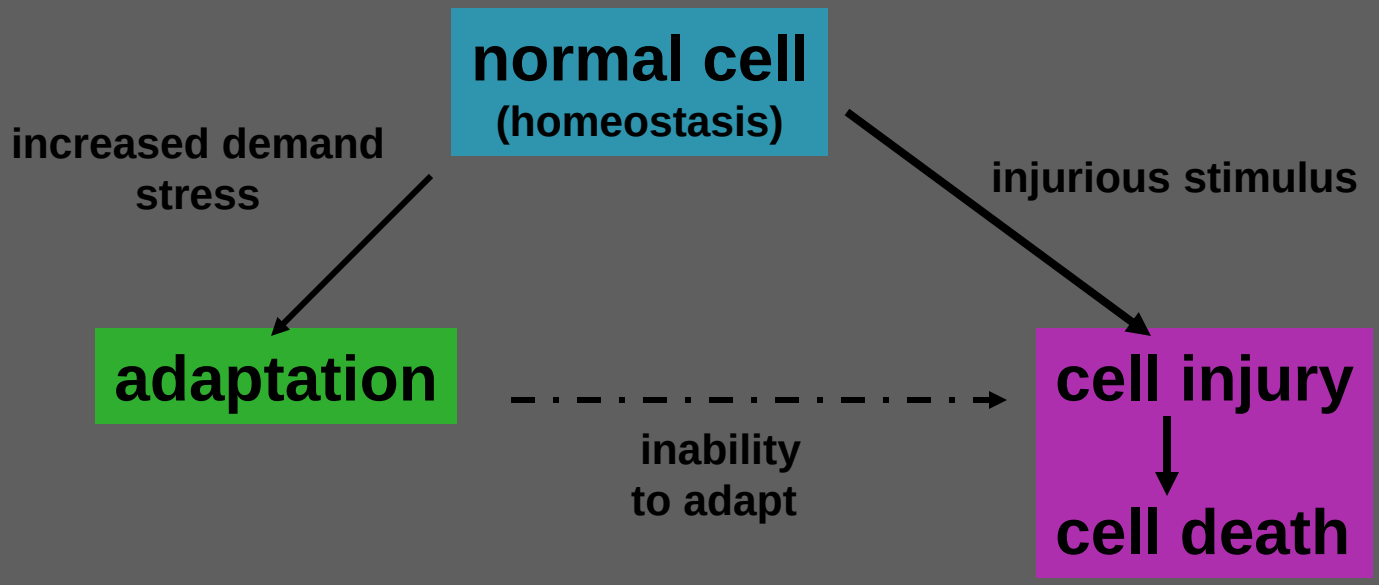
UNDERLYING MECHANISMS

the function is deranged
clinical manifestations
morphologic changes
distribution, degree

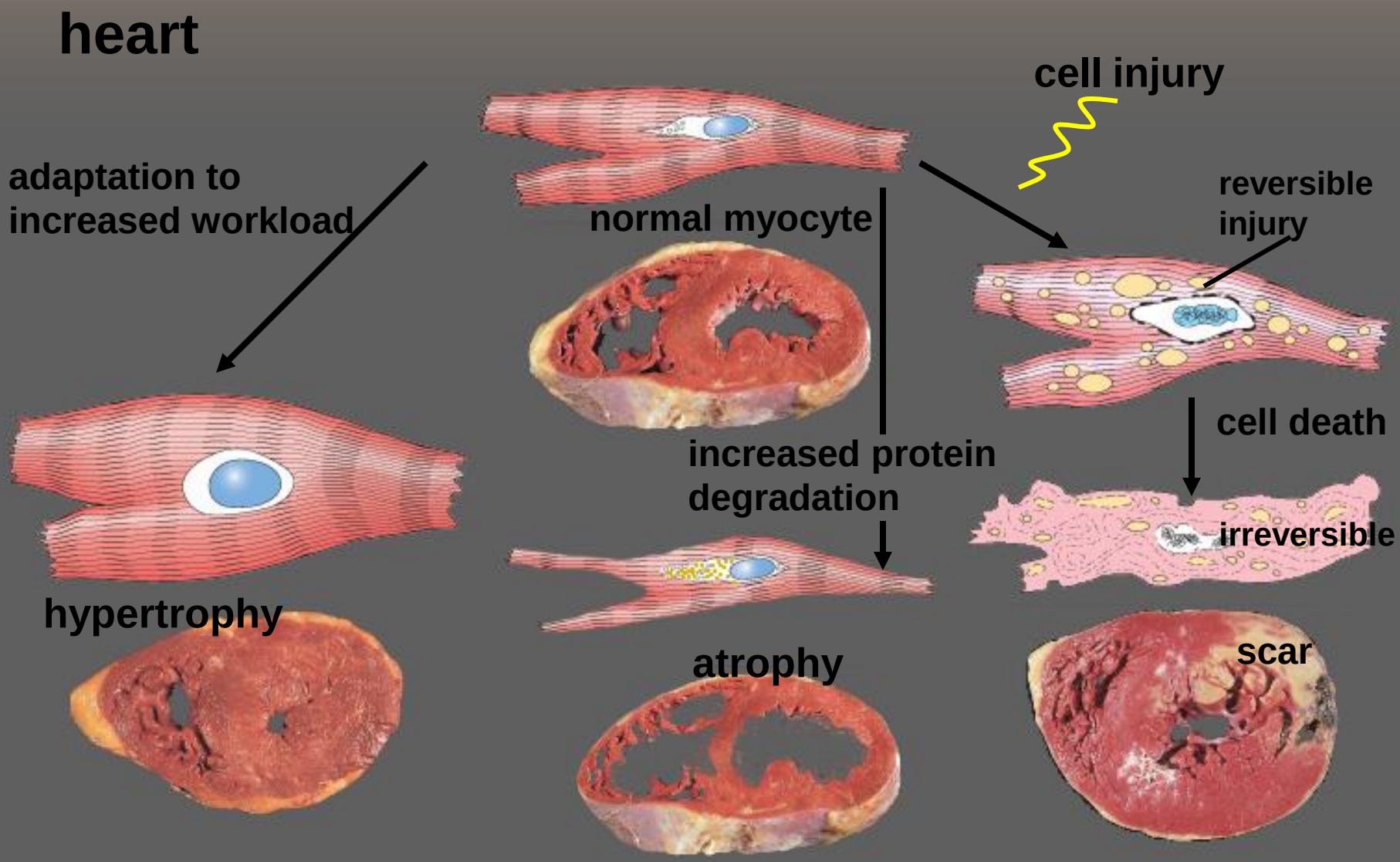
the principal changes occur at the level of the cell
molecular
structural

while the body reacts to injury the changes are happening at the cellular level

CELLULAR RESPONSE TO STIMULI



CELLULAR ADAPTATION



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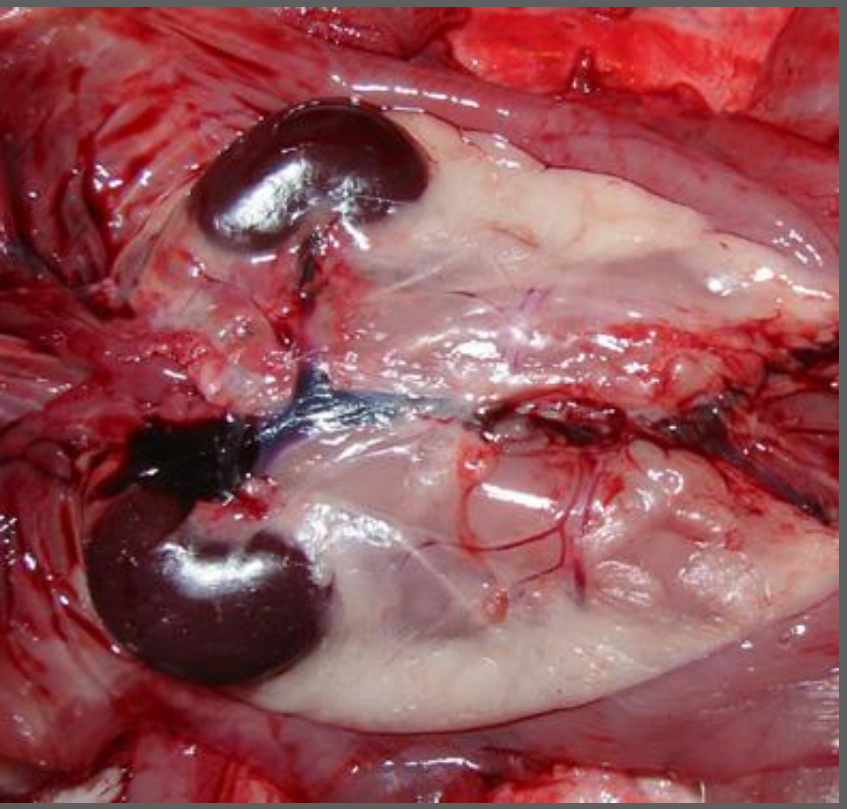
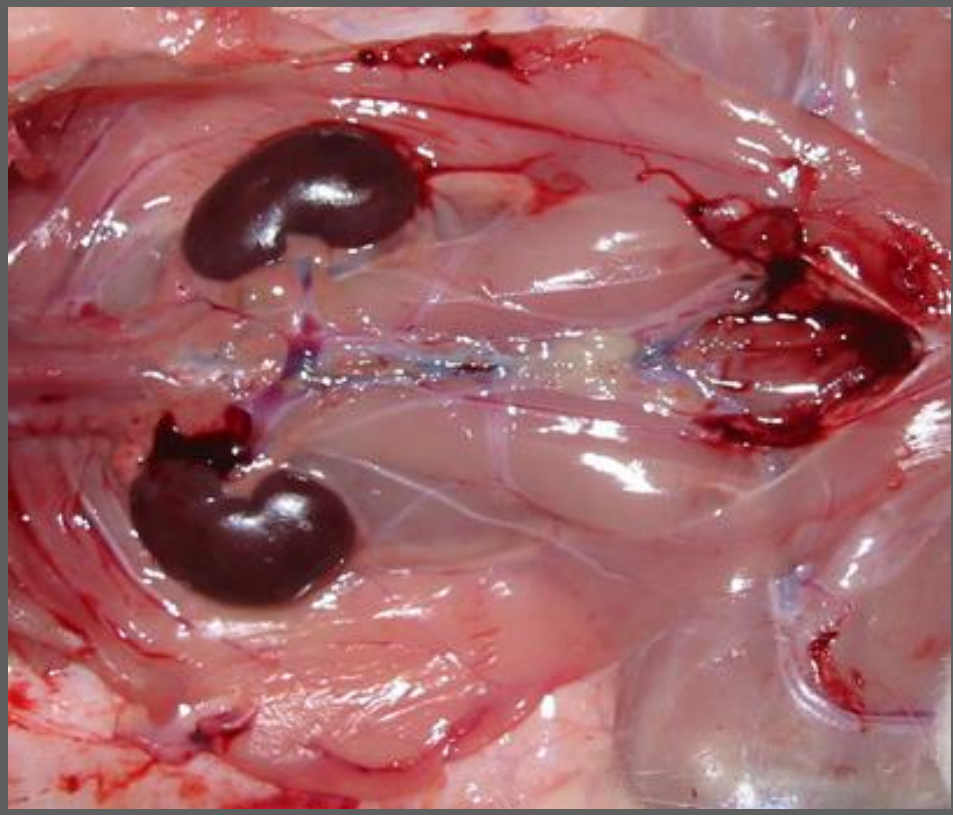
CELLULAR ADAPTATION

normal



marginal nutrition



atrophy of fat reserves around kidney

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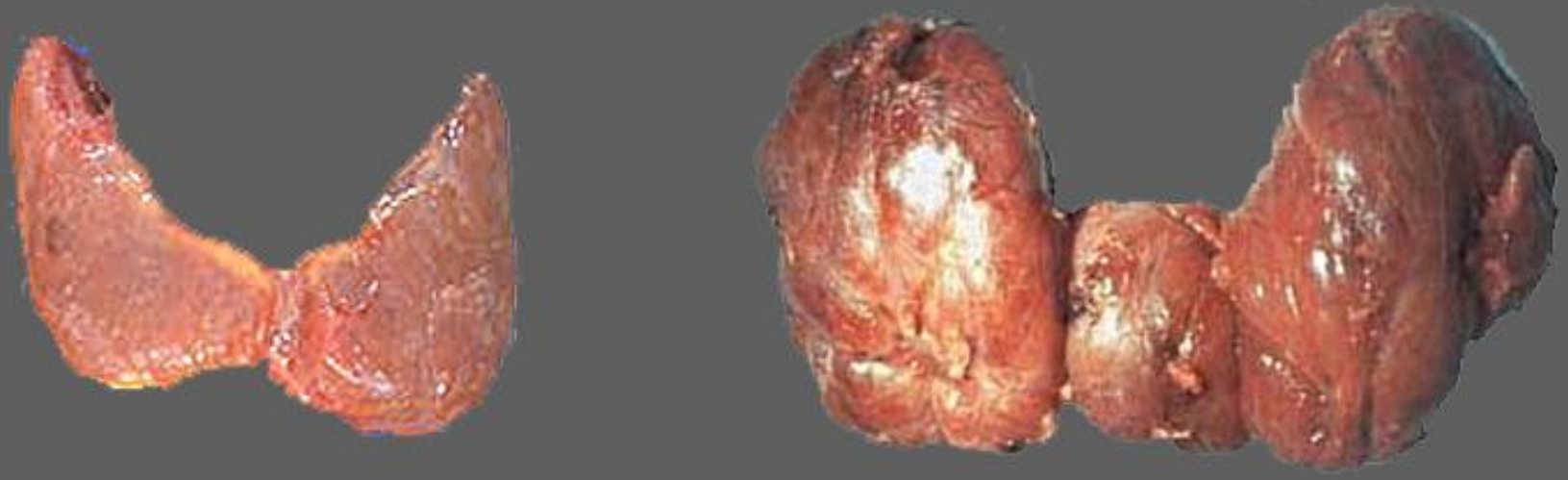
CELLULAR ADAPTATION

hyperplasia

increase in growth factors leading to cellular proliferation



thyroid hyperplasia
as a result of hormonal stimuli

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CELLULAR ADAPTATION

abnormal hyperplasia

leading to abnormal function
hyperplasia without control

could lead to tumors, cancer

CELLULAR ADAPTATION

abnormal hyperplasia — **- beyond adaptation**

leading to abnormal function — **- cells active in function**
measurable output
with secondary systemic changes

hyperplasia without control — **- growth of cells, organs**
at variable accelerated speed
cells with / without function
space occupying

could lead to tumors, cancer — **- secondary effects of cancer**
abnormal chemicals produced
space occupying

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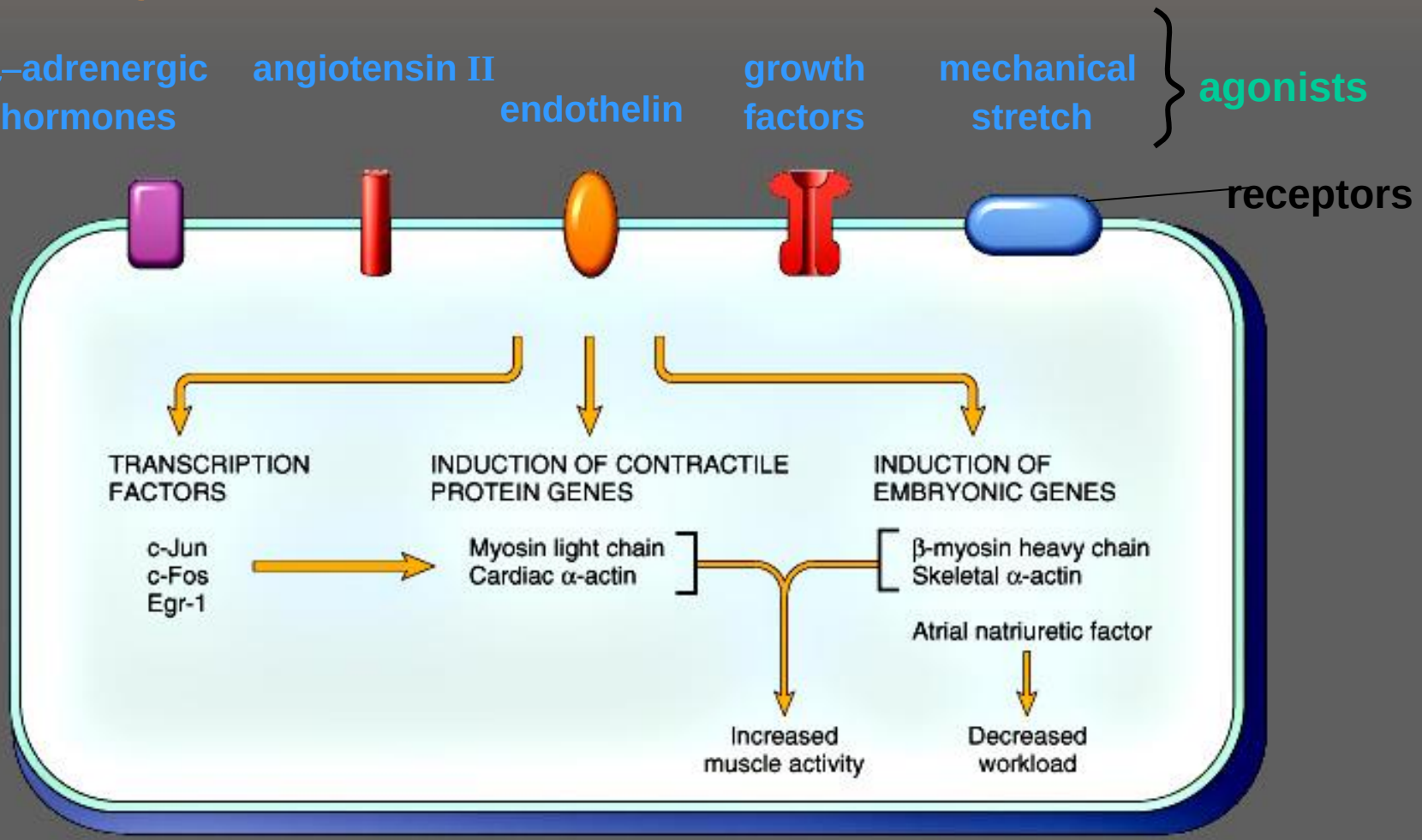
GENE EXPRESSION IN HYPERTROPHY

heart, myocardium



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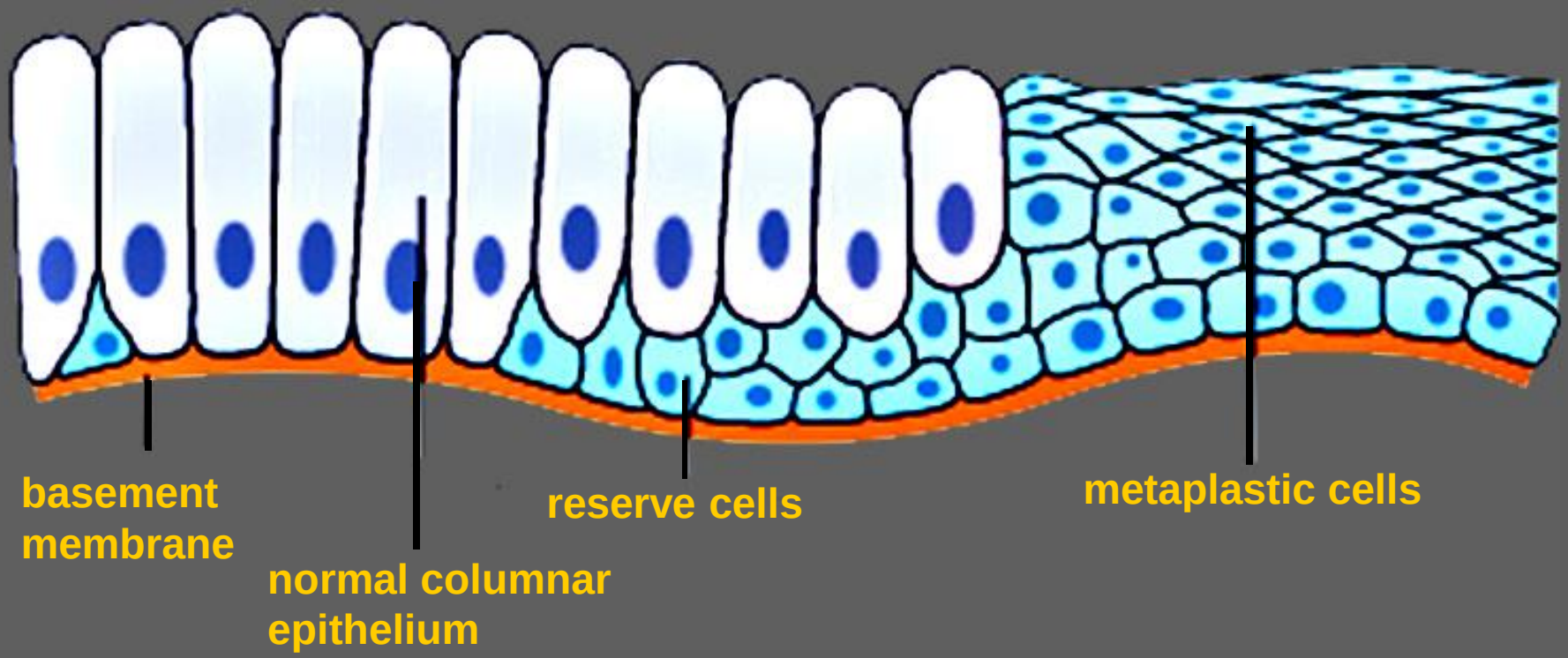
METAPLASIA

SQUAMOUS METAPLASIA OF EPITHELIUM

columnar → chronic irritation → squamous



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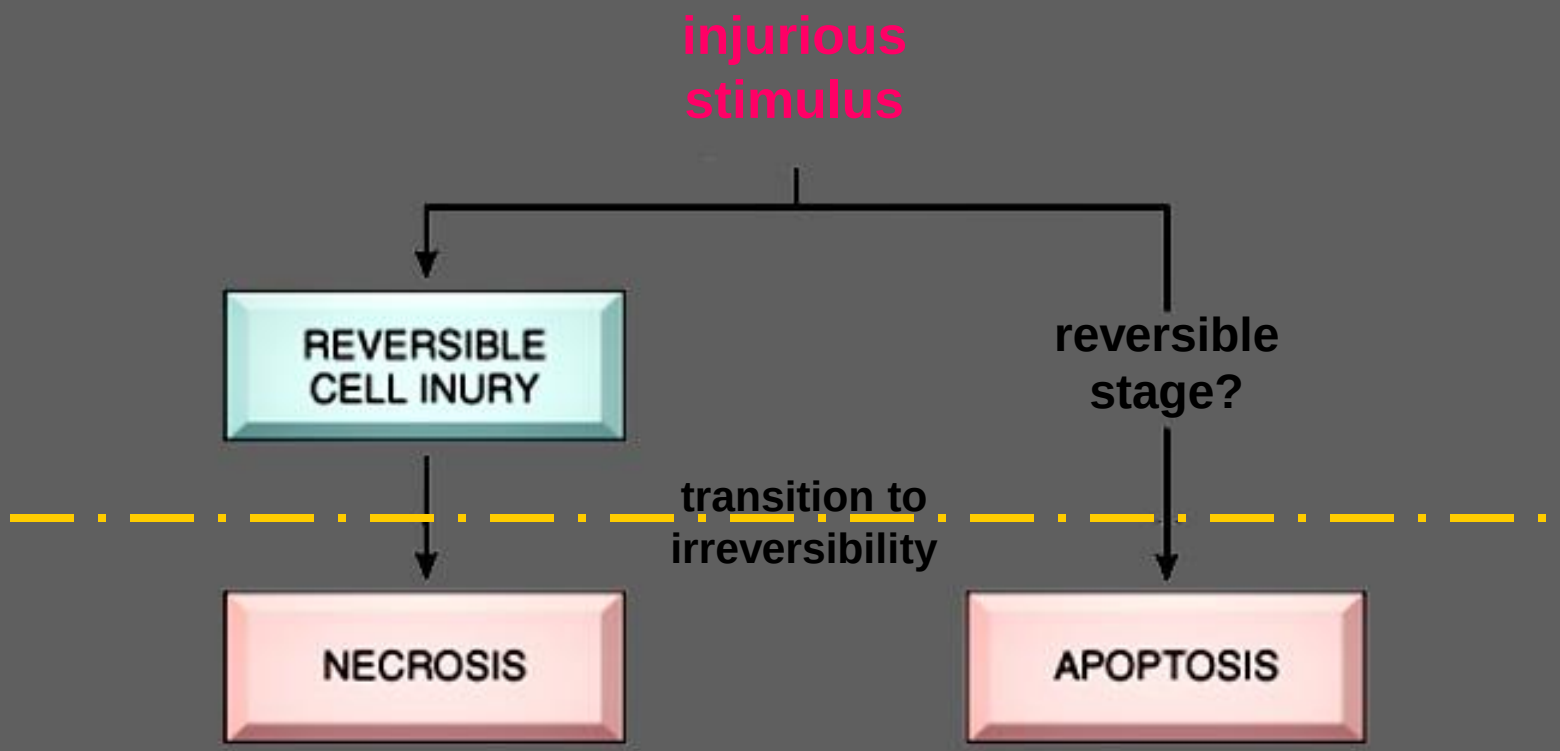
EVOLUTION OF CELL INJURY, DEATH



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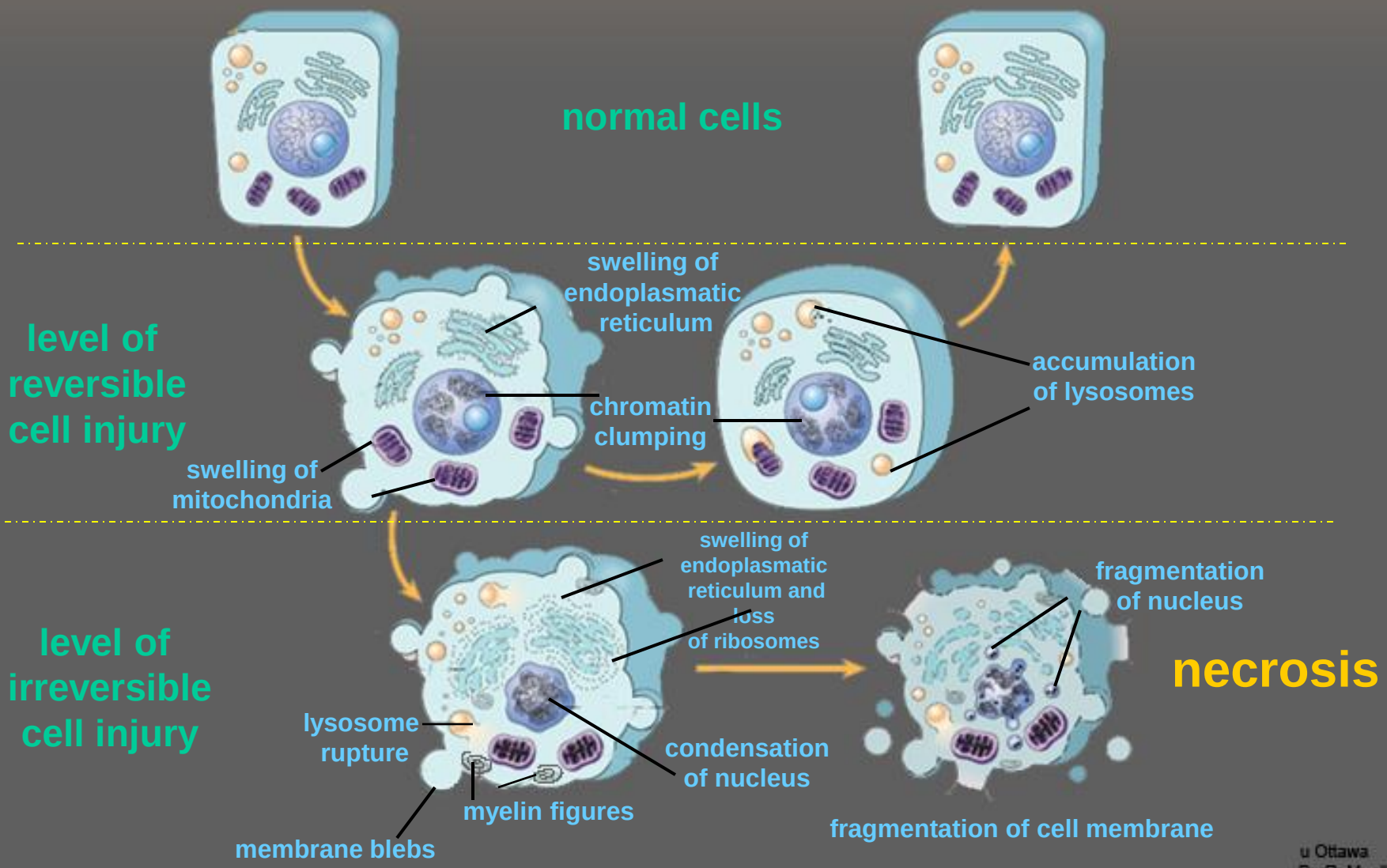
CELL INJURY



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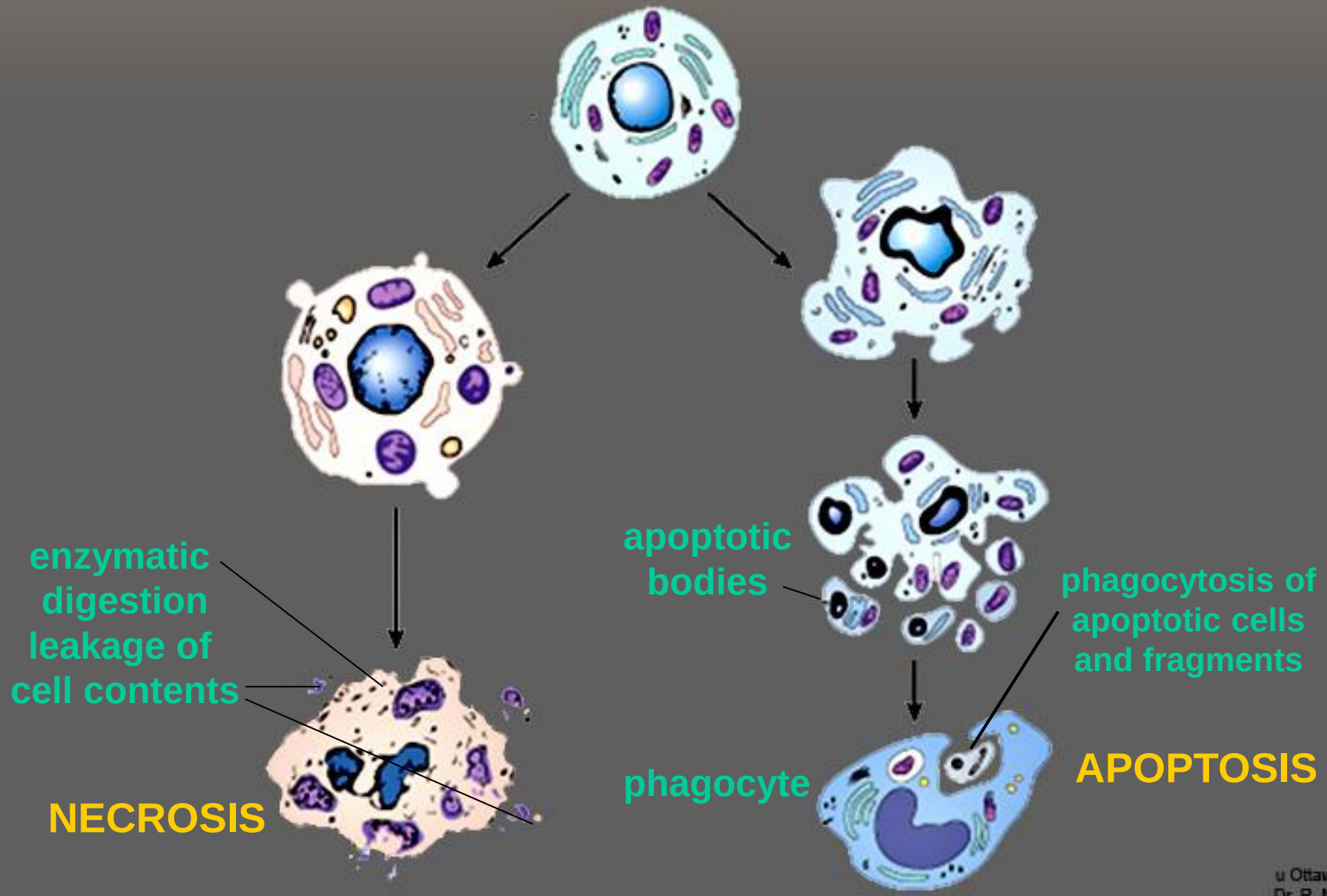
NECROSIS vs APOPTOSIS



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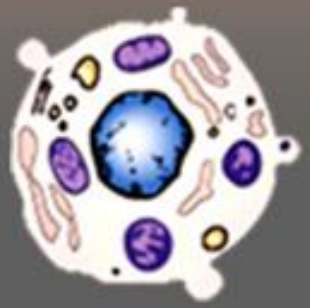
NECROSIS vs APOPTOSIS

cell enlarged, swelling		cell size reduced shrinkage
nucleus pyknosis kariorrhexis kariolysis		fragmentation nucleosome sized fragments
disrupted plasma membrane		intact plasma membrane with altered structure
enzymatic digestion of cellular contents		intact cellular contents apoptotic bodies
inflammation		no infl.
pathologic, related to disease		physiologic, often

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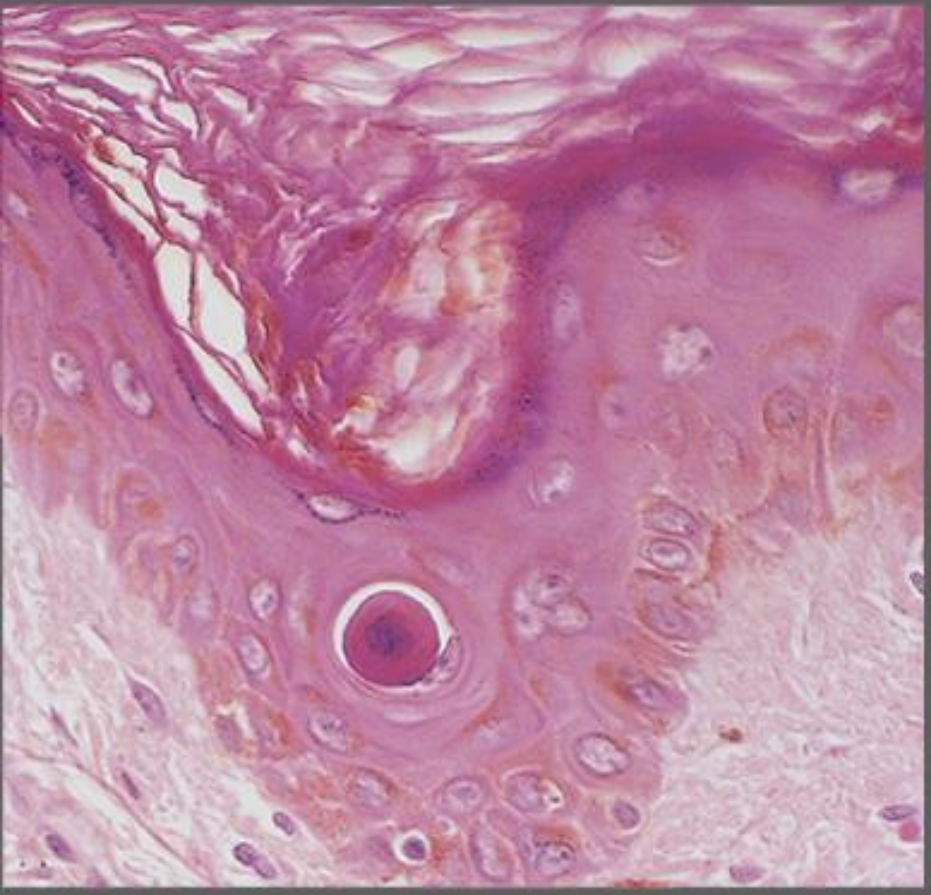
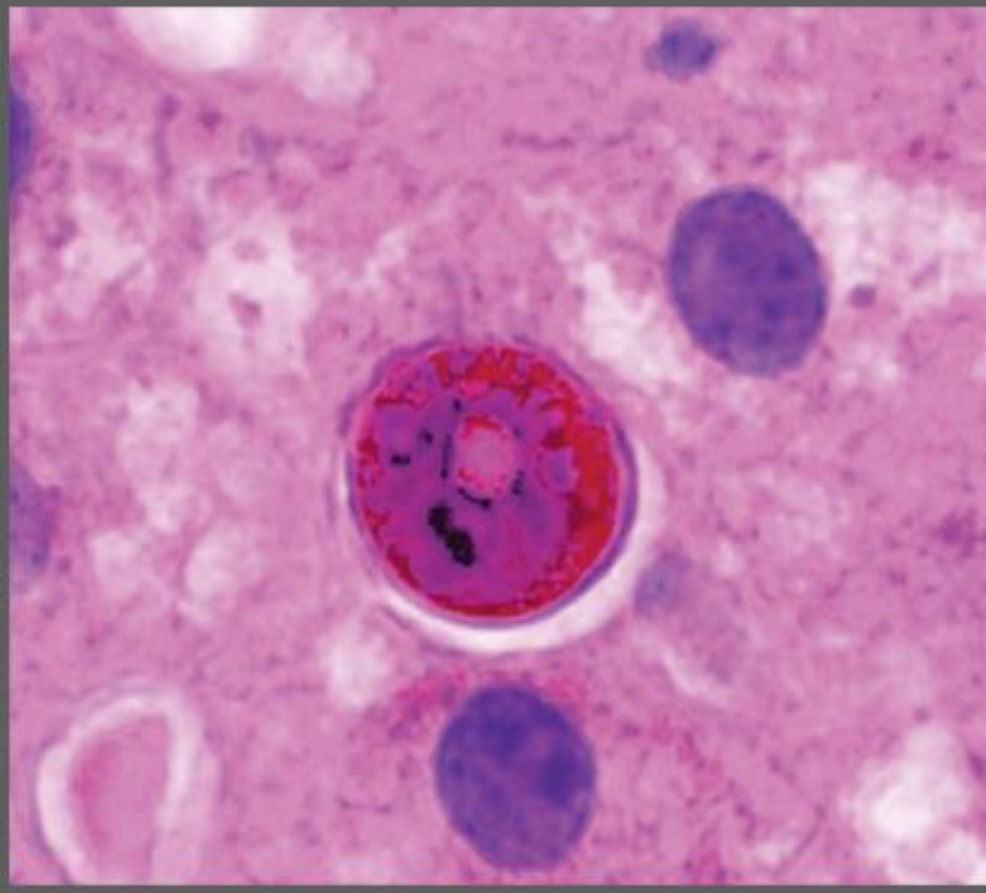
CELLULAR ADAPTATION

histology of apoptosis





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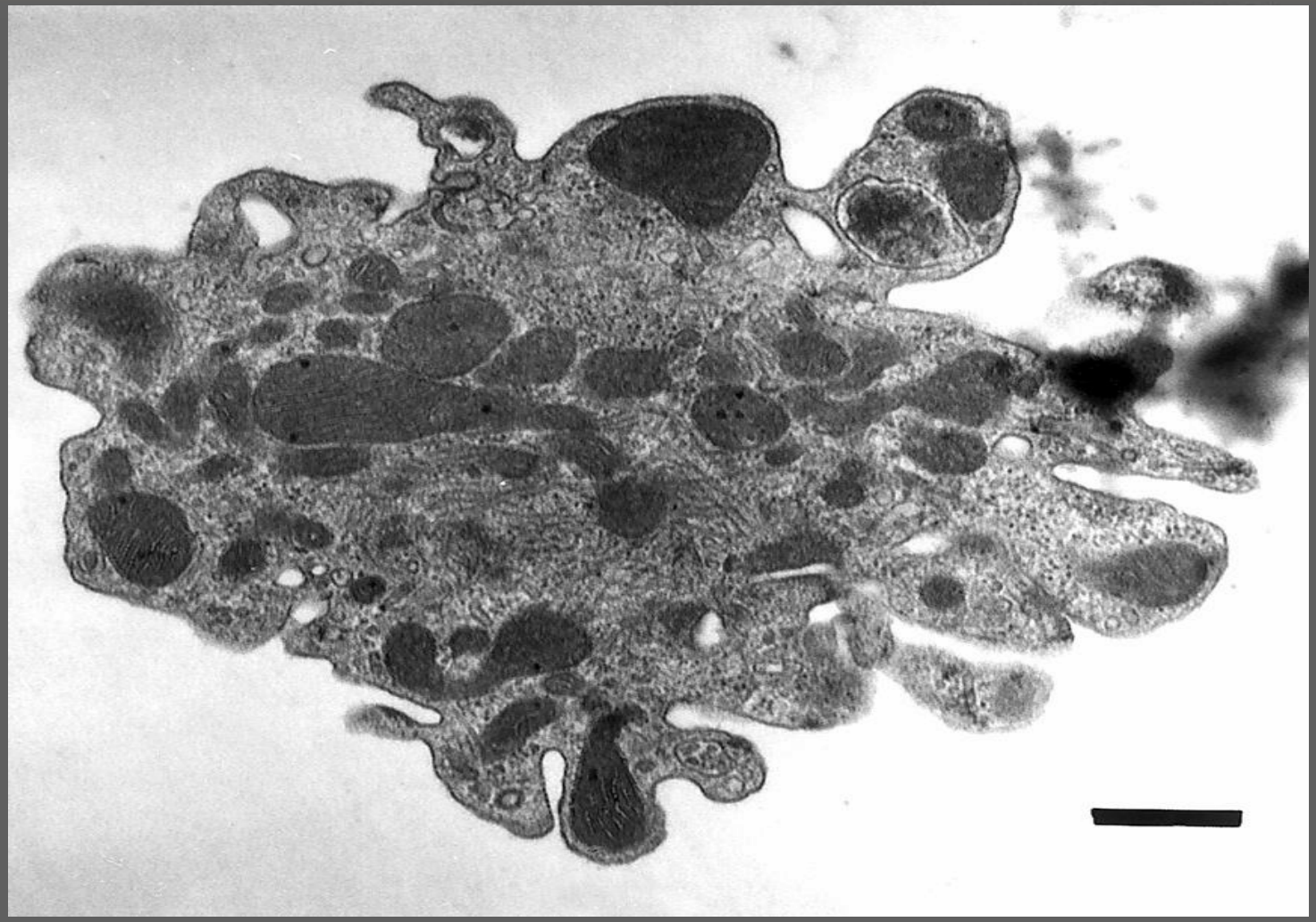
CELLULAR ADAPTATION

apoptosis electron microscopy



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MECHANISMS OF APOPTOSIS

intrinsic
(mitochondrial)

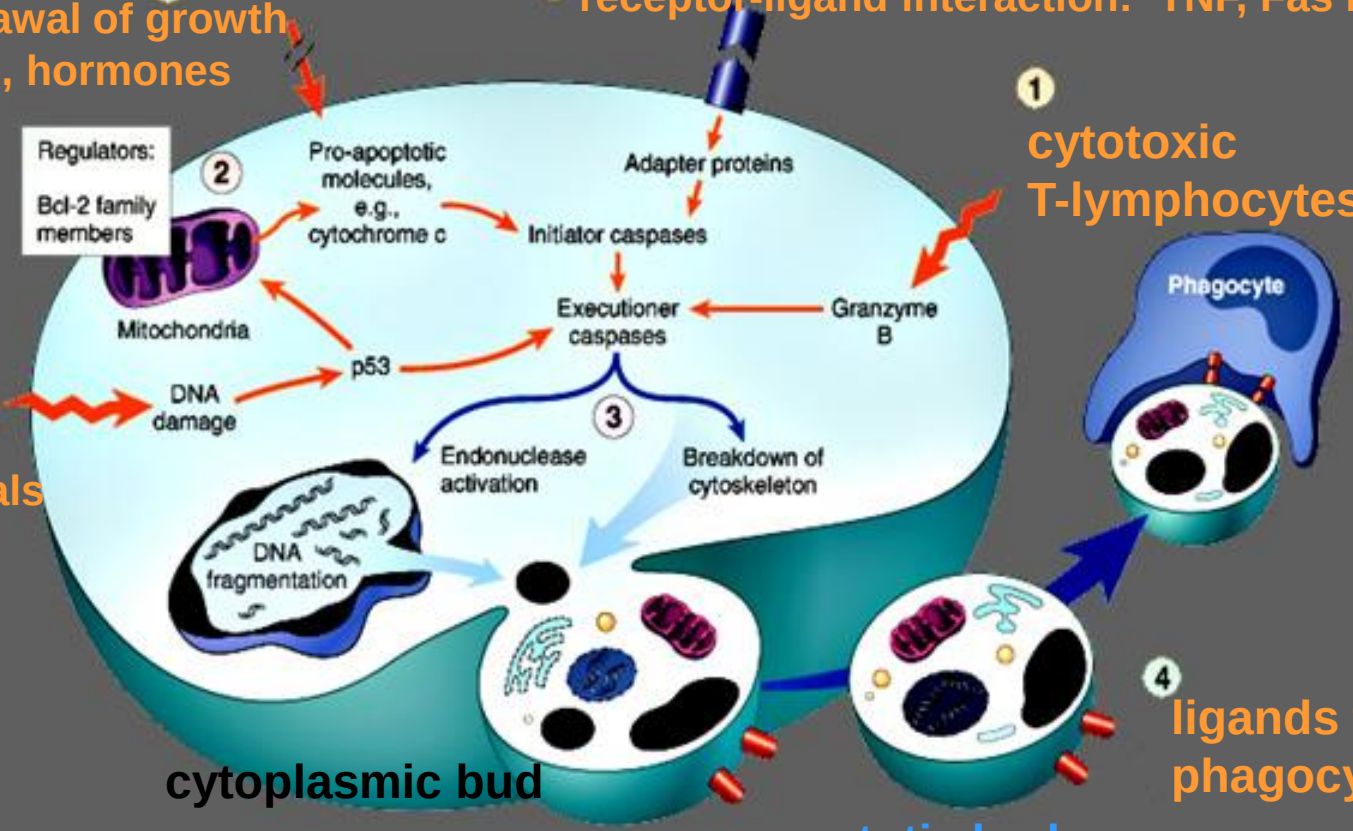
extrinsic
(death receptor-initiated)

1 withdrawal of growth factors, hormones

1 receptor-ligand interaction: TNF, Fas receptors

1 cytotoxic T-lymphocytes

1 injury
- radiation
- toxins
- free radicals



cytoplasmic bud

apoptotic body

4 ligands for phagocytic cells

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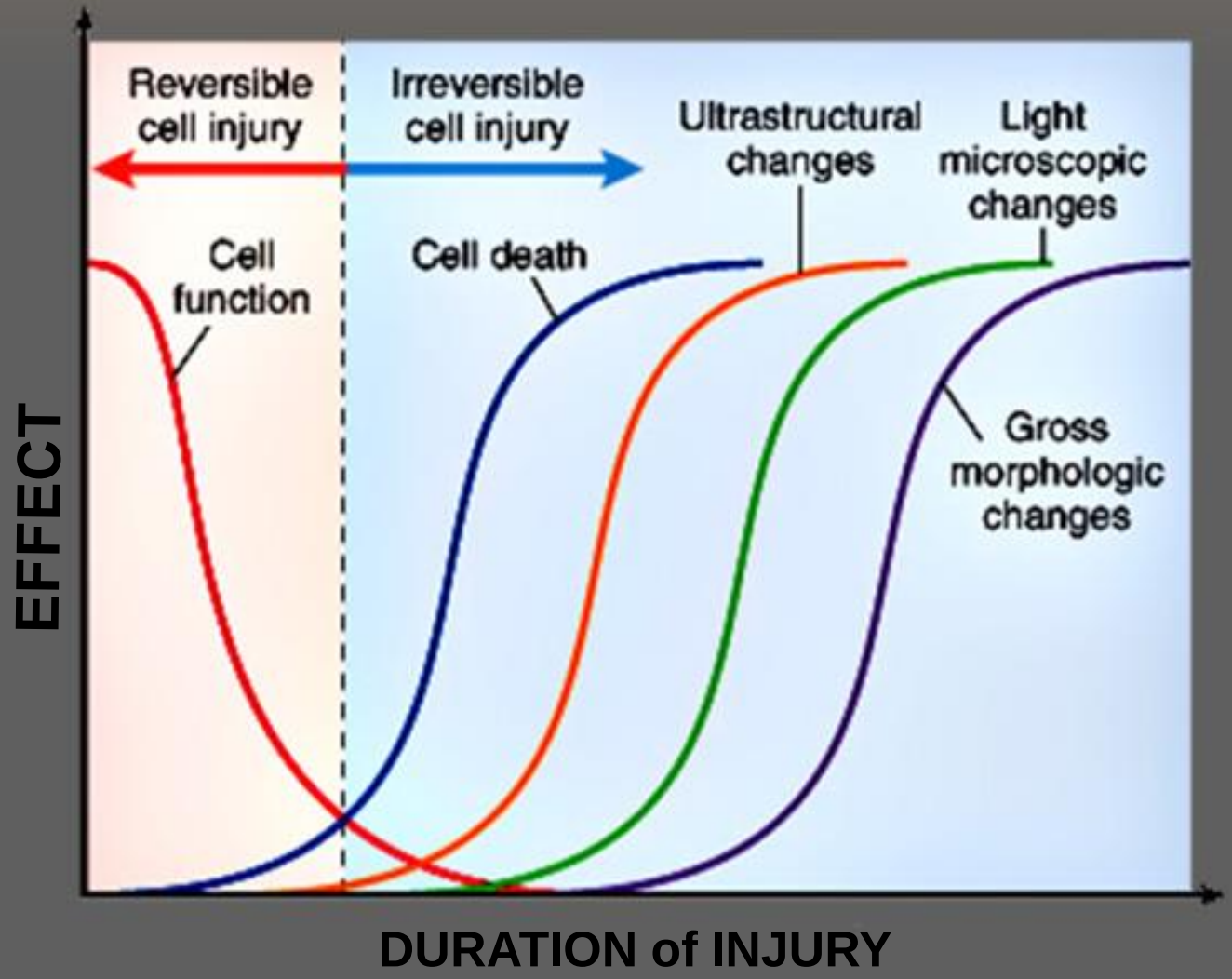
REVERSIBLE - IRREVERSIBLE



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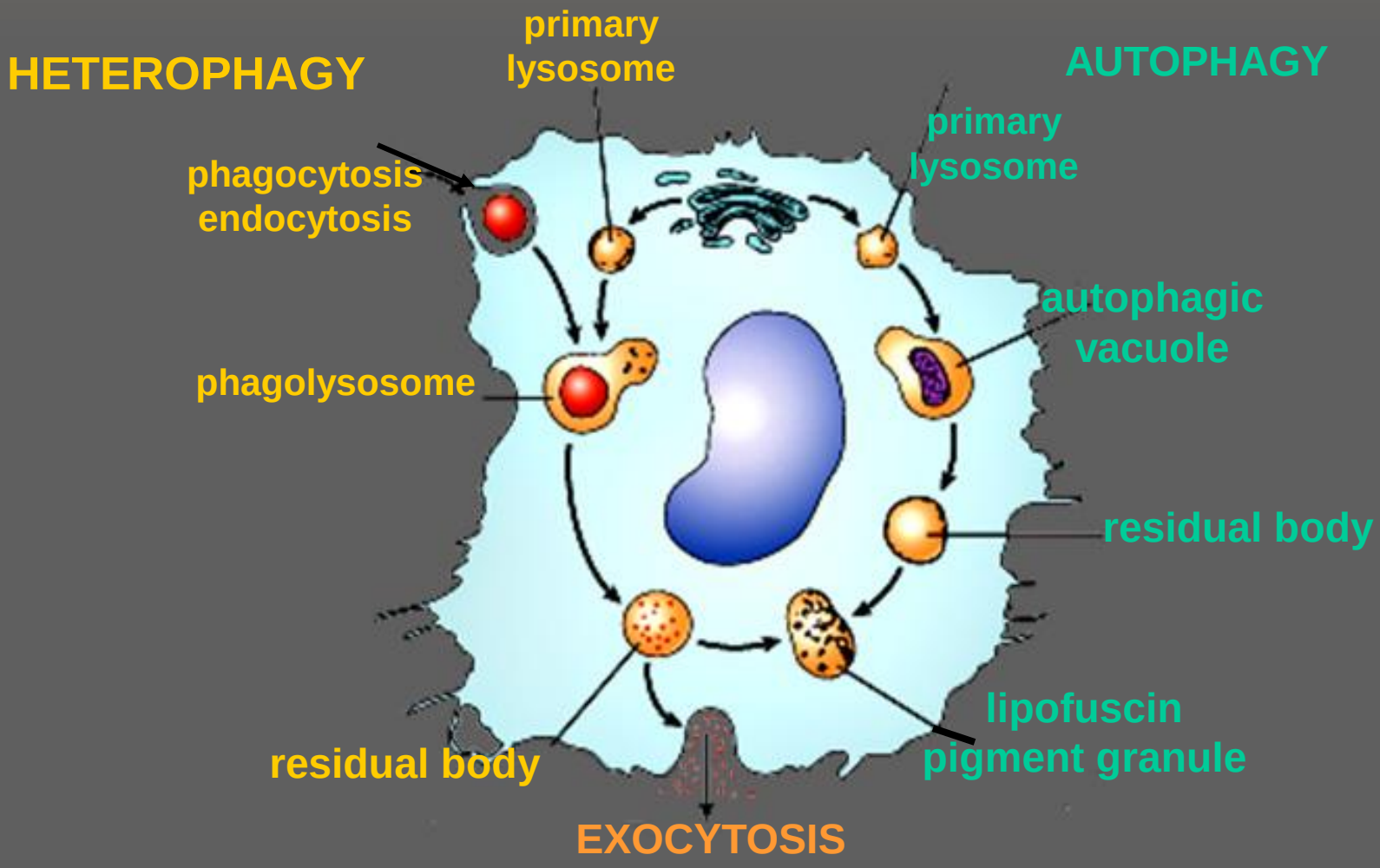
CELLULAR RESPONSE TO INJURY



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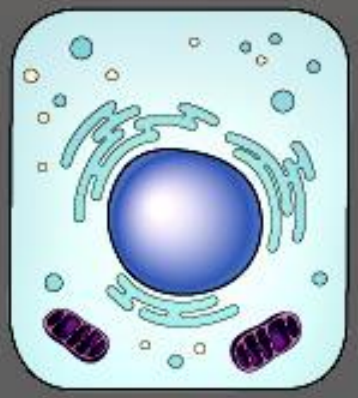
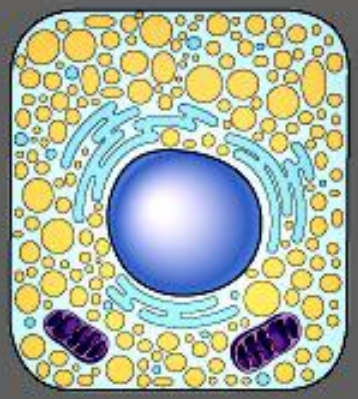
INTRACELLULAR ACCUMULATIONS

normal cell



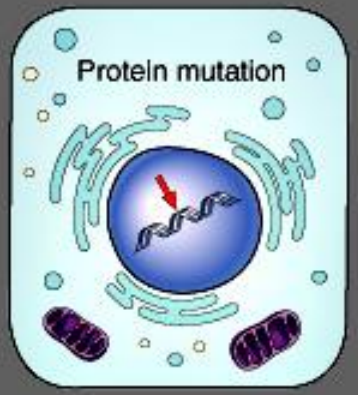
abnormal metabolism

toxins, drugs

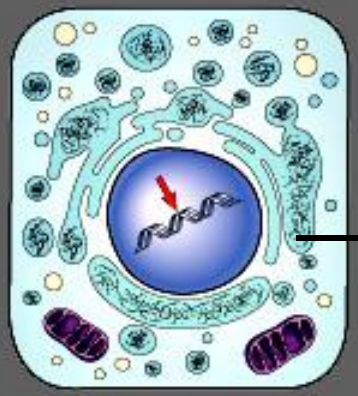


fatty liver

alteration in protein folding



protein folding transport



aggregation of abnormal proteins

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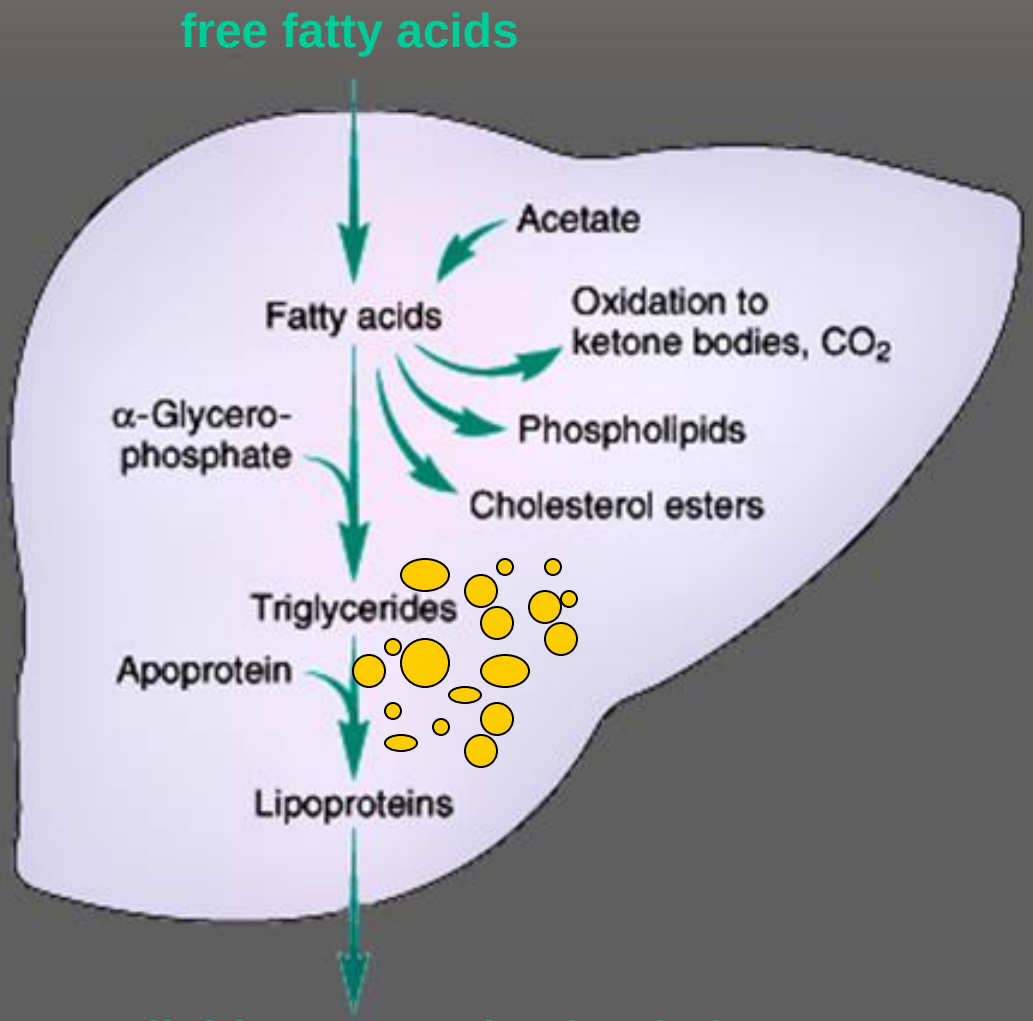
FATTY LIVER

UPTAKE

CATABOLISM

SECRETION



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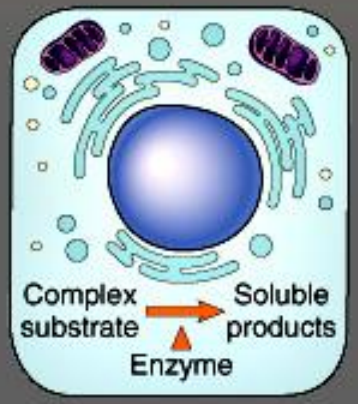
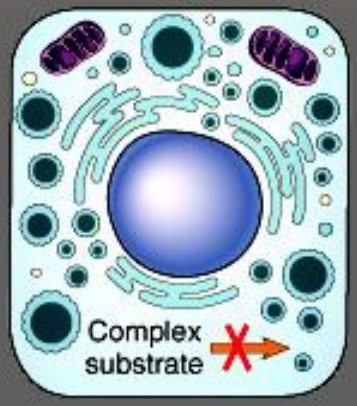
INTRACELLULAR ACCUMULATIONS

enzyme deficiency

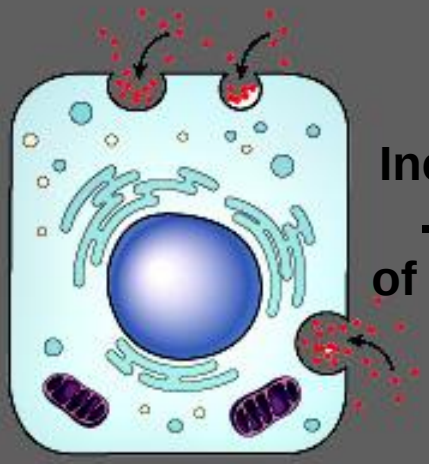


lack of enzyme → inhibition of enzyme

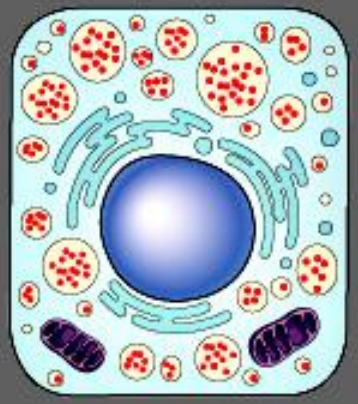


storage, accumulation of endogenous materials

phagocytosis of particles



Incorporation → of indigestible materials



accumulation of exogenous materials

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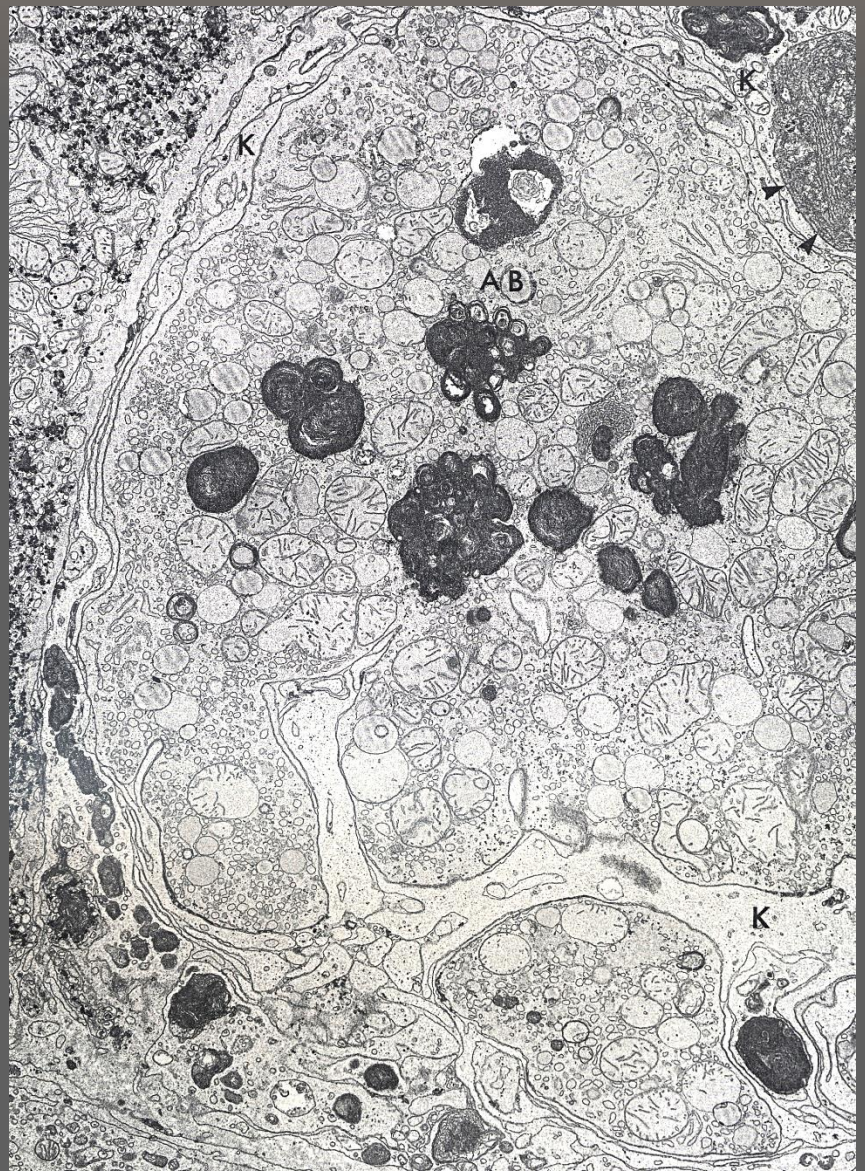
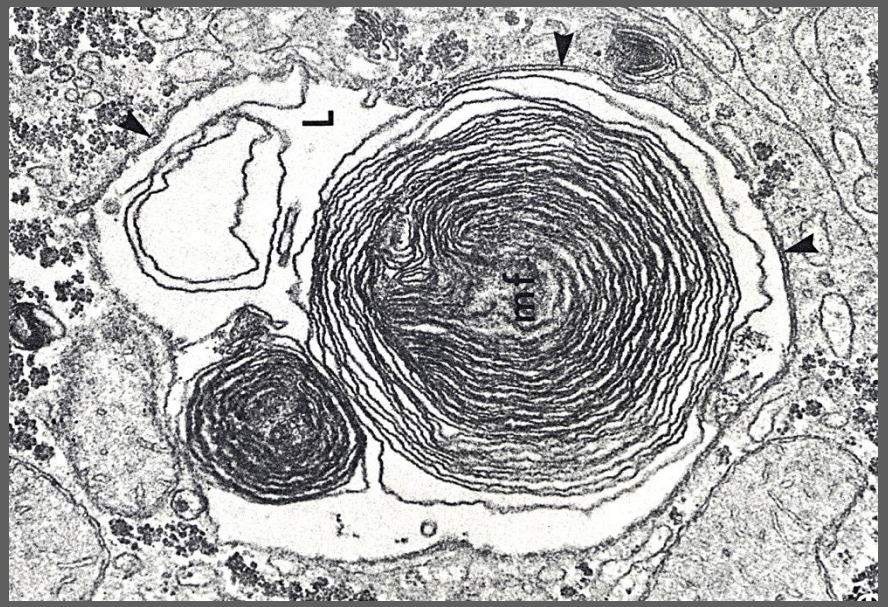
PHOSPHOLIPIDOSIS



resulting from interference with lysosomal enzymes



intracellular accumulation of phospholipids, membrane remnants

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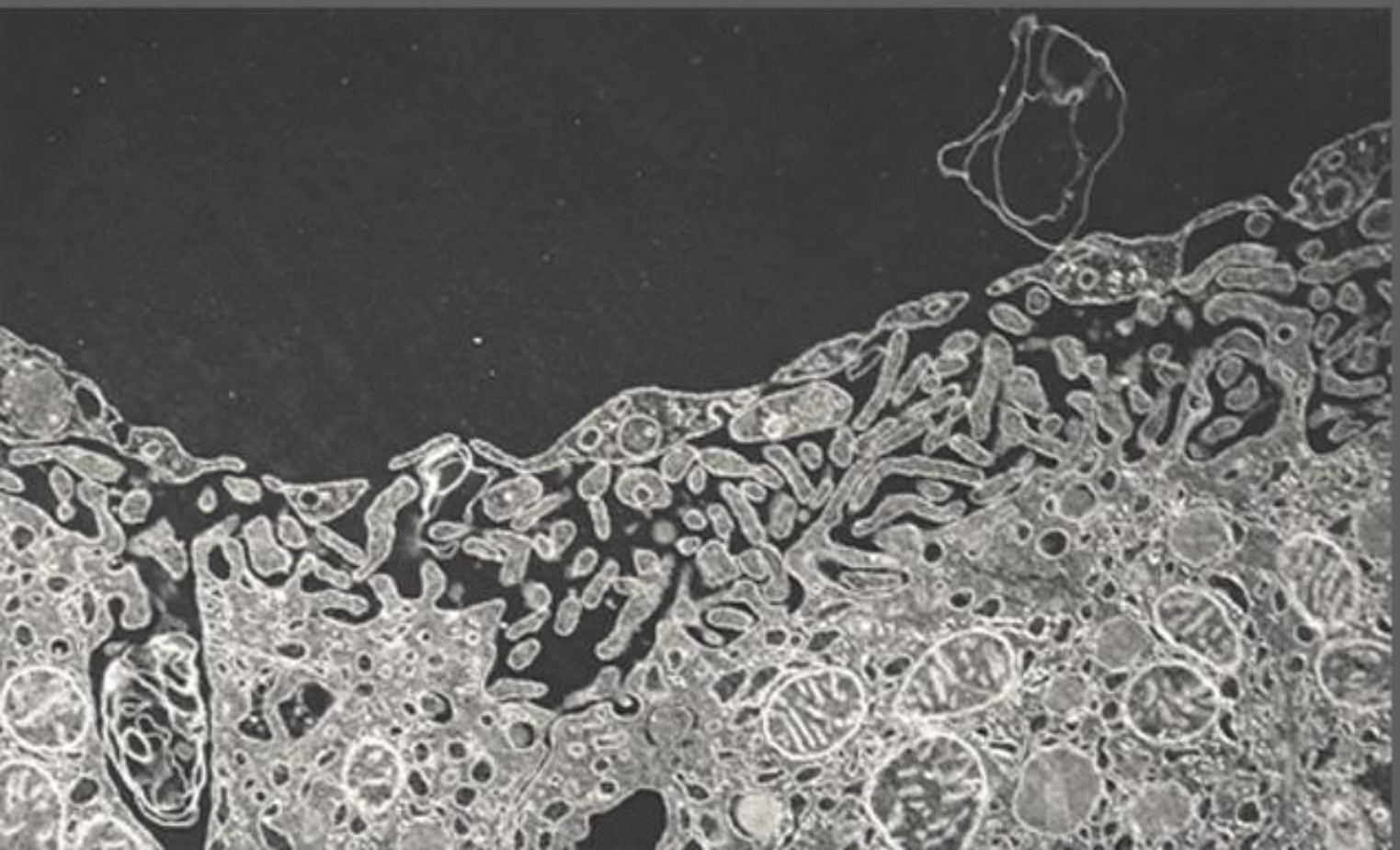
PHOSPHOLIPIDOSIS

expulsion of phospholipids from hepatocytes



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CELLULAR RESPONSE TO STIMULY

altered physiology → **cellular adaptation**

- increased demand
- decreased nutrients
- chronic irritation

- hyperplasia hypertrophy
- atrophy
- metaplasia

reduced oxygen supply
chemical injury
microbial infection → **cell injury**

- acute self limited
- progressive, severe
- mild chronic

- reversible
- irreversible: (necrosis)
- subcellular (organelles)

metabolic alteration
genetic / acquired → **intracell. accumulation**
calcification

prolonged lifespan
cumulative, sub-lethal injury → **cellular aging**

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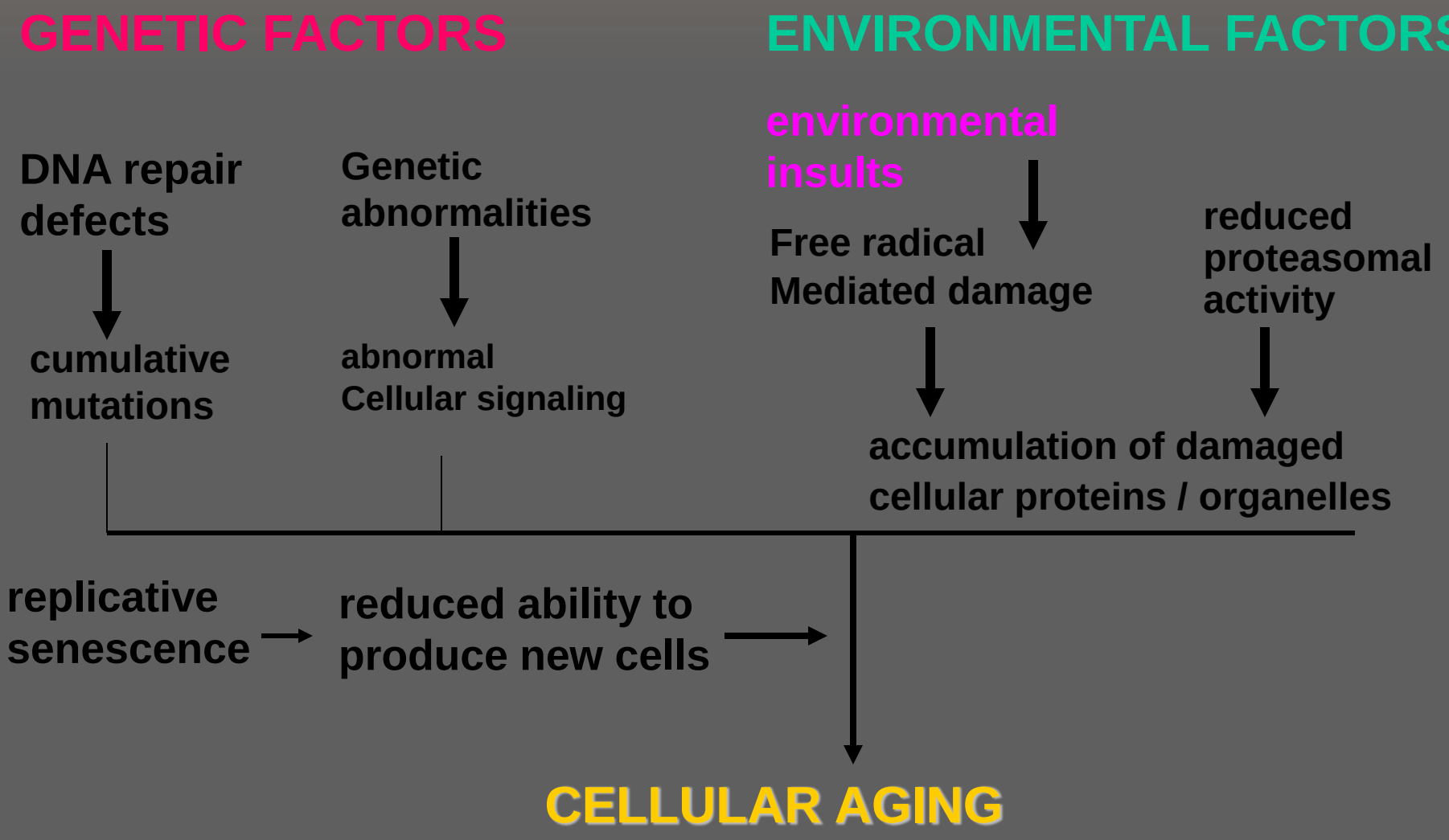
CELLULAR AGING



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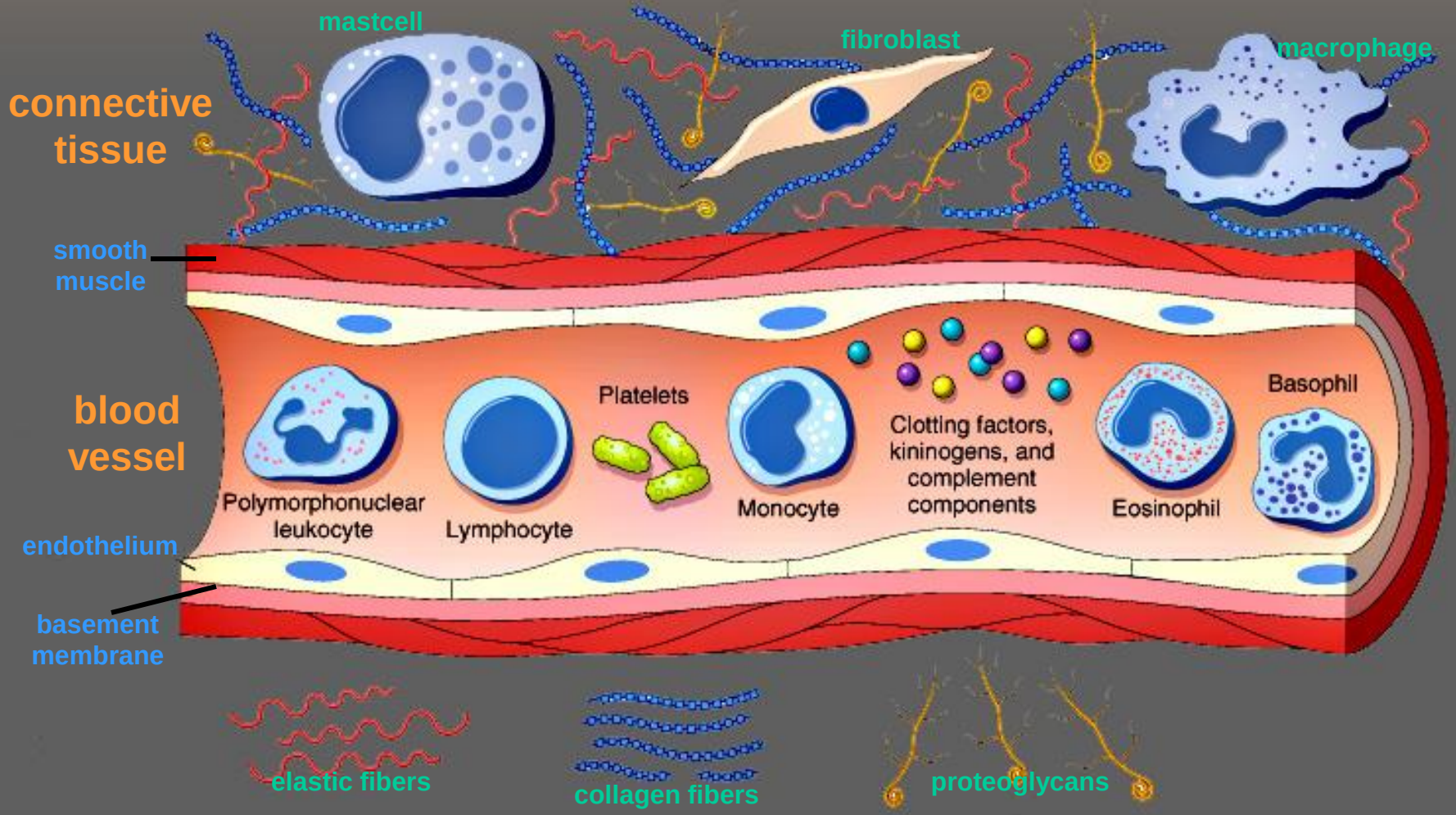
INFLAMMATION

inflammation interacts with repair

regenerative processes

stimulation of inflammation by
- **tissue necrosis**
- **foreign bodies**
- **immune reactions**

ACUTE and CHRONIC INFLAMMATION



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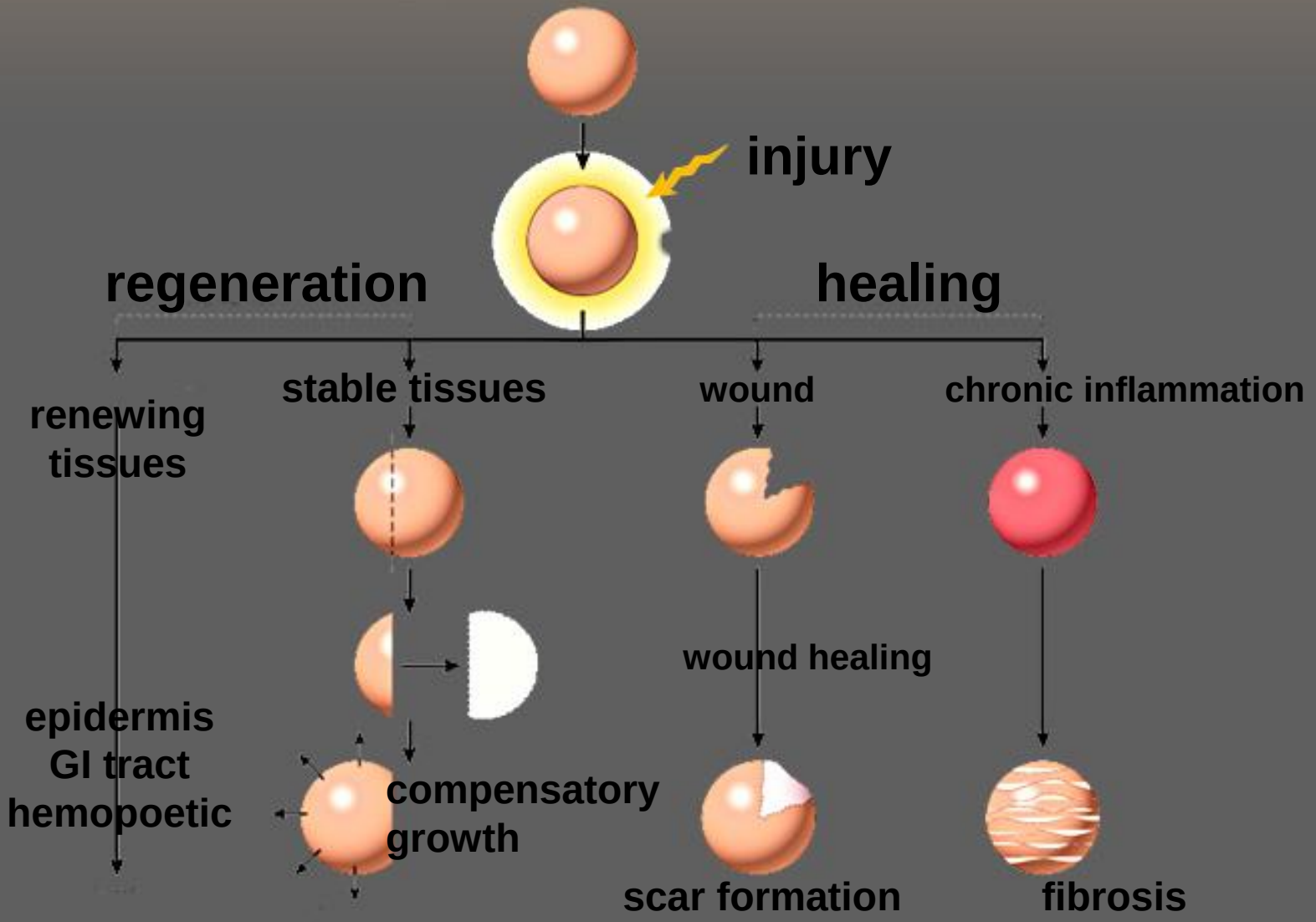
TISSUE RESPONSE TO INJURY



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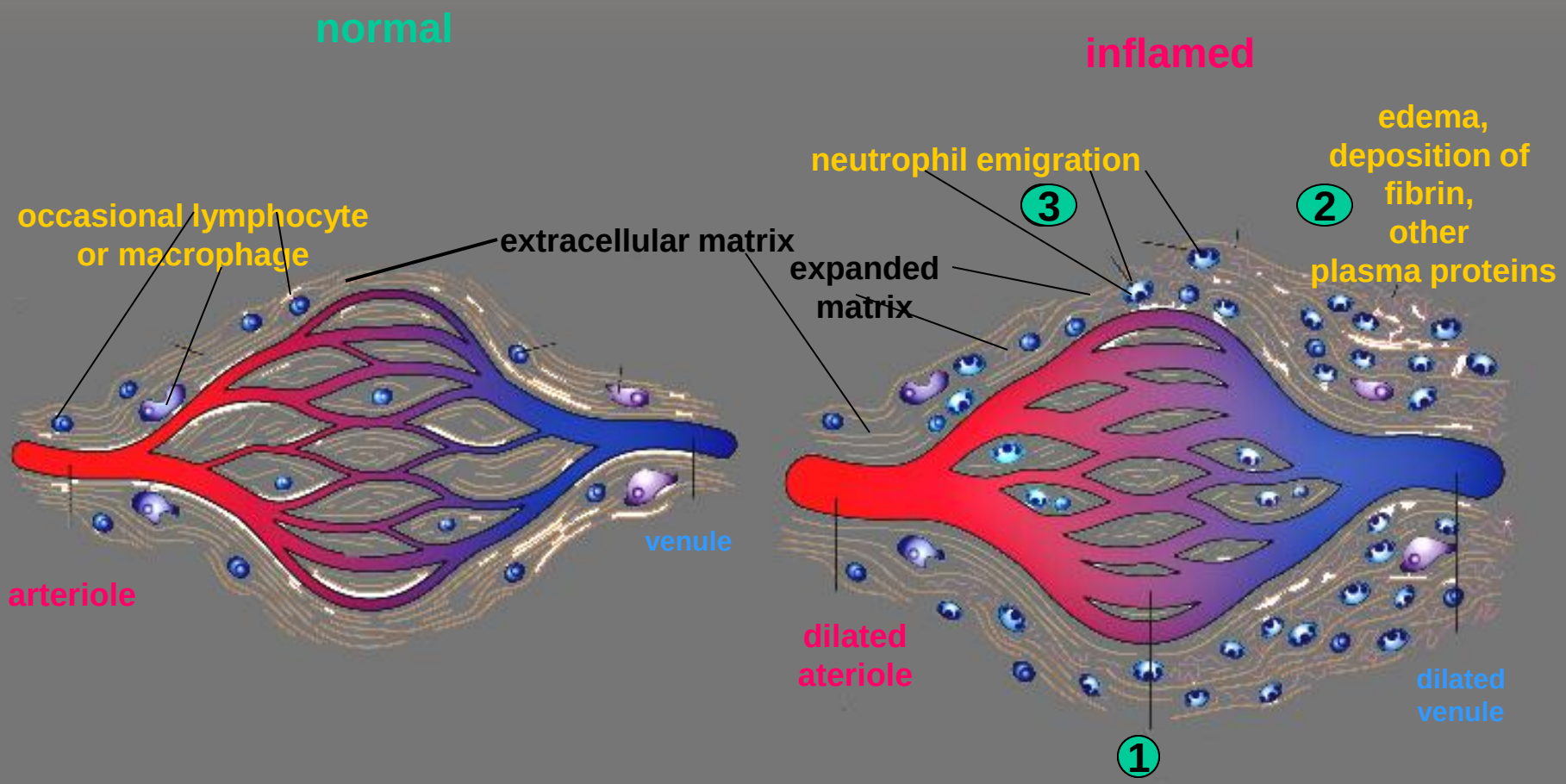
ACUTE INFLAMMATION



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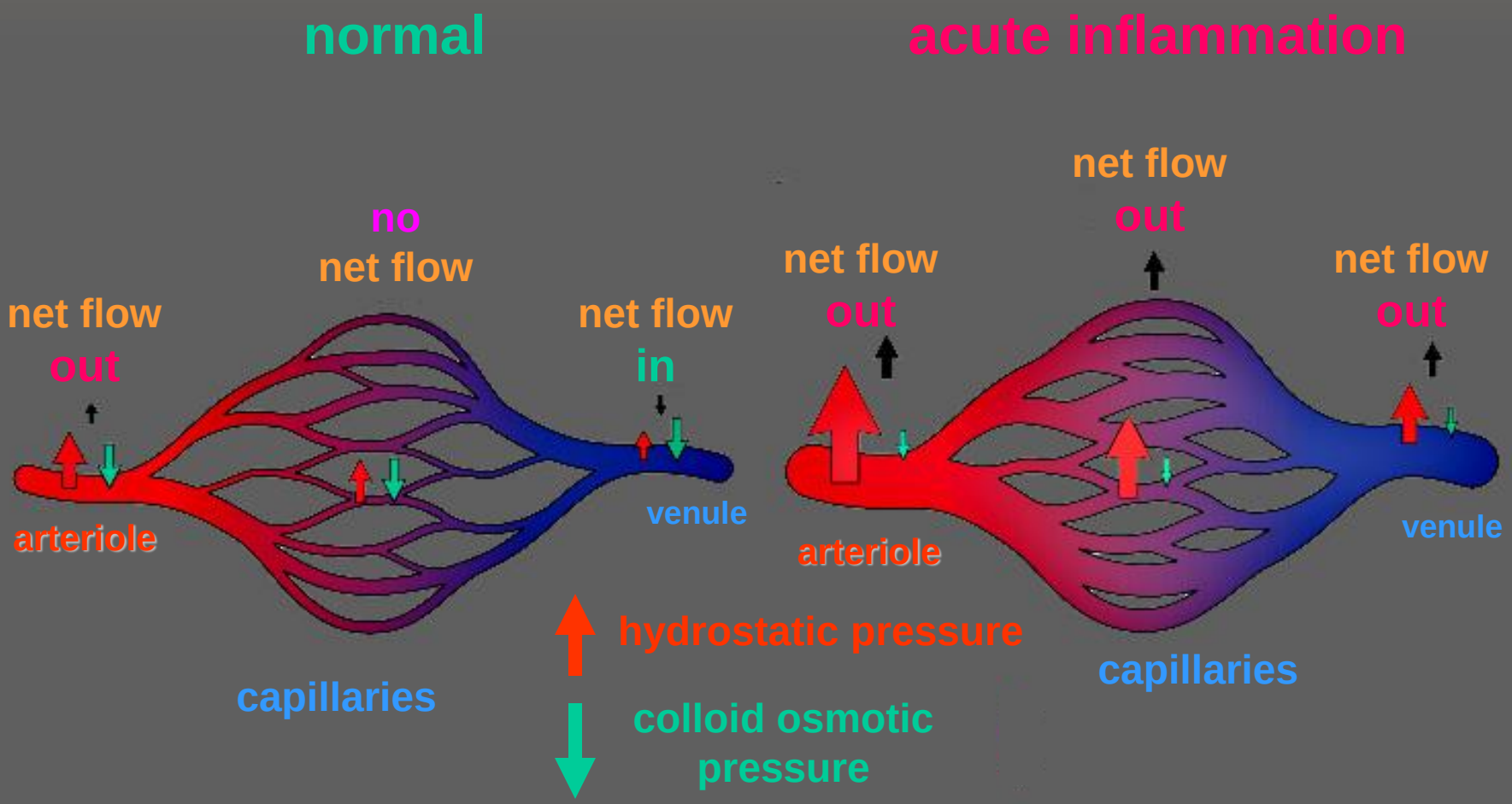
INFLAMMATION in MICROCIRCULATION



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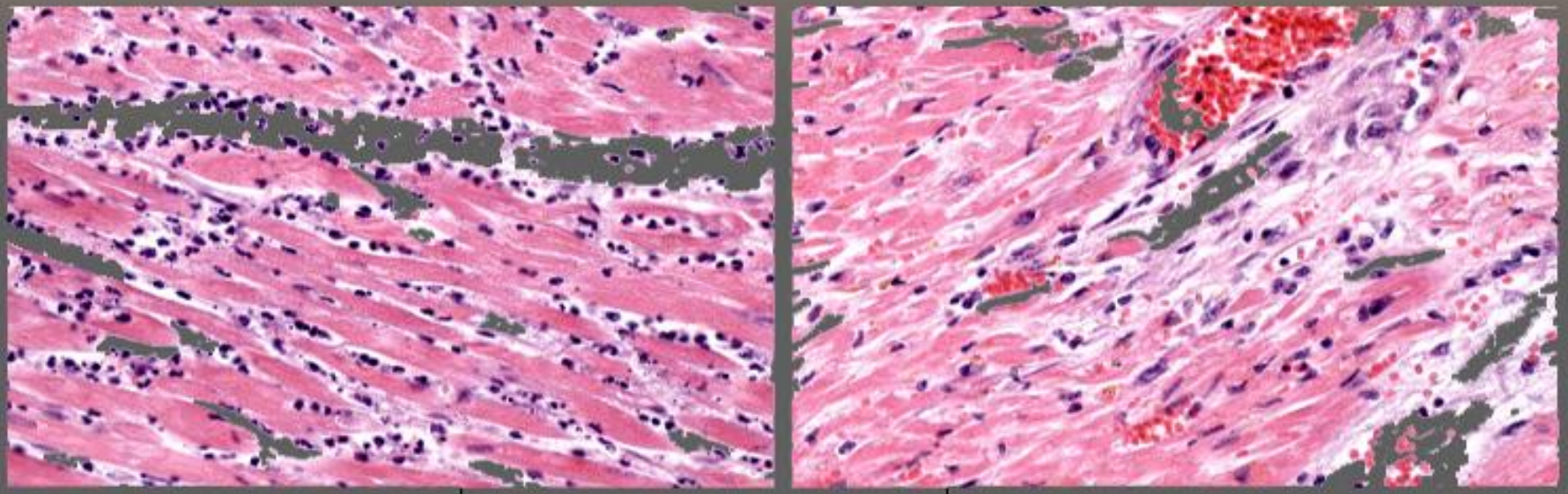
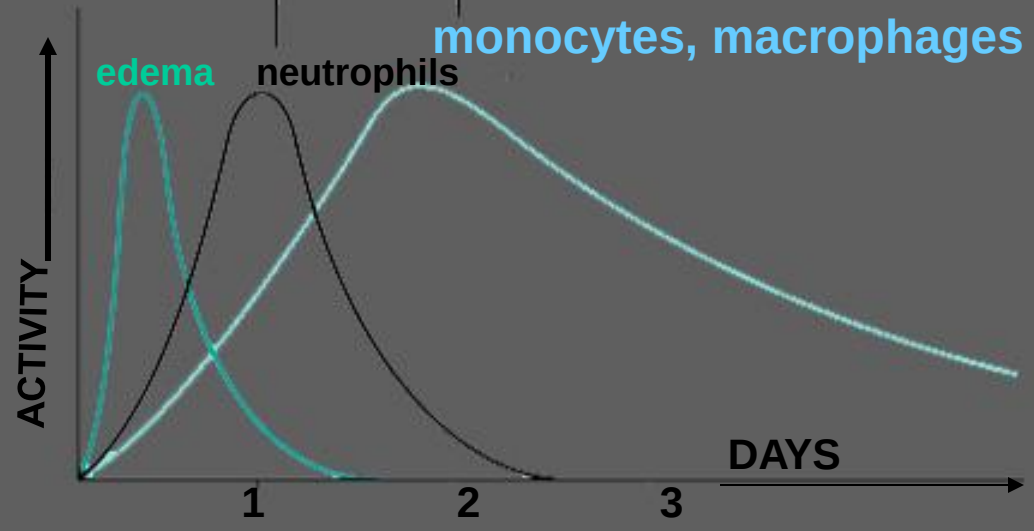
SEQUENCE IN ACUTE INJURY





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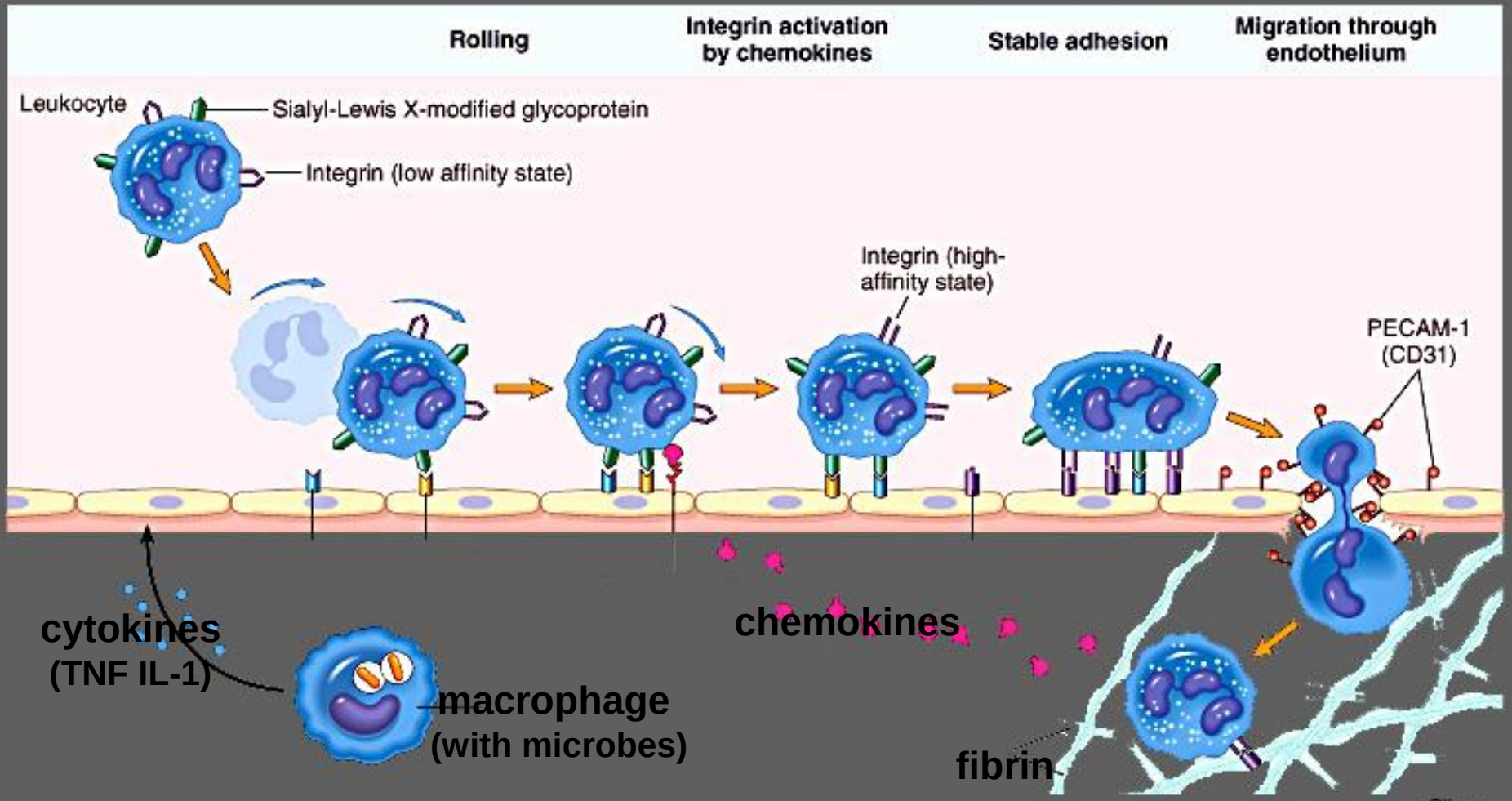
LEUKOCYTE MIGRATION THROUGH BLOOD VESSEL WALL



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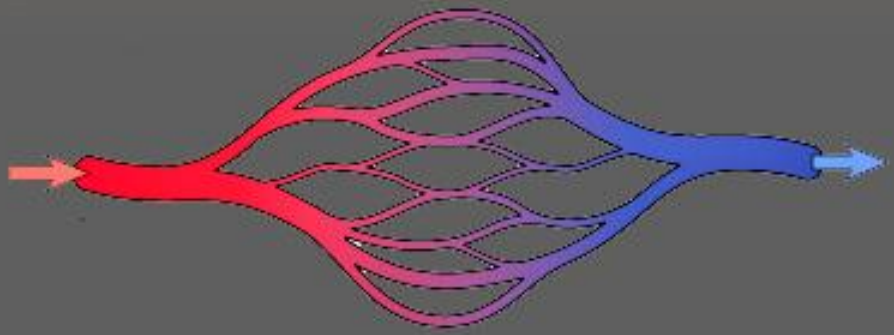
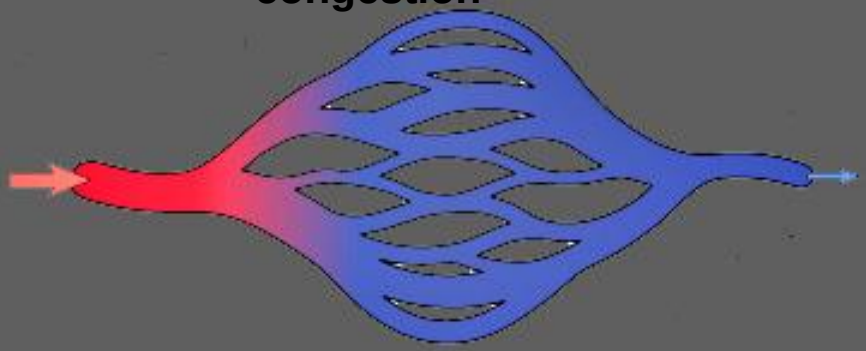
HYPEREMIA CONGESTION

normal



congestion



hyperemia

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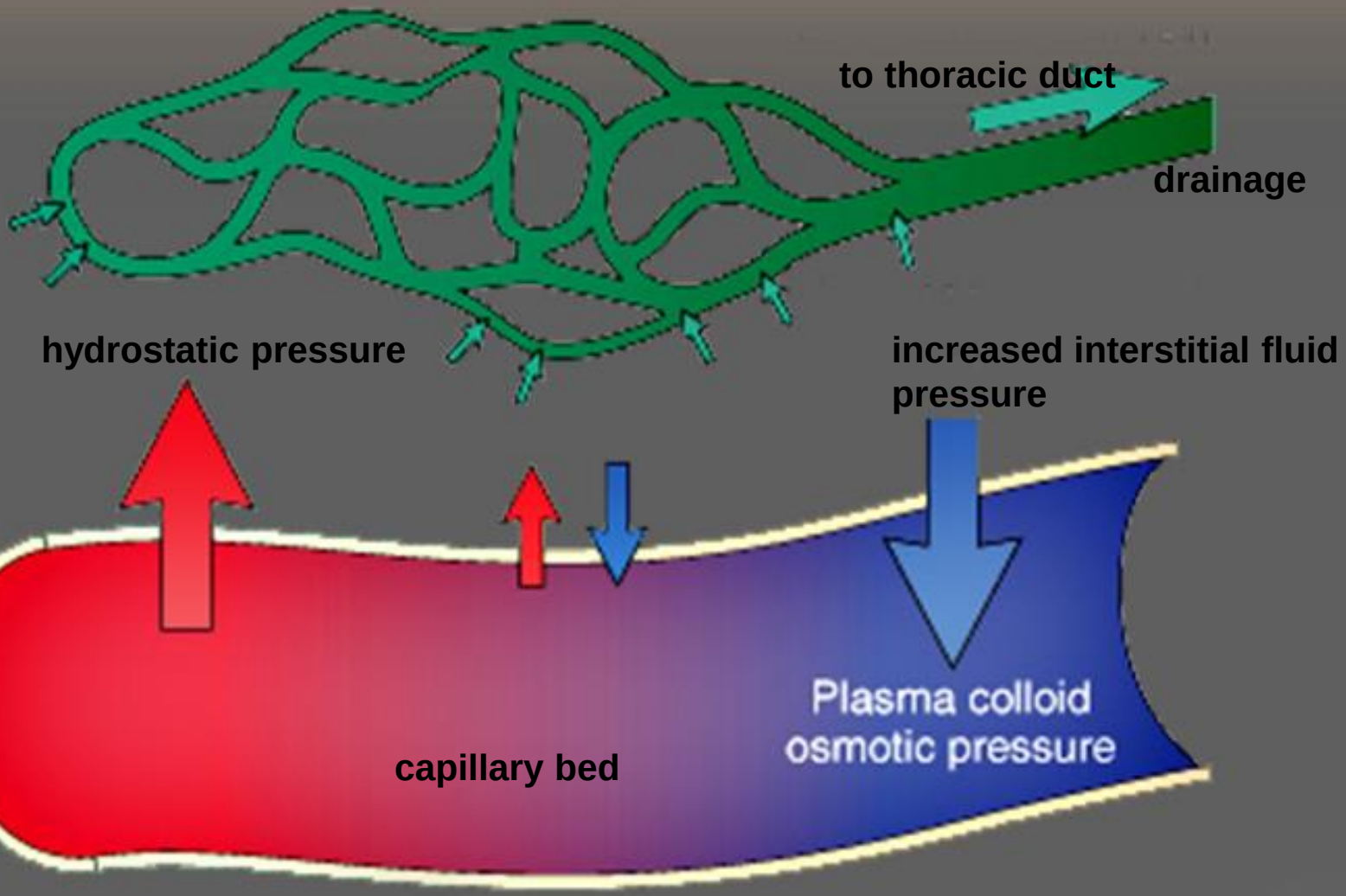
FLUID BALANCE



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FLUID BALANCE

Increased Hydrostatic Pressure

Impaired venous return

Congestive heart failure

Constrictive pericarditis

Ascites (liver cirrhosis)

Venous obstruction or compression

Thrombosis

External pressure (e.g., mass)

Lower extremity inactivity with prolonged dependency

Arteriolar dilation

Heat

Neurohumoral dysregulation

FLUID BALANCE

Reduced Plasma Osmotic Pressure (Hypoproteinemia)

Protein-losing glomerulopathies (nephrotic syndrome)

Liver cirrhosis (ascites)

Malnutrition

Protein-losing gastroenteropathy

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FLUID BALANCE

Lymphatic Obstruction

Inflammatory

Neoplastic

Postsurgical

Postirradiation

FLUID BALANCE

Sodium Retention

Excessive salt intake with renal insufficiency

Increased tubular reabsorption of sodium

Renal hypoperfusion

Increased renin-angiotensin-aldosterone secretion

HEMODYNAMIC DISORDERS

hyperemia

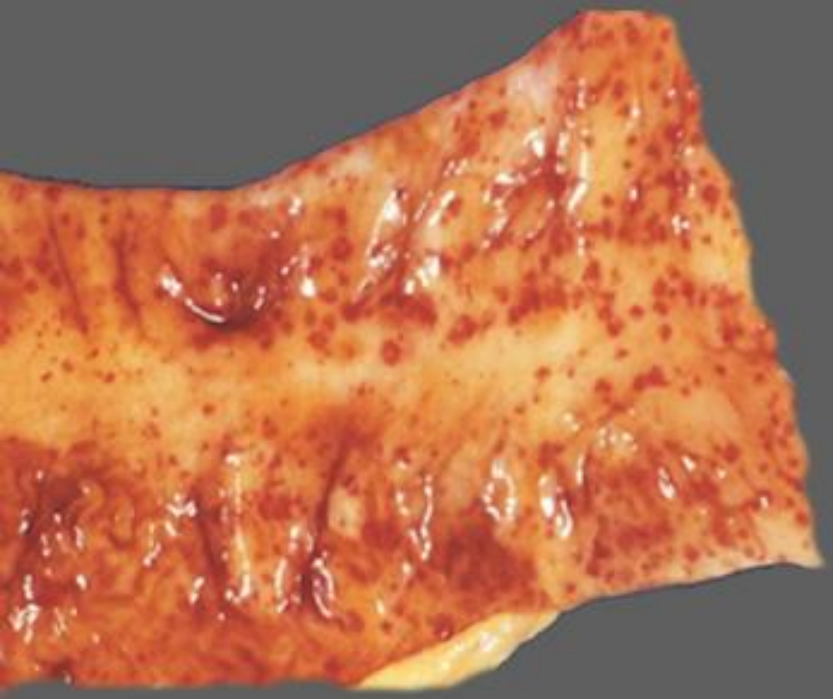
edema

hemorrhage

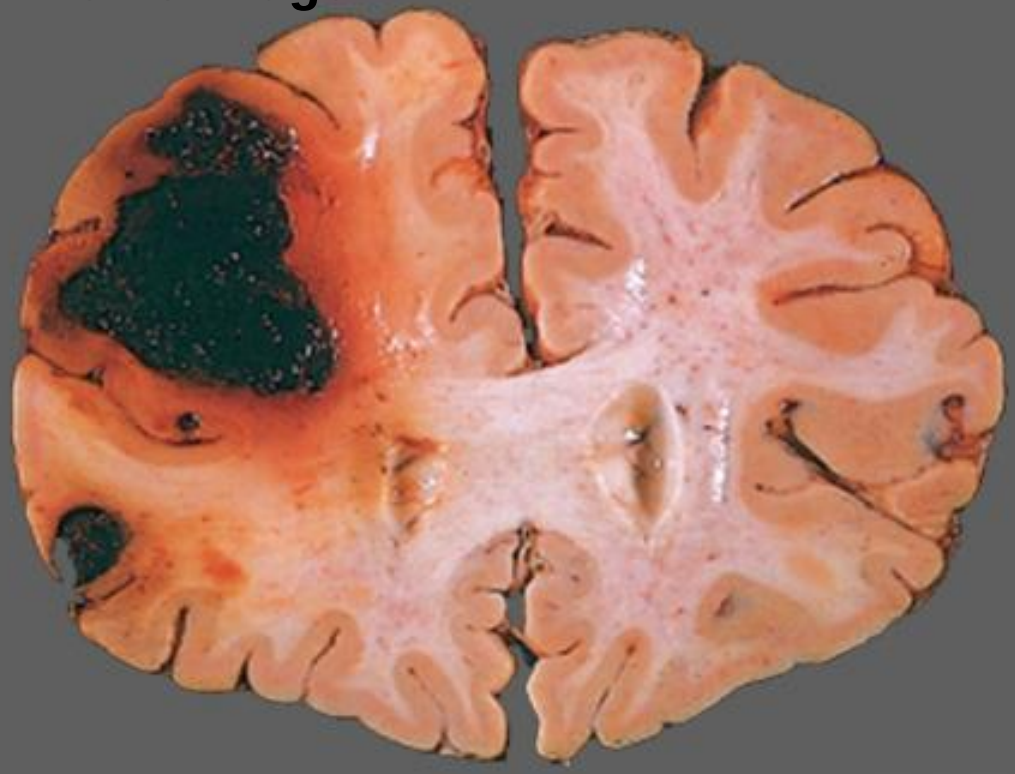
thrombosis

BLEEDING HEMORRHAGE

petechia



hemorrhage



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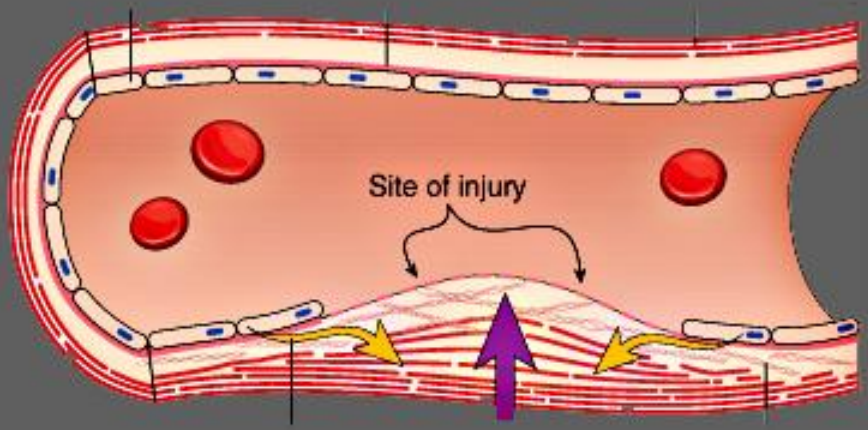
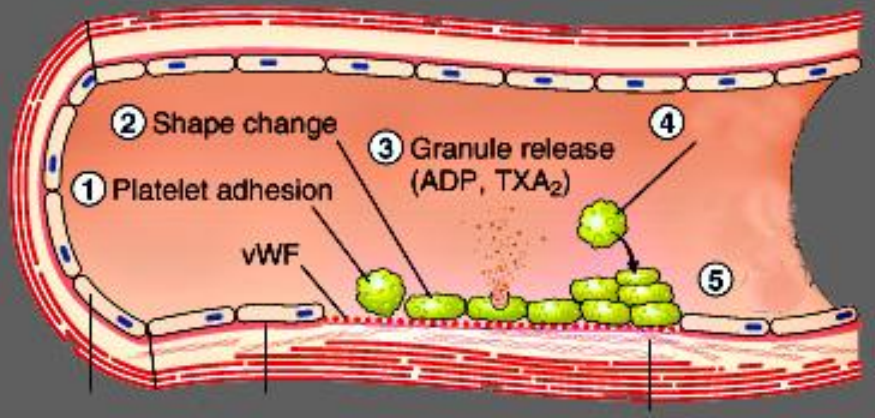
HEMOSTASIS THROMBOSIS

PRIMARY HEMOSTASIS





Endothelin release

vasoconstriction

extracellular matrix exposed

AGGREGATION HEMOSTATIC PLUG

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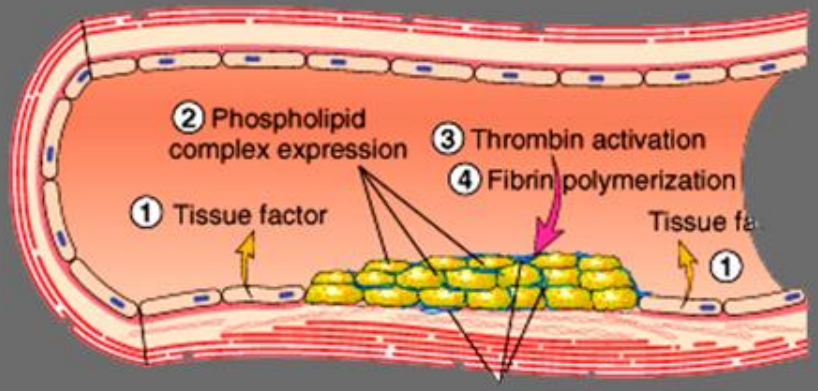
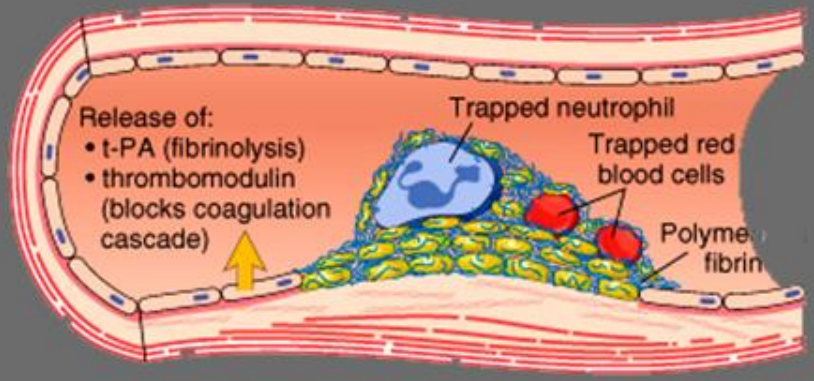
HEMOSTASIS THROMBOSIS

SECONDARY HEMOSTASIS





fibrin

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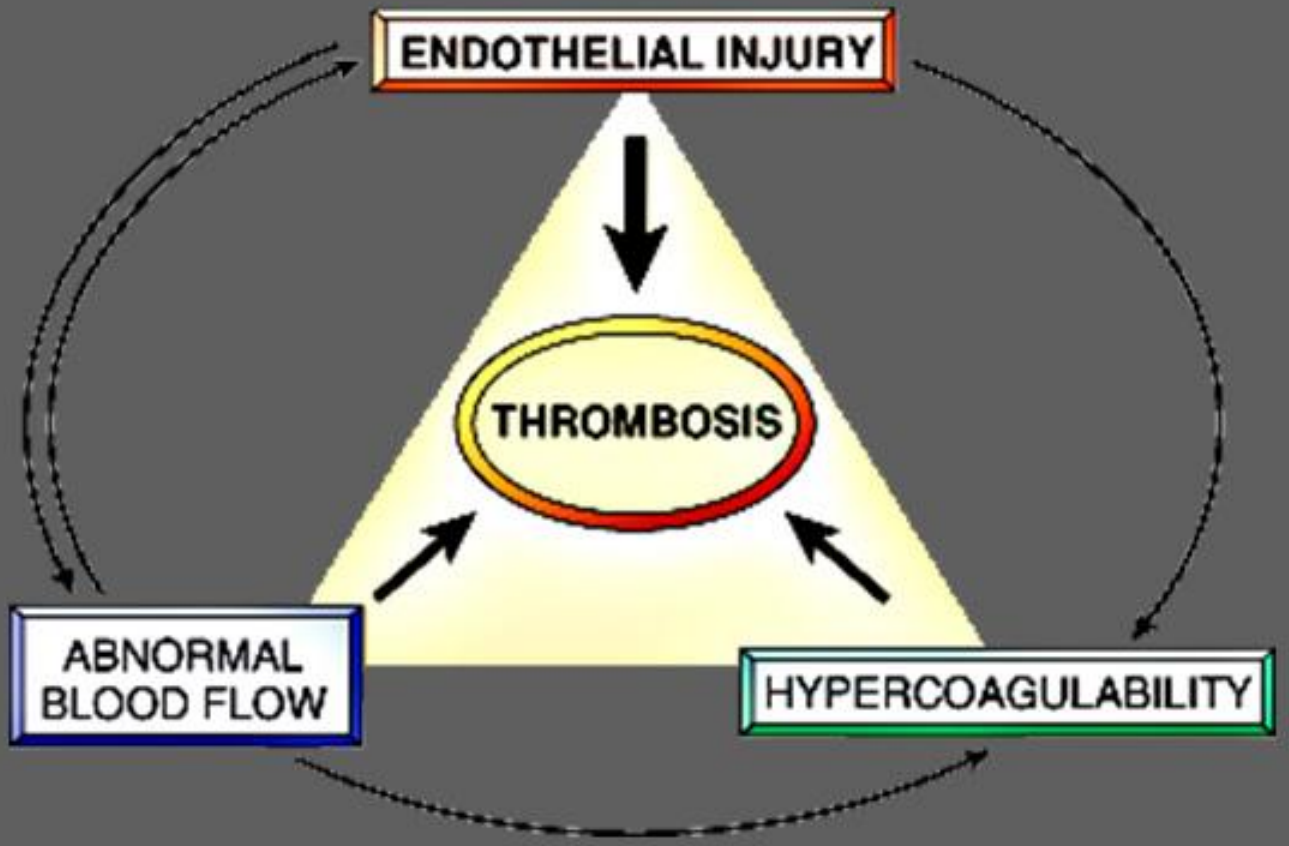
HEMOSTASIS THROMBOSIS



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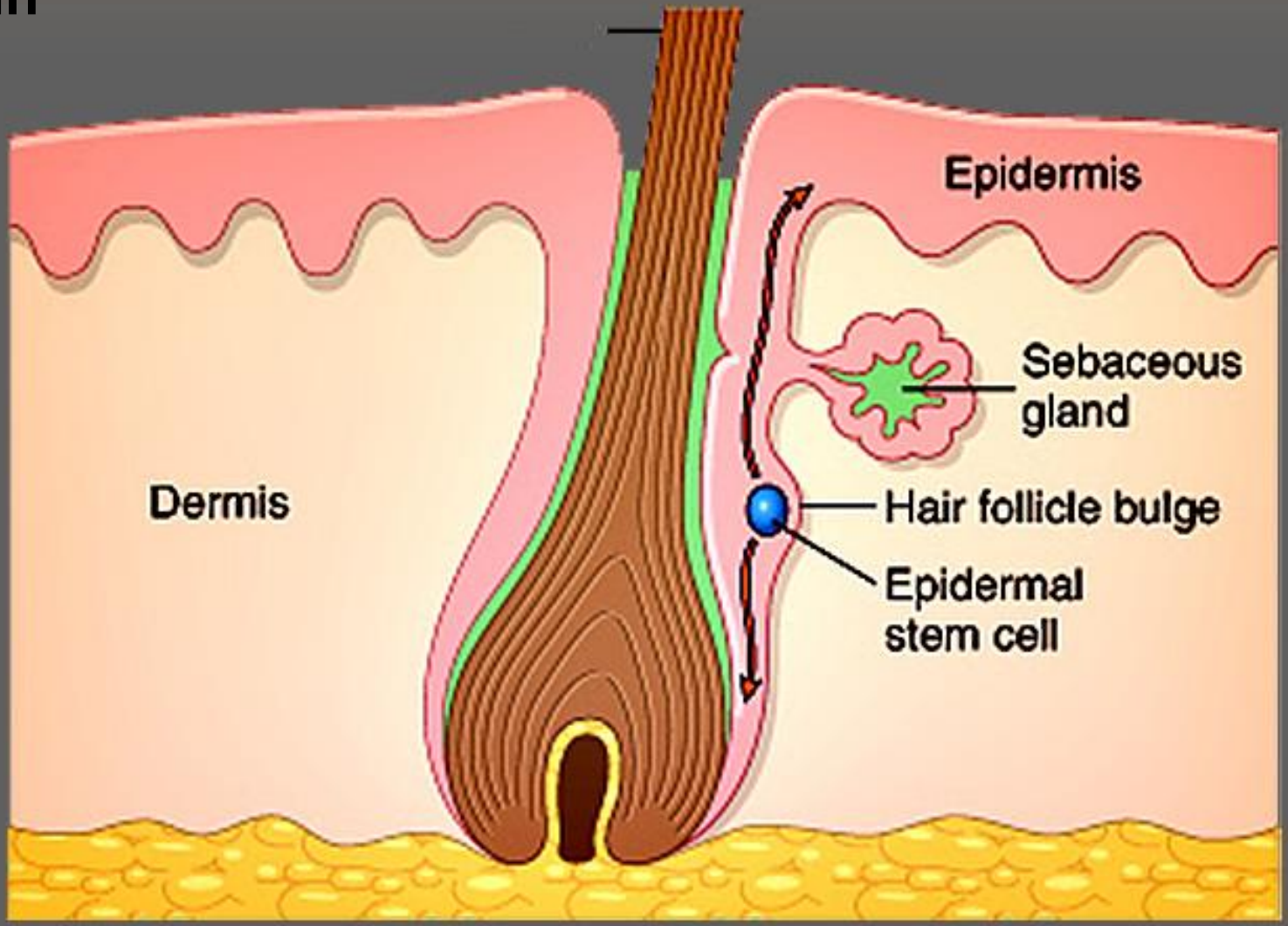
TISSUE REGENERATION

skin



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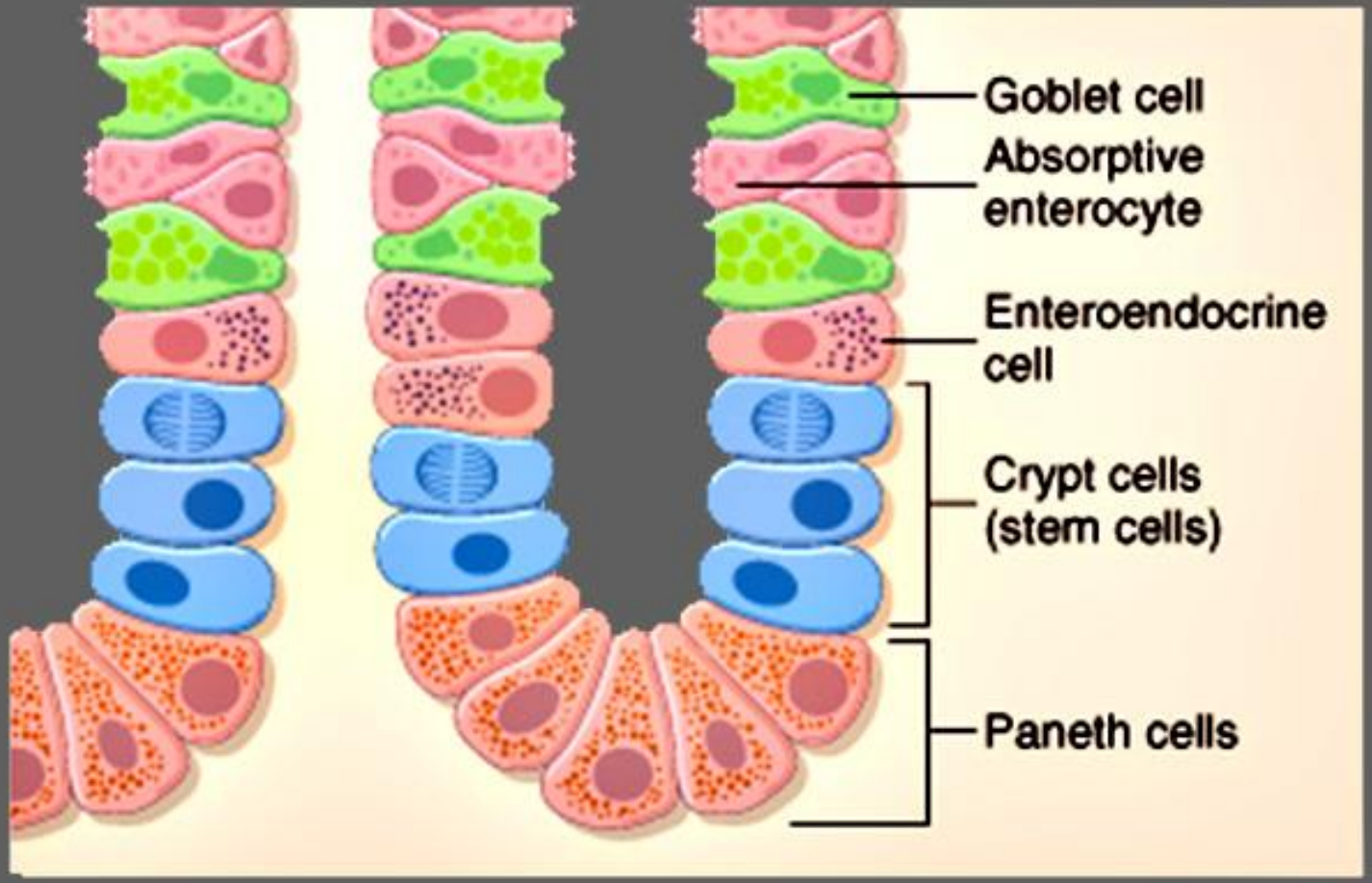
TISSUE REGENERATION

intestine



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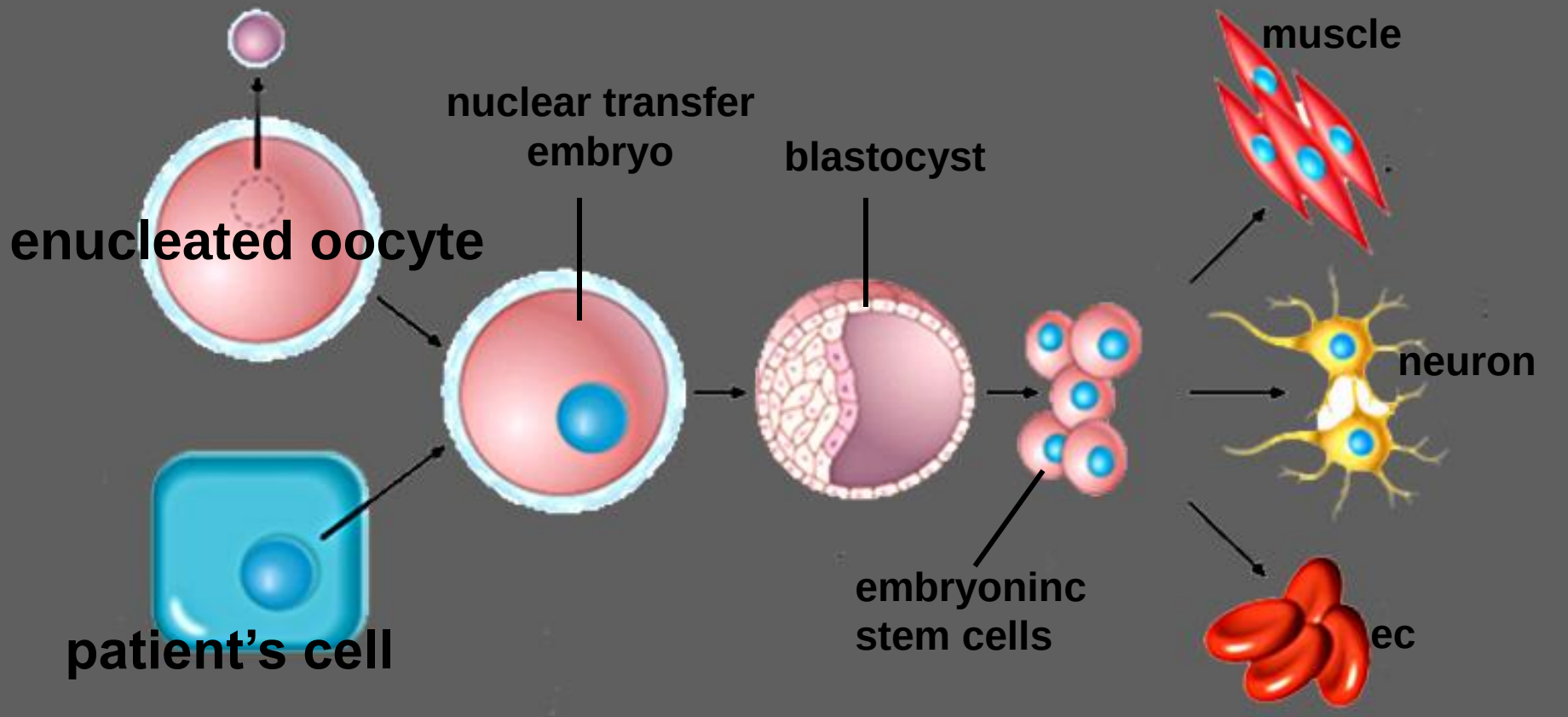
THERAPEUTIC CLONING



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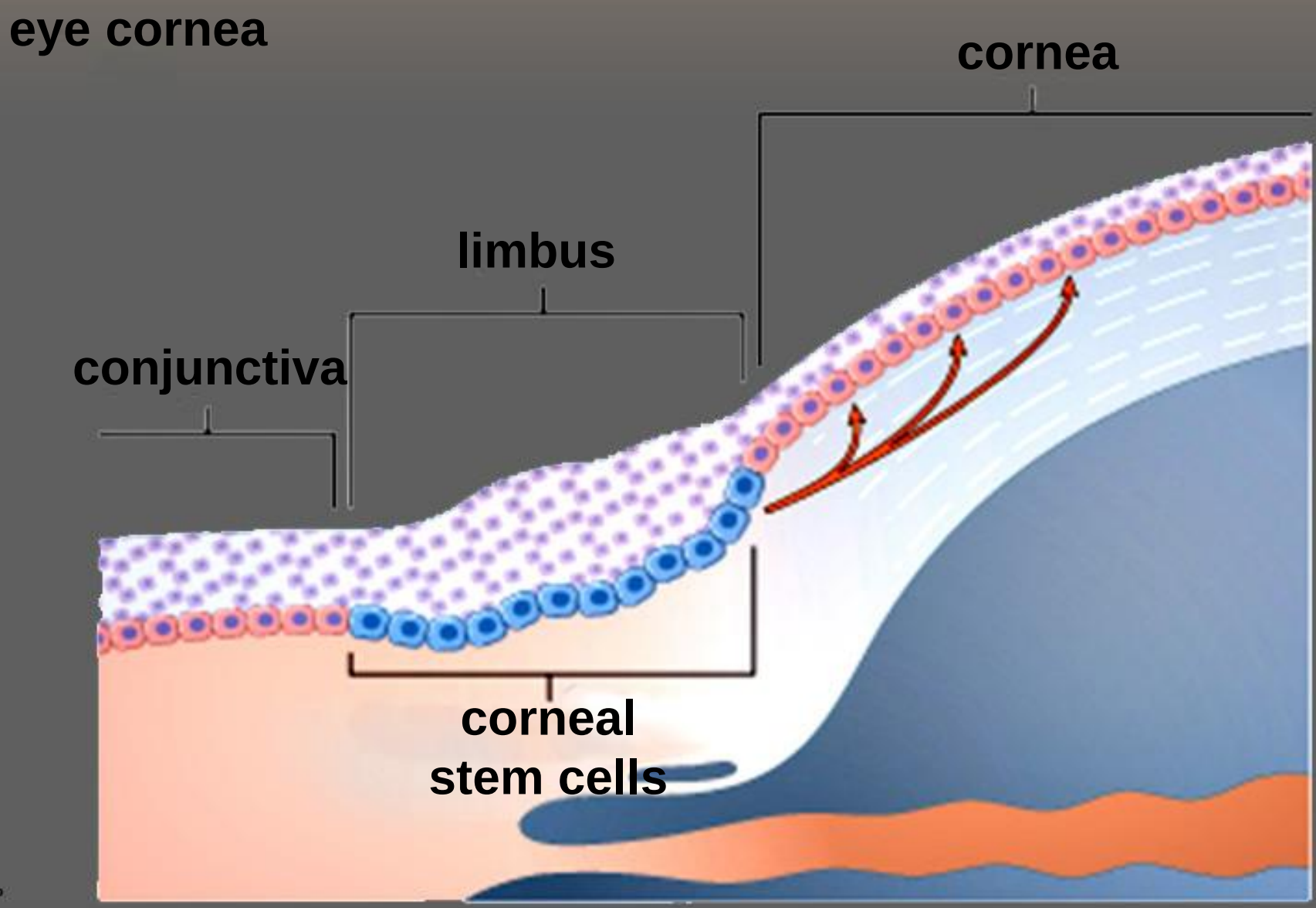
TISSUE REGENERATION



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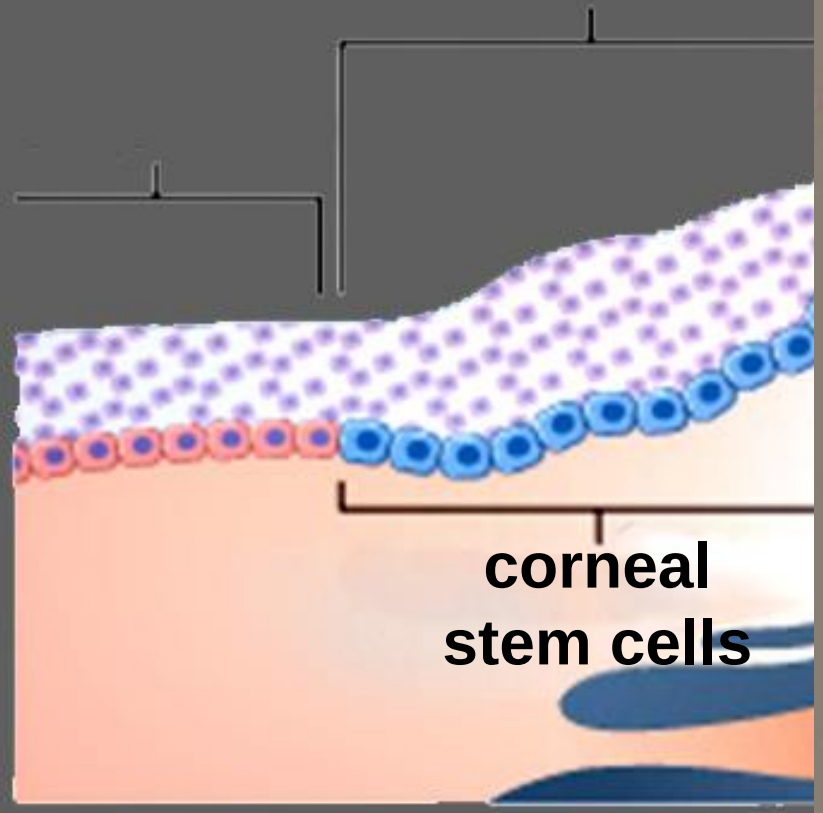
TISSUE REGENERATION

eye cornea



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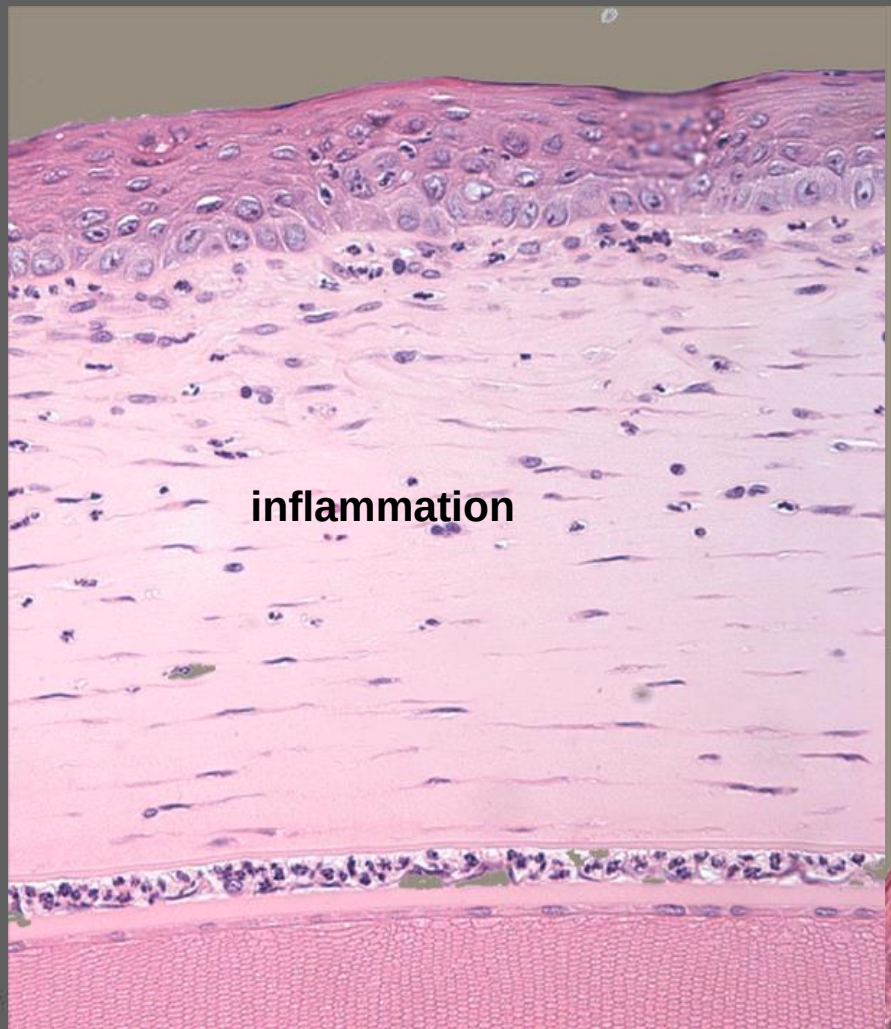
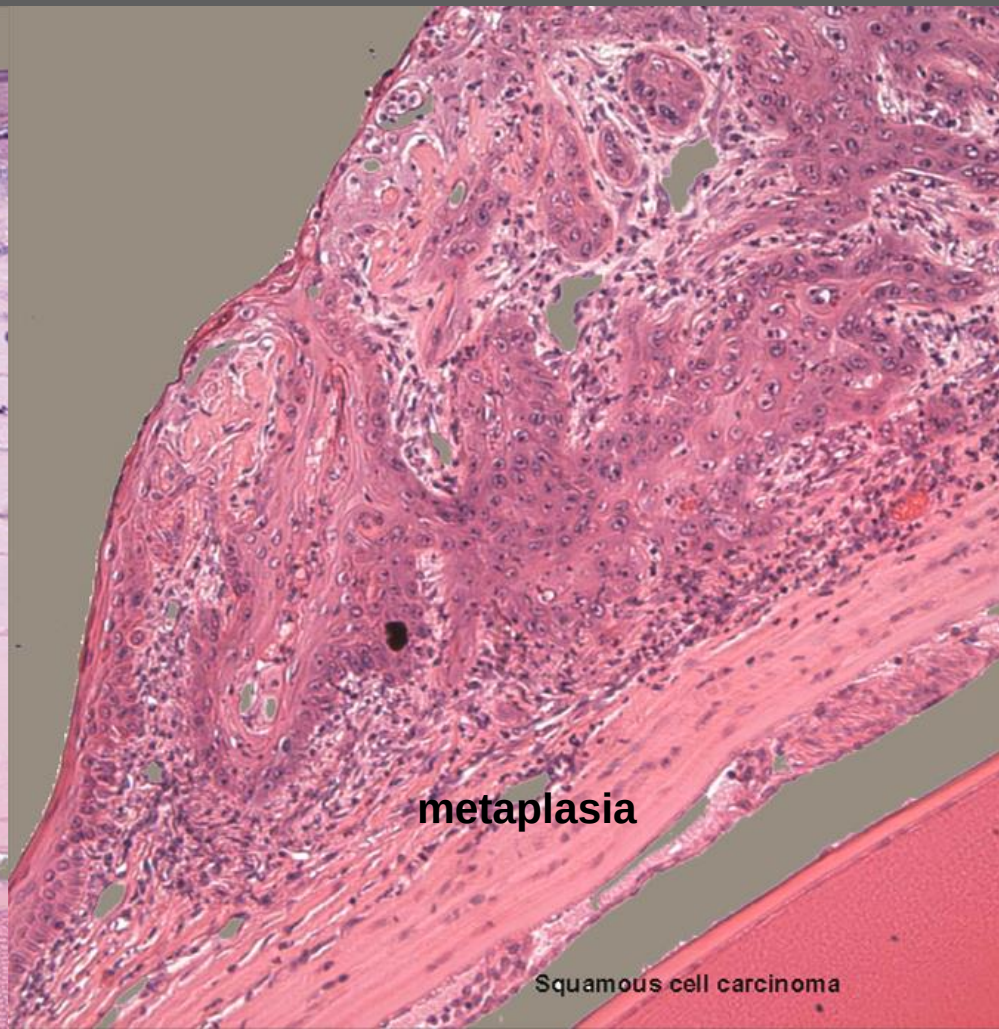
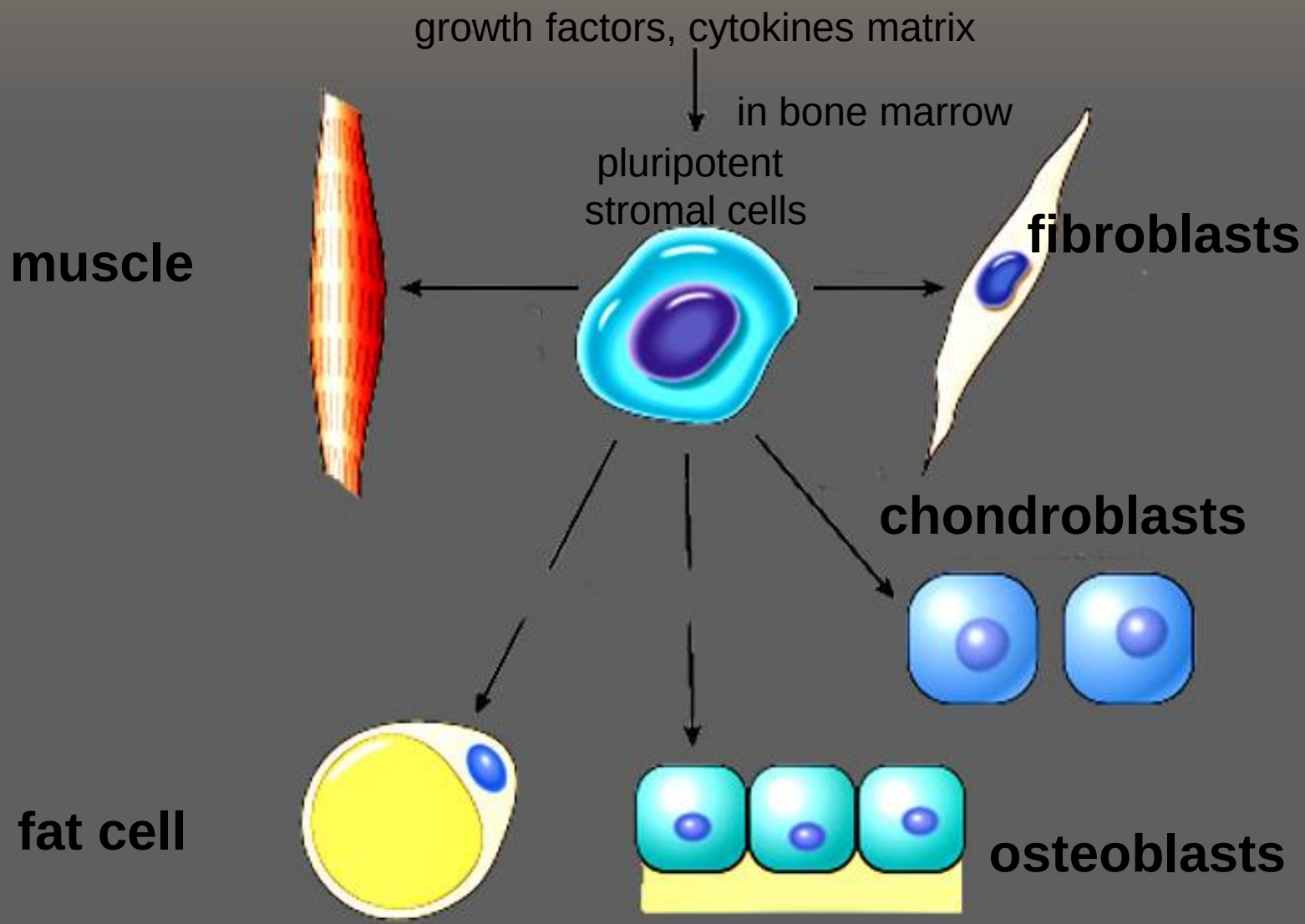
TISSUE REGENERATION

eye cornea





TISSUE REGENERATION



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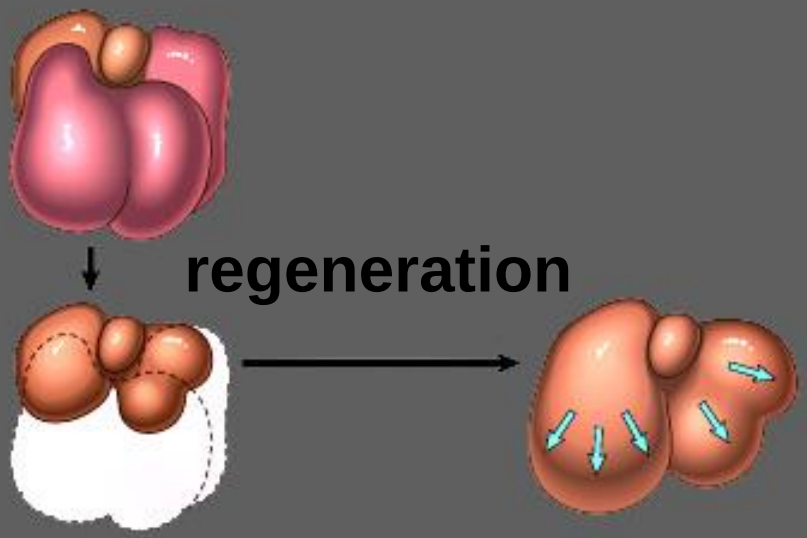
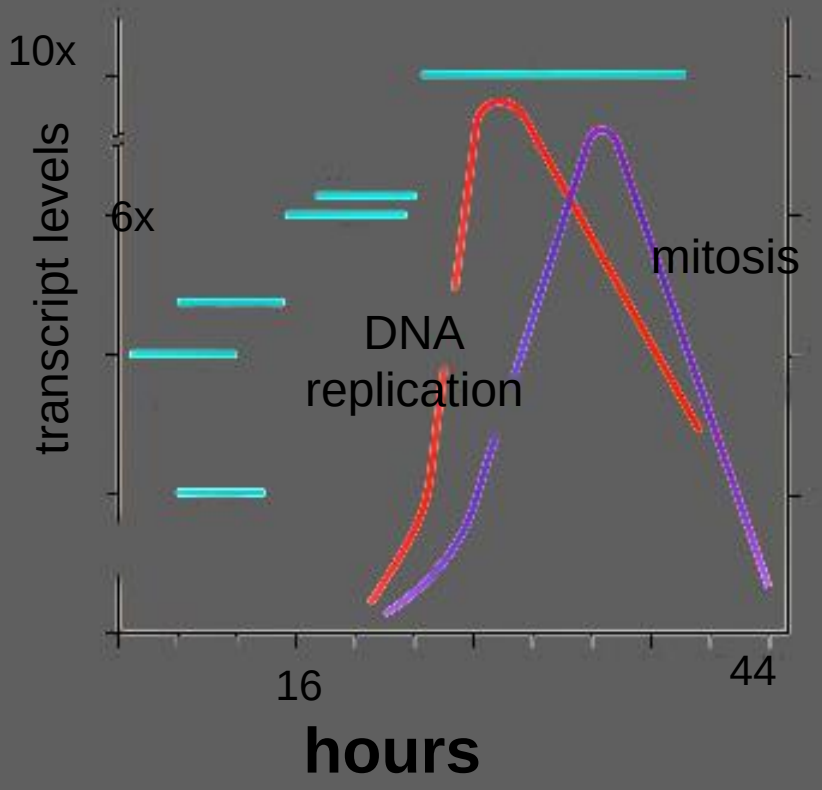
TISSUE REGENERATION

liver regeneration





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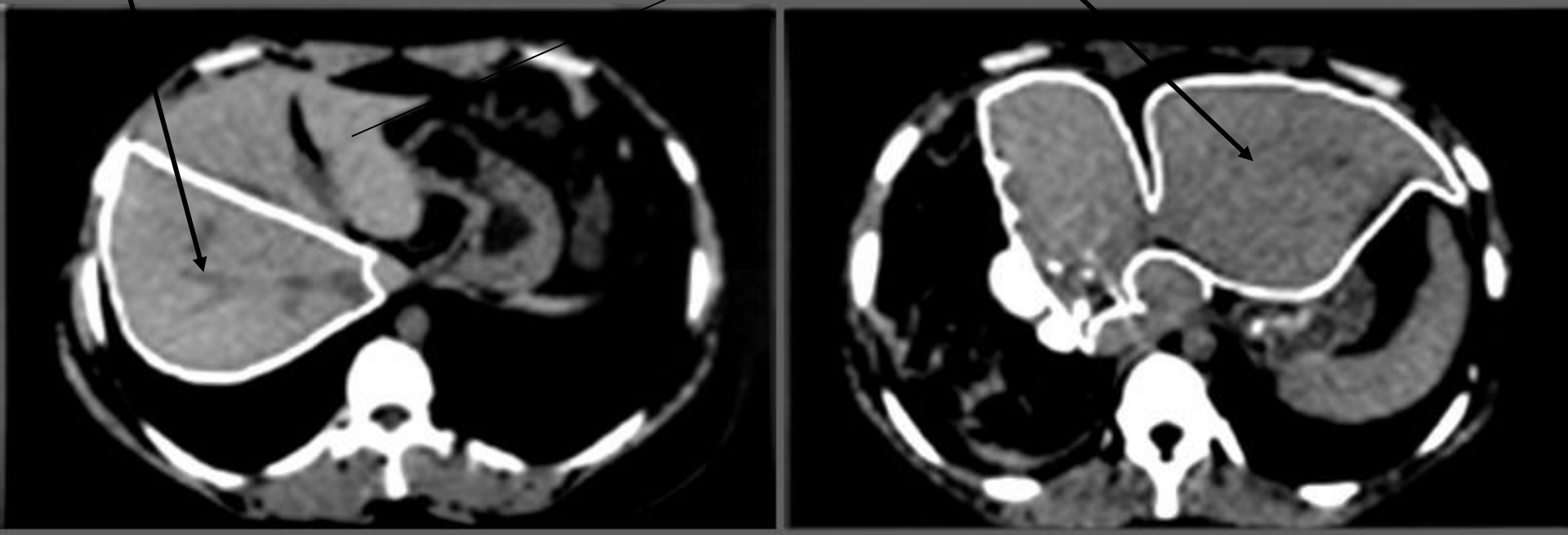
TISSUE REGENERATION

tomography

donor liver sample

regeneration



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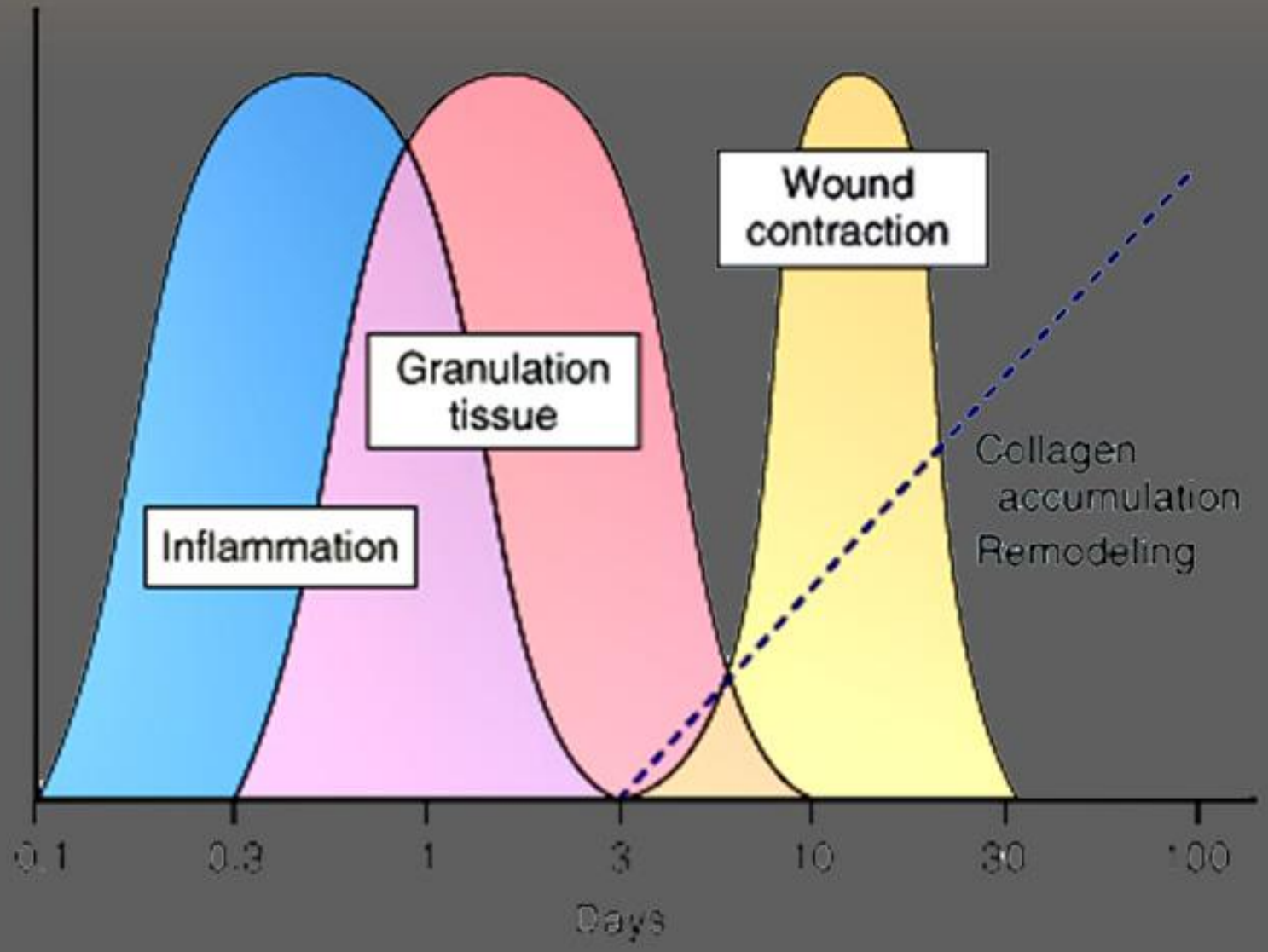
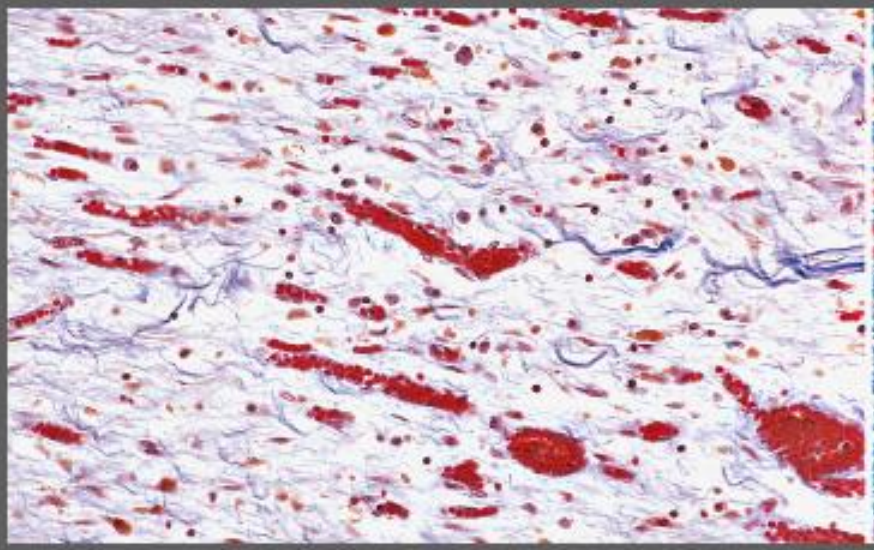
TISSUE REPAIR

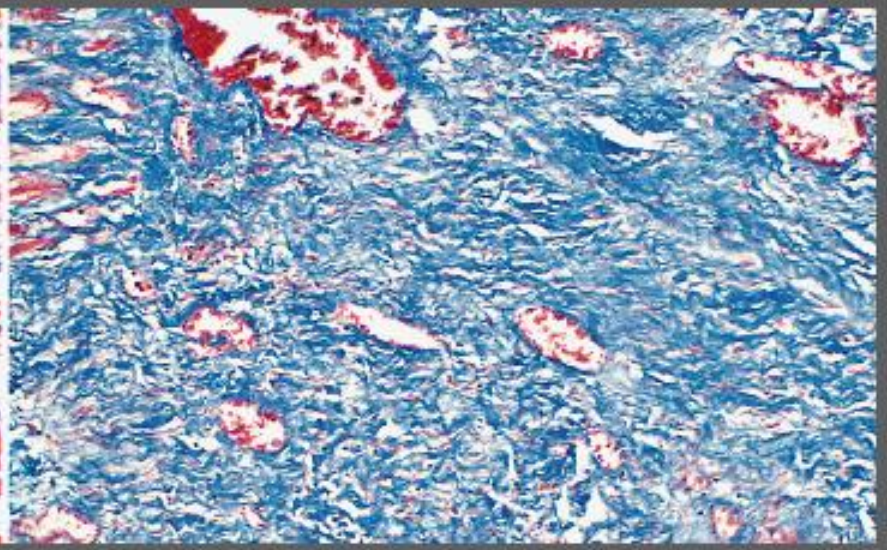


TISSUE REGENERATION REPAIR

granulation tissue

fibrosis, scar





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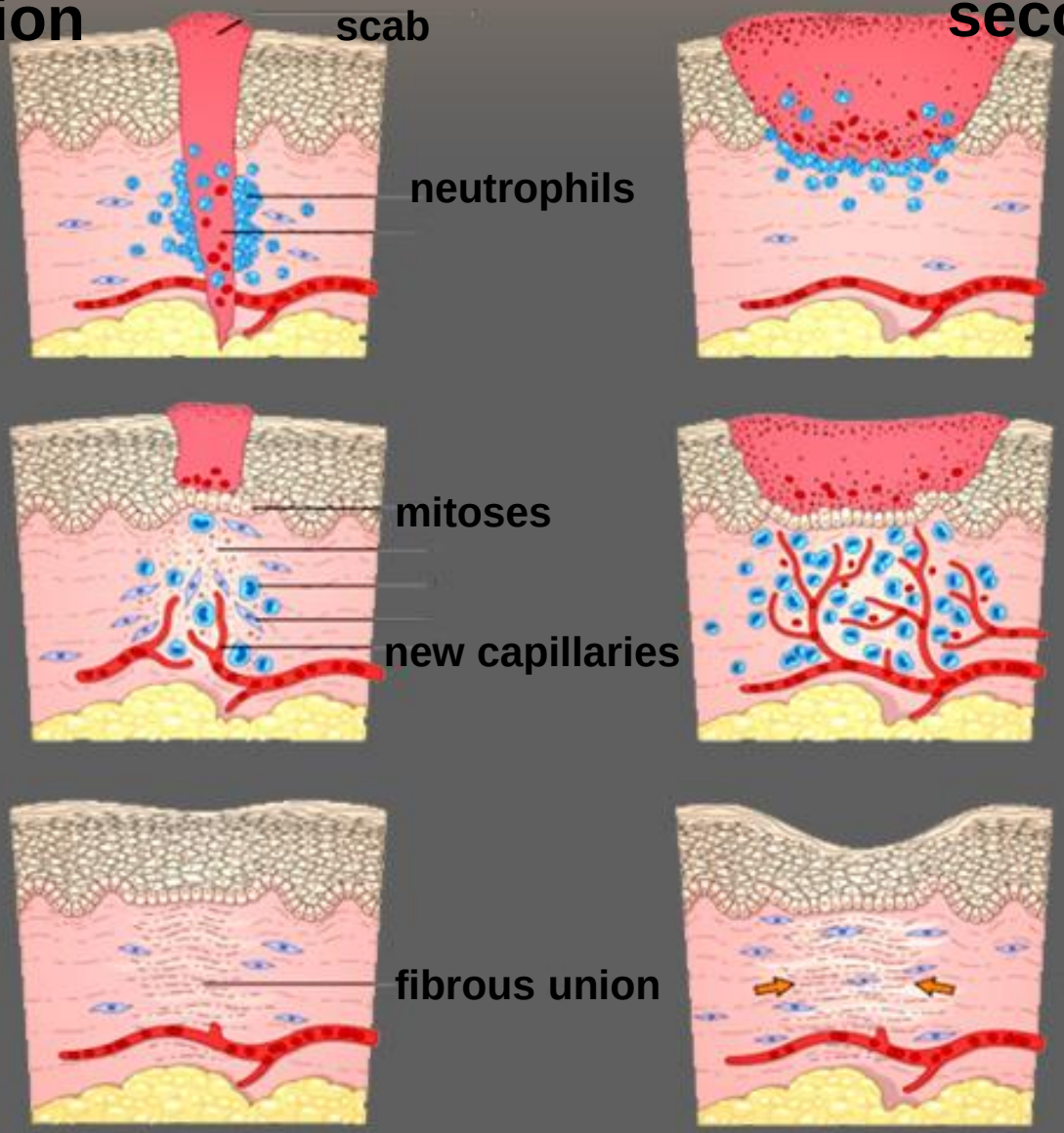
TISSUE REPAIR

first intention

second intention



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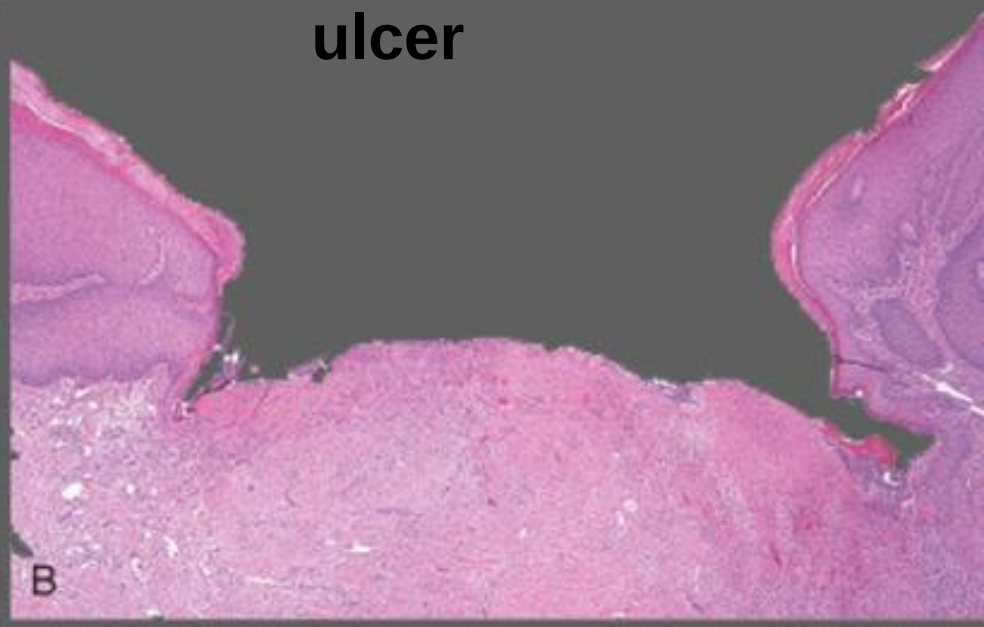
TISSUE ULCERATION

healing by second intention

skin ulcer

ulcer



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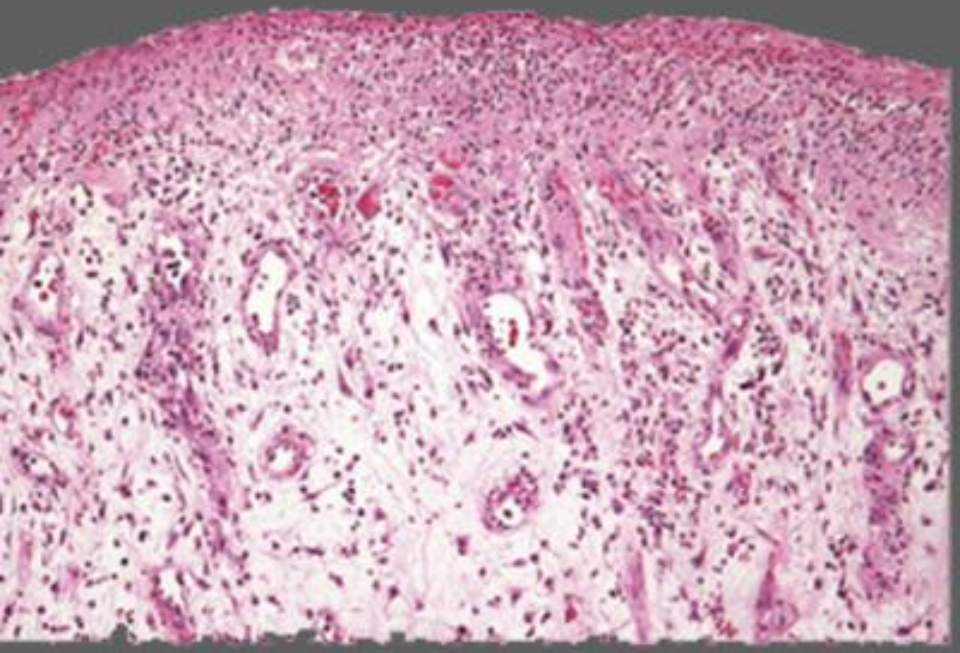
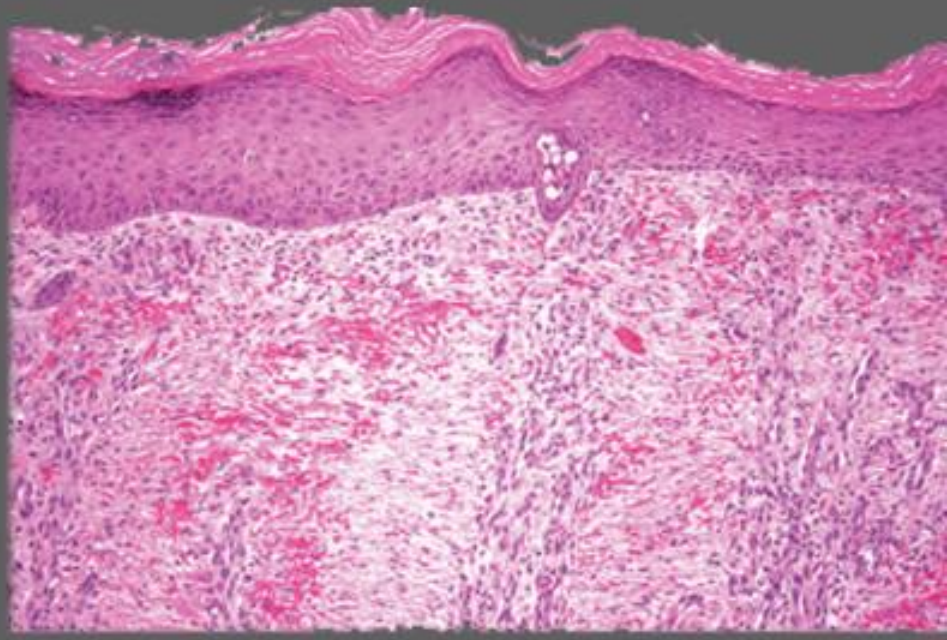
TISSUE REGENERATION

granulation tissue

reepithelialization





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TISSUE REGENERATION

Factors That Retard Wound Healing

Local Factors	
Blood supply	Mechanical stress
Denervation	Necrotic tissue
Local infection	Protection (dressings)
Foreign body	Surgical techniques
Hematoma	Type of tissue
Systemic Factors	
Age	Malnutrition
Anemia	Obesity
Drugs (steroids, cytotoxic medications, intensive antibiotic therapy)	Systemic infection
	Temperature
	Trauma, hypovolemia, and hypoxia
Genetic disorders (osteog. imp., Ehlers-Danlos syndromes, Marfan syndrome)	Uremia vitamin deficiency (vitamin C)
Hormones	Trace metal deficiency (zinc, copper)
Diabetes	
Malignant disease	

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TISSUE REPAIR

abnormal tissue reaction with excessive fibroplasia collagen deposition

keloid

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TISSUE REPAIR

Growth Factors and Cytokines Affecting Various Steps in Wound Healing

Monocyte chemotaxis	PDGF, FGF, TGF-β
Fibroblast migration	PDGF, EGF, FGF, TGF-β, TNF, IL-1
Fibroblast proliferation	PDGF, EGF, FGF, TNF
Angiogenesis	VEGF, Ang, FGF
Collagen synthesis	TGF-β, PDGF
Collagenase secretion	PDGF, FGF, EGF, TNF, TGF-β inhibits

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