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NURSING STUDIES
2nd YEAR

THERAPEUTICS & PATHOPHYSIOLOGY

October 18th: INFLAMMATION

The response of living tissues to injury; bacteria, heat, cold, electricity, radiation, trauma, chemical substances.

Manifestations: (i) Local
(ii) General

(i) Macroscopical; heat, pain, swelling, redness, loss of function.

Microscopical: increased vascularity,
increased cells; erythrocytes, polymorphonuclear leucocytes, macrophages.
Exudate: protein-rich, causes oedema.

The macroscopical varieties of acute inflammation:

(i) Serous exudate; protein-rich fluid; occurs on serous membranes, e.g. pleurisy with effusion, peritonitis, pericarditis, synovial effusions.

(ii) Fibrinous: excessive amounts of fibrin, pericarditis, alveoli in lobar pneumonia.

(iii) Sero-fibrinous: a combination of the above.

(iv) Haemorrhagic: red cell extravasation, fulminating infections, e.g. meningococcal septicaemia.

(v) Suppurative or purulent:

(a) ulcer; skin; G.I. tract.
(b) empyema; collection of pus in a closed cavity, e.g. gall-bladder.
(c) abscess: localised collection of pus, e.g. brain.

(vi) Catarrhal: respiratory tract; profuse secretion of watery or mucoid fluid.

(vii) Gangrenous: the inflamed area becomes thrombosed, i.e. oxygen supply ceases. e.g. infections due to Clostridium welchii.

(viii) Membranous: matted fibrin, mucus, forming a grey-white membrane, e.g. diphtheria.

(ix) Cellulitis: spreading inflammation due to β-haemolytic streptococci.

RESULTS OF ACUTE INFLAMMATION

(1) Resolution: Complete - normal appearance and function.
Incomplete - fibrous scar.

(2) Suppuration: abscess, ulcer, or empyema.
healing yields a fibrous scar.

(3) Chronic inflammation.

(4) Fibrosis.

(5) Spread - (i) local tissues
(ii) lymphatic tissue - lymphangitis.
(iii) bloodstream; septicaemia.

(6) Death (i) fulminating infections, e.g. meningococcal.
(ii) dangerous locations, e.g. brain.

THE GENERAL MANIFESTATIONS OF INFLAMMATION

Variation due to: (1) Infecting Agent
(2) Site of infection
(3) Resistance and host immunity
(4) Duration
(5) Localisation.

1. Fever (May also occur in infarction, haemorrhage, collagen disease, malignant disease, brain stem lesions).

Normal heat regulation:

The heat-regulating centre in the hypothalamus responds to alterations in the temperature of circulating blood.
Normally, heat production = heat loss.
Retention of heat: Vasoconstriction of blood vessels, rigors if vasoconstriction insufficient.
Loss of heat: Vasodilation of skin vessels; sweating.

Mechanism of Fever:

Increased heat production: increased adrenalin
increased thyroxine
rigors

Decreased heat loss: vasoconstriction
diminished sweating

Results of pyrexia: (1) BMR increased by 7% for each 1°F rise in temperature.
(2) Increased pulmonary ventilation and cardiac output, i.e. pulse and respiration rise.
(3) (pulse = rise of 10 beats/min. for each 1°F. rise).
(3) Excessive protein breakdown - ketonis, negative nitrogen balance.
(4) Increased insensible salt and water loss by sweating - can cause circulatory and renal failure.

Hyperpyrexia: 106°F. -

severe infections
heat stroke
brain stem change, e.g. haemorrhage

2. Changes in the Blood

(i) leucocytosis (normal count 5-10,000/cu.mm.)

Neutrophils	in pyogenic infections
Eosonophils	in parasitic infections and allergic states, eg. asthma.
Lymphocytes	in chronic infections, e.g. TB.
Monocytes	in typhoid and malaria.

(ii) red cells:

(a) depression
(b) haemolysins - intravascular destruction
(c) haemorrhage - localised areas, e.g. peptic ulcer
generalised areas, e.g. Weil's disease.

3. Changes in Organs

(i) Liver, spleen and bone marrow - reactive hyperplasia.
(ii) Degenerative - toxic substances, e.g. carbon tetrachloride in the liver.
(iii) Septicaemia.
(iv) Pyaemia - metastatic abscesses.

REPAIR

When cells are destroyed, they are removed from the site by phagocytes. This leaves a defect, e.g. an ulcer, or abscess cavity. The defect is repaired by:

(i) regeneration of the parenchymal cells of the organ.
(ii) growth of the supporting connective tissues.

Repair Mechanisms:

(1) Primary Union - occurs when there is minimal loss of tissue. Invasion of the blood clot by fibrillants and capillary loops between fibrin strands. Retroblasts lay down collagen which matures. Vascularity then decreases and epithelial cells cover surface.

(2) Secondary Union: Granulation

There is loss of tissue, e.g. as in an ulcer cavity.

Stages:
(i) infection overcome by inflammatory response and debris removed by macrophages.
(ii) repair commences in floor of defect - proliferating capillary loops and fibrilloblasts.
(iii) epithelial cells proliferate and grow over the granulation tissue.
(iv) the vascular granulation tissue mature from the base until the area is a mass of fibrous tissue; the scar becomes avascular, and contracts.

Special Points:

(i) sweat glands, sebaceous glands and hair follicles do not regenerate.
(ii) the presence of infection retards growth of granulation tissue and delays healing.
(iii) dirt and foreign bodies delay healing (e.g.gauze).

Repair by resolution

Only occurs with minimal tissue damage, e.g. after surgical incisions; lobar pneumonia.

Repair by organisation

Unabsorbed fibrin is invaded by fibrilloblasts - scar tissue results. e.g. heart valves following rheumatic carditis; pleura following fibrinous pleurisy - i.e. there is a permanent scar.

Repair by regeneration

Some tissues show great powers of regeneration, e.g. liver, thyroid, pancreas, salivary glands, kidneys (to lesser extent).

Regneration in special tissues

(1) Will regenerate in most instances, e.g. bone, fibrous tissue.
(2) Will regenerate in favourable circumstances, e.g. liver, thyroid, kidney tubules; pancreas. (Kidney glomeruli cannot regenerate).
(3) Cannot regenerate: e.g. C.N.S. Tissue, striated muscle.

Epithelium

(i) Surface epithelia; retain powers of regeneration throughtout life.
(ii) Glandular tissue:
  (a) if the organ is removed, no regeneration is possible.
  (b) if the supporting framework is present, the regeneration may be complete.

Connective Tissues

(1) Fibrous tissues - excellent regeneration.
(2) Bone - excellent regeneration.
(3) Cartilage - replaced by fibrous tissue.
(4) Muscle - striated, cardiac and smooth muscle fibres do not regenerate, although hypertrophy of remaining fibres may occur.
(5) Mesothelium - complete regeneration.
(6) Blood vessels - mixed: the muscle and elastic tissue does not regenerate, the endothelial lining does.
(7) Lymphoid tissue - good regeneration.
(8) Nervous tissue -
  (i) C.N.S. - no capacity for regeneration - replaced by gliosis.
  (ii) Peripheral nerve tissue - regeneration if only axon is destroyed; cell body must be intact.

Factors influencing Repair

(1) Tissue involved.
(2) Vascularity - adequate blood supply is essential.
Avascular tissues do not heal and necrosis occurs.
(3) Protection, e.g. immobilisation of a fracture.
(4) Infection - retards granulation tissue.
(5) Nutrition - protein deficiency delays healing.
(6) Vitamins - Vitamin C essential for soft tissues.
Vitamin D essential for bone.
(7) Age.
(8) Endocrines: thyroid hormone is essential for healing.
steroids retard healing.
(9) Temperature
(10) Size.
(11) Foreign bodies - suture material, swabs, foreign fragments such as glass.
(12) Sinuses and fistulae - an open track joining two epithelial surfaces.
(13) Irradiation.
(14) Sensory nerves - absence delays healing, e.g. diabetics.

IMMUNITY

Immunity = freedom from infection (rarely complete).
Resistance = the capacity to deal with pathogenic (disease-producing) organisms.

Resistance

(1) Inborn:
(a) Species - e.g. gonococcus pathogenic to man, but not to other species.
(b) Race - white races more resistant to TB.
(c) Age - very young and very old.

(2) Increasing resistance:
(a) previous attack of same infection.
(b) artificial immunisation.

(3) Decreasing resistance:
General: (a) cold
(b) fatigue
(c) starvation
(d) debilitating diseases, e.g. diabetes.
(e) drugs and chemicals, e.g. anaesthesia.

Local: (a) wards
(b) necrotic tissue, foreign bodies
(c) impaired blood supply
(d) chemical substances, e.g. silica.

Mechanism of Resistance

(1) Mechanical: Skin;
Intact mucosal surfaces;
Trapping of particles by respiratory mucus and removal by ciliary action.

(2) Chemical: organism subjected to drying and low pH on the skin;
bacterial substances in sweat;
lysogen in tears;
in respiratory mucus
and in stomach.

(3) Ecological: inter-species competition;
e.g. skin, nose, otopharynx, gut, vagina and urethra possess normal 'commencal' bacterial flora.
These compete and usually outnumber pathogenic bacteria.

(4) Serological: (a) non-specific inhibitors, e.g. complement, lysins.
(b) specific antibody; gamma globulins; these are specific to the organism introduced.
Substances which give rise to antibody production are called antigens - any foreign substance.

Antigen - Antibody Reactions

Definitions of an antigen:
A substance which, when introduced into the body, invokes synthesis of new proteins (antibodies) with which it reacts characteristically and specifically.

Host Factors

(1) Self and 'not-self':
Substances recognised as not-self are antigenic and stimulate antibody production - usually high molecular weight proteins.

(2) Hetero-immunity:
Immunity common to all members of that species.

(3) Iso-immunity:
Antigens present in some members of the species and not others, e.g. ABO blood group antigens - non-antigenic to the individuals that possess them but antigenic to those who do not.

(4) Auto-immunity:
Some tissues may give rise to antibodies which may damage the same tissue. Immunity to tissues of the same individual arising from that individual is auto-immunity, and the antibodies, autoantibodies.

(5) Immune-tolerance.
The body may fail to recognise foreign protein as not-self - no antibodies are formed.

Immune Antibodies

Characteristic globulins which develop in response to antigenic stimuli and which react specifically with infoking antigens.
Types of antibodies:

(i) agglutinins
(ii) lysins
(iii) opsonins (allow cells to be phagocytised)
(iv) precipitins
(v) neutralising, e.g. antitoxins.
(vi) incomplete; block against other antibodies.

Antibody Formation

(1) Reticulo-endothelial system:
spleen, liver; kidney.
The RE system is concerned with antigen uptake rather than antibody synthesis.
(2) Lymphoid tissue:
(a) high concentration of antibody production.
(b) activation of germinal follicles within lymph glands.
(3) Plasma cells:
The splenic pulp. Production of antibody.

Responses to Antigenic Stimuli

(1) Primary Response:
Dose dependent - differs with route of invasion.
Time-lag of 5-7 days after which antibody is detectable.
Circulating antibody then falls over a number of weeks.

(2) Secondary response:
A further dose of antigen given after antibody synthesis has been established leads to prompt and active synthesis of antibody - high titres obtained for long periods.

Natural Antibody:

(1) Antibacterial antibody: already described. Non-specific, low-titre.

(2) Iso-haemogglutins: directed against red cell antigens - important in blood transfusions.

The clinical manifestation of the antigen-antibody response.

(1) Fever.

(2) Lymphadenopathy.

(3) Local reactions around invasion site, e.g. tonsillitis.

Allergy

Hypersensitivity to antigen-producing an exaggerated antibody or immune response - an exaggerated form of secondary reaction.

(1) Anaphylactic shock; restlessness, vomiting, convulsions, irregular and laboured respiration, heart failure. Recovery may not occur (depends on antigen).

(2) Cutaneous reaction: erythema (redness) and oedema (swelling).

(3) Asthma - bronchial constriction.
e.g. pollens, housedust mite, dander.

(4) Hay fever, e.g. pollens.

(5) Vomiting and diarrhoea, e.g. milk, sea-foods.

(6) Skin allergies, e.g. contact dermatitis.

(7) Serum sickness.

There may be a family history of hypersensitivity - the mechanism may be inborn or inherited (e.g. idiosyncrasy, atopy).

Artificially-acquired immunity

Passive Immunity
Gamma globulin containing antibodies can be injected into an individual to prevent disease, e.g. gamma globulin to protect against infectious hepatitis. Protection is immediate but lasts only up to three months.

Active Immunity
Antigens in a harmless form, e.g. modified avirulent virus can be introduced so that the individual can create his own antibodies. Modified toxin can also be used (known as toxoid).

The Clinical Use of Vaccination (immunisation).
Repeated doses of vaccine are necessary to procure immunity:

Active immunity: (toxoid or avirulent organisms are used to create the individual's own antibody response) -

smallpox	tetanus
diphtheria	whooping-cough
tuberculosis	poliomyelitis
typhoid	rubella

Passive immunity: Can be conferred in emergency situations, at-risk situations and travelling:

diphtheria	measles
tetanus	infectious hepatitis

Drugs which suppress immunity:

steroids	cytotoxic drugs.

DEGENERATION, INFILTRATION AND NECROSIS

(1) Degeneration : accumulation of metabolites in a cell damaged by preceding injury.

(2) Infiltration : the cell is overloaded by foreign substances.

(3) Necrosis : cell death.

Degeneration:

Causes :
- (i) infections
- (ii) physio-chemical agents, e.g. burns, anaesthetic agents
- (iii) nutritional - local, e.g. ischaemia,
  - general, e.g. anaemia, anoxia, malnutrition.
- (iv) severe water and electrolyte disturbance, especially K+ depletion.
- (v) systemic disease: diabetes, hepatic failure.

Necrosis:

Causes : ischaemia
infections
physio-chemical

Abnormalities of Cell Growth:

(1) Aplasia : Failure of development of a tissue or organ - intra-uterine.

(2) Hypoplasia : Failure of organs to develop full size.

(3) Atrophy:
- (i) Physiological: normal manifestation, e.g. thymus gland at puberty.
- (ii) nutritional: wasting due to protein deficiency.
- (iii) disuse: paralysed limb.
- (iv) vascular: ischaemia = necrosis.
- (v) pressure: vascular insufficiency due to pressure.
- (vi) infections: e.g. T.B.
- (vii) endocrine: e.g. adrenals in Addison's disease; uterus at menopause.
- (viii) metabolic: e.g. thyrotoxicosis.
- (ix) malignant disease: cachexia.

(4) Hypertrophy and hyperplasia:

Hypertrophy: increase in size of the tissues due to increase in individual cell size.

Hyperplasia: increase in total cell numbers.

Types:
- (i) endocrine: breast in lactation.
- (ii) compensatory: kidney.
- (iii) functional: L ventricular in hypertension.
- (iv) replacement: healing of liver by regeneration.
- (v) reactive: lymphoid tissue and bone marrow in response to infection or anaemia.
- (vi) neoplastic: localised areas of increase in cell numbers.

(5) Metaplasia: Definition - a change from one cell type to another, usually reversible.

(i) epithelial: prolonged irritation or chronic infection, e.g. calculi in urinary tracts or biliary tracts.
sites: endocervix, gall bladder, urinary bladder, repiratory tract, stomach.
columnar or transitional epithelium changes to squamous.

(ii) connective tissue: association with repair.
fibroblasts can change to osteoblasts.
Squamous epithelium undergoing metaplasia can undergo malignant change. This tendency is reversible if the irritant cause is removed.

(6) Dysplasia: Definition - alteration in size, shape and orientation of epithelial cells.
Cause: chronic irritation.
Sites: cervix, skin, oesophagus, endometrium.

Reversible - may undergo malignant change if cause persists.

(7) Neoplasia: Definition - an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of normal tissues and persists in the same excessive manner after cessation of the stimuli which evoked the change:

		Benign	Malignant
(i)	Connective Tissue	lipoma osteoma	sarcoma
(ii)	Epithelium	papillomata adenoma	carcinoma
(iii)	Lymphoid Tissue	benign lymphoma	malignant lymphoma
(iv)	Naevus Cells	benign naevus	malignant melanoma
(v)	Nervous System		meningioma glioma
(vi)	'Mixed' Tissues	ovarian dermoid	malignant Wilm's tumour
(vii)	Endothelium	haemangioma lymphangioma	haemangiotheloma

Differences		Benign	Malignant
(1)	Structure	structural differentiation	imperfect differentiation
(2)	Mode of Growth	expansion and compression	invasion
(3)	Rate of Growth	slow-growing, normal cells	rapid-growing, abnormal cells.
(4)	Continuation	may stop or regress	continue to grow
(5)	Metastisis	never	almost all metastasise.
(6)	Results	harmless except for compression effects or incidental complications, e.g. tension. May undergo malignant change.	kill by invasion and by metastasis.

Characteristics of Malignancy:

(1) Invasion.

(2) Atypical structure - (a) undifferentiated
(b) differentiated.

(3) Evidence of rapid growth.

(4) Irregular cell growth.

(5) Atypical blood vessels.

(6) Metastases.

Spread:

(1) Direct - (a) expansion
(b) invasion

(2) Lymphatic spread.

(3) Blood spread - (a) invasion of blood vessel.
(b) via lymphatic system into bloodstream.

(4) Implantation - (a) natural
(b) induced

(5) Transcoelomic - (a) peritoneum
(b) pleura
(c) pericardium.