Multicellular organisms are big, aggregated lineages (clones) of cells (plus various symbions, parasites, mutants etc.). Each cell is plasma-membrane bound aqueous system, with homeostatic mechanisms to maintain stasis (or growth) by regulating exchange: energy, nutrients ‘raw materials’ etc IN & wastes, hormones, ‘products’ etc OUT.

Diffusion through tissues is very slow & inefficient.

Large animals are masses of tubes w/ ↑ surface/vol & ↓ diffusion dist. Bulk flow through tubes (gut, lungs, arteries & veins, lymph etc)

The vertebrate body is a tube within a tube. The endoderm gut tube passes through the coelom. In mammals the coelom is divided by the diaphragm into the peritoneal cavity – contains stomach, intestines, liver and the thoracic cavity – subdivided into pleural cavities – lungs and pericardial cavity - heart.

Animals are multicellular organisms with their specialized cells grouped into tissues. Tissues are integrated groups of cells with a common structure and function. Combinations of various tissues make up functional units called organs, and groups of organs that work together form organ systems. All organs are made of the four basic tissue types:

**Epithelial tissue** is derived from all three germ layers; functions to protect surfaces (e.g., skin), secrete material (e.g., glands), absorb material (e.g., intestine).

**Epithelial tissue**

- The mouth, esophagus, uterus and vagina, ducts of the pancreas and liver, urethra and ureters, blood vessels (where it is called endothelium), tubules of the kidney, air sacs (alveoli) of the lungs...

Epithelial tissue is classified according to:

1. The 
   - squamous: flat, linings - diffusion
   - cuboidal: glands & tubules - transport
   - columnar: linings - secretion & absorption or transitional, *discrete categorization is an 'ideal'*

2. Whether or not the tissue is
   - simple: lungs & capillaries
   - stratified: skin, mouth or pseudostratified: glands & mucous membranes

3. Whether or not the cells are
   - ciliated: lungs & capillaries
   - glandular, ex: goblet cell...

Glandular epithelia, absorb or secrete chemical solutions. Glandular epithelia secrete hormones into the blood (ch 45). Glandular epithelia that line the digestive & respiratory tracts form mucus membrane. They secrete a slimy solution called mucus that lubricates the surface.

Glandular epithelia line the digestive & respiratory tracts; they secrete a slimy solution called mucus that lubricates the surface.

The epithelium of our respiratory tract has... that move the film of mucus along the surface, helping keep our lungs clean by trapping dust, 'germs' and other particles and sweeping them back up the trachea (windpipe) to esophagus.

Cancer biology: Breaking and entering

To spread, or metastasize, cancer cells must escape from their site of origin. S Weiss and colleagues have identified three enzymes that allow tumors to degrade proteins in the basement membrane, allowing cancer cells to escape. Knowing the enzymes could enable future cancer therapies to target this process.

Cancer biology: Breaking and entering

To spread, or metastasize, cancer cells must escape from their site of origin. Doing so requires crossing the basement membrane, a barrier of connective tissue. S Weiss and colleagues have identified three enzymes that allow tumors to degrade proteins in the basement membrane, allowing cancer cells to escape. Knowing the enzymes could enable future cancer therapies to target this process.
In the inactive mammary gland, the glandular elements consist only of ducts: lined by cuboidal or columnar epithelium ...

Dramatic changes in the mammary gland occur during pregnancy. Ducts proliferate and secretary alveoli sprout from them. Alveoli are collections of cuboidal or columnar epithelial cells that become active milk-secreting structures.

The lipid (water insoluble) component of milk is released in an envelope by apocrine secretion. (homogenization breaks up large globules)
The protein (water soluable) component of milk is released by merocrine secretion.

During the menstrual cycle slight development of secretary alveoli may begin ...

... an increasing number of menstrual cycles increases the stimulation of breast ductal epithelial cells and one's risk of breast cancer. ... the risk for breast cancer is associated with...

Breast Cancer Risk Factors: Estrogens


Menstrual and reproductive factors and endometrial cancer risk ...

Fibrous connective tissue is dense, due to its large numbers of collagenous fibers.

In tendons, which attach muscles to bones, and in ligaments, which join bones together at joints, the fibers are organized into parallel bundles ...

The "unhappy triad" is where the ACL is torn at the same time as the MCL and the lateral meniscus (one of the shock absorbing cartilages in the knee).

Cartilage has collagenous fibers embedded in a rubbery matrix of chondroitin sulfate, a protein-carbohydrate complex. ... secreted by cells called chondrocytes.

... articular (meniscus) cartilage lining the bones of your knee joint

Blood capillaries do not penetrate the joint capsule. (similar to 'the blood-brain barrier'). Synovial fluid, secreted by synovium (membranes), lubricates the joint and carries nutrients to the cartilage.

Connective Tissue derives from embryonic mesoderm, functions mainly to bind and support other tissues. ... has a sparse population of cells scattered through an extracellular matrix.

The major types of connective tissue in vertebrates are

Loose connective tissue (Fig 40.5) (including Adipose tissue = fat)
Fibrous (dense) connective tissue regular- ligaments & tendons irregular – sheathing membranes

Cartilage
Bone
Blood

Rheumatic diseases are diseases.
Arthritis means joint inflammation.
... arthritis is a kind of rheumatic disease.
Osteoarthritis, the most common type, affects cartilage, the tissue that cushions the ends of the bones within the joints.

Rheumatoid arthritis is an ... the immune system attacks a person's own synovium, the tissue inside the joint capsule. {one type of antibody attacks the 'tail' of another type}

http://en.wikipedia.org/wiki/Rheumatoid_arthritis

The cause of RA is unknown ...the "mistaken identity" theory suggests that an offending organism causes an immune response that leaves behind antibodies specific to that organism. They begin an immune attack against the synovium, because a molecule in the synovium "looks like" one on the offending organism. 50% of patients with RA have the cluster of markers known as the HLA-DR4/DR1 cluster, whereas only 40% of controls do. 
Thus, in theory, RA requires susceptibility to the disease through genetic endowment and an infectious event that triggers an autoimmune response.
Bone is an extracellular mineralized connective tissue (from mesoderm).
Bone-forming cells called osteoblasts deposit a matrix of collagen.
Calcium, magnesium, and phosphate ions combine and harden within the matrix into the mineral hydroxyapatite – rigid but brittle.
The structure of hard mammalian bone consists of repeating units called osteons (or Haversian systems).
Each osteon has concentric layers of the mineralized matrix, which are deposited around a central canal containing blood vessels and nerves that service the bone.
Mature osteocytes maintain, remodel and repair mineral bone.

Blood functions differently from other connective tissues (mesoderm) but it has an extensive extracellular matrix: a liquid called plasma, consisting of water, salts, and a variety of dissolved proteins.
Suspended in the plasma are two classes of blood cells, and cell fragments called platelets.
Blood will be discussed later (Chapters 42, 43 & 44).

Nervous tissue (from ectoderm) senses stimuli and transmits signals from one part of the animal to another, & stores memories.
The functional unit of nervous tissue is the neuron, or nerve cell, discussed later in ch 48.

Muscle tissue (from mesoderm) is composed of long cells called muscle fibers that are capable of contracting when stimulated by nerve impulses.
Arranged in parallel within the cytoplasm of muscle fibers are large numbers of myofibrils made of the contractile proteins actin and myosin.
Recall actin in eukaryotic cytoskeleton (see ch 6).

Smooth muscle is found throughout animals.
In vert’s – ‘visceral’ muscle, sheets surround larger blood vessels and bronchia, gut, iris of eye. Not striated (lined up) Not ‘voluntary,’ spontaneous waves in gut;

Skeletal muscle is usually attached to tendons & bones at origin & insertion; antagonists flex & extend.
Lined up in orderly, multinucleate myofibrils – ‘striated.’ ‘Voluntary,’ excited at neuromuscular synaptic junctions

Cardiac (heart) muscle ‘striated’ but single cells (& nuclei) linked by gap junctions into single functioning myocardium
Specialized ‘autogenic’ cells maintain rhythmic contractions, modified by sympathetic (+) and parasympathetic (-) nerves

Optimization of bone growth and remodeling in response to loading ...
limb bones initially optimize (growth) responses to loading ...
In juveniles, exercise induces higher rates of (remodeling) ... [but less so in adults]

Archeo-Cell Biology: Carbon Dating Is Not Just for Pots and Dinosaurs
In this issue of Cell, Spalding et al. (2005) describe a clever strategy for birth dating human cells in vivo, based on incorporation of 14C during a peak in atmospheric levels resulting from above-ground nuclear arms testing in the 1950s.
The amount of 14C in neurons of the human cerebral cortex corresponds to the amount in the atmosphere at the time of birth ...
occipital neurons are as old as the individual

Contraction:
Somatic motor neurons release acetylcholine Ach (blocked by Botox)
Ach depolarizes muscle ... starting the power cycle

Power cycle (see Fig 49.30);
(a) myosin splits ATP
(b) cross-bridges w/ actin,
(c) myosin head bends (power stroke -rowing)
(d) new ATP releases bridge, straightens →(a)

Rigor mortis → actin Z bands get closer, Sarcomeres shorten muscle contracts
From venoms to toxins to drugs:

Toxins have been used to elucidate physiological mechanisms; the pure alkaloid, **tubocurarine**, isolated from the arrow poison **curare**, has been used as a muscle relaxant to accompany general anaesthetic.

**Essentially We Have Two Fibre Types:**

- **Fast-twitch (Type 2)**: high intensity, anaerobic, short-burst activity, engages the fibres, which are lighter in coloring than slow-twitch fibres due to the low levels of myoglobin (stores oxygen for use in cell respiration) and mitochondria they possess – quickly fatigue.

- **Slow-twitch (Type 1)**: high intensity, anaerobic, short-burst activity, engages the fibres, which are lighter in coloring than slow-twitch fibres due to the low levels of myoglobin (stores oxygen for use in cell respiration) and mitochondria they possess – quickly fatigue.

**ACTN3 genotype is associated with human elite athletic performance.**


There is increasing evidence for strong genetic influences on athletic performance and for an evolutionary "trade-off" between speed and endurance ...

... the skeletal-muscle actin-binding protein α-actinin-3 is specifically expressed in fast-twitch (type 2) myofibers responsible for generating force at high velocity ...

... is absent in 18% of healthy white individuals because of homozygosity for a common stop-codon polymorphism in the ACTN3 gene, R577X.

*alleles R577T codes for α-actinin-3; R577X is a defective ACTN3.*

*homozygote R577XX results in no α-actinin-3*

... highly significant associations between ACTN3 genotype and athletic performance. Both male and female elite sprint athletes have significantly higher frequencies of the R577 allele than do controls. The differential effects in sprint and endurance athletes suggests that the R577 vs R577X polymorphism (at the ACTN3 locus) may have been maintained in the human population by balancing natural selection.

Loss of ACTN3 gene function alters mouse muscle metabolism and shows evidence of positive selection in humans


**All animals eat other organisms**

An adequate diet must satisfy three nutritional needs:

1. Chemical energy for all cellular work of the body:
   - (empty calories in junk food serve this purpose OK)

2. The organic raw materials animals use in biosynthesis:
   - Given a source of [essential amino acids](http://en.wikipedia.org/wiki/Essential_amino_acid) (8 or 9, see [Table 41](http://en.wikipedia.org/wiki/Essential_fatty_acids)) an animal can fabricate a great variety of organic molecules - carbohydrates, proteins, and lipids;

3. **Essential nutrients** substances that the animal cannot make for itself from any raw material and must obtain in food in prefabricated form: essential fatty acids (omega-3 & -6: http://en.wikipedia.org/wiki/Essential_fatty_acids) and minerals (Table 41)
Teeth and Guts are great indicators of diet

... as is the number of copies of the gene coding for the salivary enzyme amylase, which digests complex starches into simple sugars ...

news@nature Ewen Callaway, Published online: 9 September 2007: The gene that makes your mouth water

Ability to digest starch could have spurred human evolution.

Compared with chimpanzees, humans boast of the gene that makes salivary amylase – a saliva enzyme that breaks down starch into digestible sugars. And carbohydrate-loving societies than those that follow low-carbohydrate diets, says a new study in Nature Genetics.

Over the long term, homeostatic mechanisms, involving hormones in feedback circuits to a “satiety center” in the brain control the body's storage and metabolism of fat.

The complexity of weight control in humans is evident from studies of the hormone, a long-term appetite regulator in mammals, is produced by adipose (fat) cells. As adipose tissue increases, levels in the blood rise, which normally suppresses appetite. Loss of body fat decreases levels, signaling the brain to increase appetite.

Glucose Regulation as an Example of (push-pull –FB) Homeostasis

When an animal takes in more calories than it needs ... the liver and muscle cells store energy in the form of glycogen, a polymer made up of many glucose units.

If the body's glycogen depots are full, the excess is usually stored as fat. When fewer calories are taken in than are expended ... the body expends liver glycogen, then muscle glycogen and fat. (released as glucose, into blood)

Blood glucose levels are regulated by complementary ‘push-pull’ negative feedback systems:

- insulin pulls high blood glucose down
- glucagon pushes low glucose up

(Figs 41.3 & 45.12)

Type 1 diabetes mellitus:
- loss of insulin-producing beta cells;

Type 2 diabetes is often due to reduced responsiveness to insulin,

Body fat mass, leptin and puberty.


By modulating the hypothalamo-pituitary-gonadal axis both directly and indirectly, leptin may thus serve as the signal from fat to the brain about the adequacy of fat stores for.

Normal leptin secretion is necessary for normal reproductive function to proceed and leptin may be a signal allowing for ...

Role of leptin in reproduction.

Bajari et al. CURRENT OPINION IN LIPIDOLOGY 15 (3): 315-319 JUN 2004

The development of therapeutic agents against obesity must consider the consequences of treatment on the bioactivity of leptin in the context of growth, glucose homeostasis, and last but not least, fertility.