MUST TO KNOW IN IMMUNOLOGY AND SEROLOGY	
IMMUNOLOGY	
Emil von Behring	Serum antitoxins
Robert Koch	TB
Elie Metchnikoff	Phagocytosis
Paul Ehrlich	Immunity
Charles Richet	Anaphylaxis
Jules Bordet	Complement
Karl Landsteiner	ABO blood group SSR
Gerald Edelman Rodney Porter	Structure of antibodies
Rosalyn Yallow	RIA
Snell Dausset Benaceraf	MHC
Niels Jerne	Immunoregulation
Kohler Milstein	Monoclonal antibody
Susumu Tonegawa	Antibody diversity Déjavu
Thomas Murray	Transplantation
Peter Doherty Rolf Zinkernagel	Dual recognition
Barré-Sinoussi Luc Montagner	HIV
Pope Innocent VII	1st: blood transfusion
Christopher Columbus	Old world → New world = smallpox New world → Old world = syphilis
1984	Year of discovery of T cell receptor gene
1979	(-) Small pox
US Russia	Pure culture of smallpox
Lysozyme	Attacks bacterial cell wall Ineffective against *Mycoplasma* and *Ureaplasma* (no cell wall)
LAK cells	NK cells + IL-2 Against cancer
NK/Null/3rd population lymphocyte	(-) Markers on T/B cells Kills virus and tumor cells CD 16, CD 56
Complement	Major humoral immunity (natural)
Phagocytosis	"ICED": Initiation, Chemotaxis, Engulfment, Digestion
Direct phagocytosis	Primitive pattern recognition receptor
Indirect phagocytosis	Via opsonins
Initiation	CR3 (3rd C' component) Laminin receptor Leucyl-formyl-methionyl-phenylalanine receptor
Chemotaxis	C5a (potent chemotaxin) Job's syndrome = N-RA/Abn-CA Lazy leukocyte syndrome = Abn-RA and CA Boyden Chamber assay = test for chemotaxis

Engulfment	C3b (opsonin)
Histamine	From eosinophils and mast cells Vasodilation
IL-1	Lymphokine activating factor Secreted by monocytes and macrophages Mediates fever, ↑APR's
CRP Serum amyloid A	APR's ↑20-1,000x
Fibroblasts	Young cells Stabilize the wound area
IFN-α	Leukocyte IFN (Type 1) Produced by viral-induced leukocyte culture Major producer: NK cell
IFN-β	Fibroepithelial IFN (Type 1) Produced by dsRNA fibroblast cells
IFN-γ	Immune interferon (Type 2) Produced by immunologically-stimulated lymphocytes
TNF-α	Cachectin Produced by macrophages
TNF-β	Lymphotoxin Produced by CD4+ and CD8+ lymphocytes
H. influenzae *N. meningitidis* *S. pneumoniae*	Large capsule Cause meningitis
CGD	(-) NADPH oxidase
NBT dye test	Test for CGD
Granulocyte concentrate	Appropriate blood component for CGD patients
Hypothalamus	Regulates body temperature (fever)
Chronic inflammation	↑ γ-globulins (↑plasma cells)
Heterophile antigens	Antigen in unrelated plants and animals but are closely linked that they cross react with one another
Order of activation (C')	$C_{142356789}$
Properdin	Serum protein Bactericidal and viricidal Needs C3 and Mg^{2+}
Betalysin	Released by platelets Against Gram (+) except *Streptococcus*
Active immunity	Antibody production is done by the body Advantage: Long term Disadvantage: slow response
Active natural	Infection (Ag)
Active artificial	Vaccination (Ag) Vaccines: 1. Live = smallpox 2. Attenuated = BCG (*M. bovis*) 3. Dead = cholera, typhoid 4. Toxoid = *C. tetani* 5. Modified virus = poliovirus
Passive immunity	Antibody production is not done by the body Advantage: Immediate Disadvantage: short term
Passive natural	Transfer in vivo (Ab)

Passive artificial	Immune serum Ig's administration (Ab) Ex. anti-rabies
Quellung	German word: Swelling
T. spiralis	Highest eosinophil count
1' lymphoid organs	Maturation of T and B cells
2' lymphoid organs	Proliferation and differentiation of T and B cells Spleen = Ag injected IV or IP Peyer's patches = Ag ingested Lymph nodes = Ag injected subcutaneously
Lymph nodes	Cortex = B cells Paracortex = T cells
T lymphocytes	80% of total lymphocytes CD2 = Sheep RBC receptor, classical T-cell surface marker CD3 = part of T cell Ag-receptor complex CD4 = MHC class II (Th) CD8 = MHC class I (Tc/Ts)
Ontogeny of T cells (Thymus)	Cortex = Immature (85%) Medulla = Mature (15%)
CD4+: CD8+ ratio	NV = 2:1 Abn = 0.5:1 or 1:2 (HIV)
AIDS	CD4+ cells: <200/μL (NV = 500-1300/μL)
Double (-) thymocytes	Immature T cell (+) CD2, CD5, CD7 (-) CD4, CD8
Double (+) thymocytes	(+) CD4, CD8
Mature T cell	CD4+/CD8+
Activated T cell	2' lymphoid organ CD25+ = receptor for IL 2 → lymphocyte proliferation
Sensitized T cell	Secretes lymphokines
Th_1 cells	Secrete IFN-γ and IL2 Activation of Tc, DH
Th_2 cells	Secrete IL4 and IL5 Activate B cells
Pro-B cells	BM CD19, CD45 receptor HC = chromosome 14
Pre-B cells	BM μ chains on cytoplasm κ = chromosome 2 λ = chromosome 22
Immature B cells	BM IgM on surface (monomer) (+) CD21, CD35 CD 21 = receptor for EBV
Mature B cells	IgD on surface ↑↑ IgM density
Activated B cells	CD25+
Plasma cells	(-) surface Ig (-) surface markers ↑ cytoplasmic Ig's → Ab's
CD10	CALLA

Cell flow cytometry	Light scatter Forward LS = cell size Side/90^0 LS = cell granularity/complexity	
Fluorescence microscopy	Labeled monoclonal antibodies	
Rosette test	E-rosette assay = T cells (CD2) EAC (Erythrocyte Ab Complement rosette) = B cells	
Differentiate T cells and B cells		
	T cell	**B cell**
Function	CMI	HI
Organ	Thymus	BM (1^{st}: Bursa of Fabricius – birds)
Concentration	60-80%	20-35% (10-20%)
Lifespan	Longer	Shorter
Soluble substances	Lymphokines	Antibodies
ID	E-rosette	Surface immunoglobulins
Mitogen	Concanavalin A Phytohemagglutinin Pokeweed mitogen	Lipopolysaccharide Pokeweed mitogen
Mitogen	Substances that cause cells to divide	
Lymphocyte capping	B cells	
HLA	Chromosome 6 (short arm)	
Class I MHC	Endogenous antigen Locus/Ag = HLA - A, B, C Chain structure = α-chain + β_2 microglobulin Cell distribution = all nucleated cells Presents antigen to CD8+ cells	
Class II MHC	For antigen found on surface of the cell Locus/Ag = HLA - DP, DQ, DR Chain structure = α-chain + β-chain Cell distribution = B cells and macrophages Presents antigen to CD4+ cells	
Class III MHC	"CCTB" Locus/Ag = C2, C4, TNF, Factor B	
Dendritic cells	Most efficient APC	
Langerhans cells	DC in skin	
IL-2	T cell growth factor Stimulates lymphocyte proliferation	
IL-3	Growth of stem cells and differentiation of blood cells	
IL-4 IL-5	B cell growth factor 1 B cell growth factor 2 Differentiates B cell → plasma cell IL-5: eosinophil differentiation	
IL-6	Enhance antibody production of plasma cell	
IL-12	NK stimulating factor Activates NK cells and cytotoxic T lymphocytes	
Heteroantigen	↑↑↑ Antigenic	
Graft rejection	1. Hyperacute = w/in mins 2. Accelerated = 2-5 days 3. Acute = 7-21 days 4. Chronic = >3 months	
Potent antigen	>10 kDa	
Albumin	40 kDa Good immunogen	

Hemocyanin	1M Da Excellent immunogen
Proteins	Most immunogenic (complex)
Haptens	Substance that is non-immunogenic but which can react w/ the products of a specific immune response
Agglutinoids	Agglutinins that are modified by heat
Adjuvants	Added to vaccines to enhance immune response 1. CFA = H_2O in oil emulsion of *M. butyricum* or *B. pertussis* (MTB), stimulates T cells 2. LPS = stimulates B cells 3. Synthetic MDP (muranyldipeptide) = stimulates T cells 4. Alum adjuvant = stimulates phagocytic cells 5. Squaline = from shark's oil, for HIV vaccine (MF59)
Allograft	Ex. Fetus on mother's womb
BM	Most immunogenic graft
Cornea	Least immunogenic graft Avascular, privilege site
Lymphocytotoxicity testing	Determines class I and II Ag's Ficolle-Hypaque solution: separates T and B cells from other cells Rgts: Trypan blue and C' (from Guinea pig cells), antisera of known HLA spec. (+) Blue (-) Unstained
Polyspecific reagents	ID by elimination
Nylon Wool technique	For class II Mixture of T/B cells ---(Straw w/ nylon wool)---> B cells adhere to nylon wool B cells + antiserum of known HLA spec. ---(C' + trypan blue)---> (+) Blue (-) Unstained
MLR: Mixed Lymphocyte Reaction	For D-related antigens = Class II One way = one is inactivated Pt. lympho. + <u>Donor lympho.</u> (inactivated: irradiated/treated w/mitomycin) If incompatible → proliferation of patient lymphocytes Tritiated hydrogen = ↑radioactivity
Antibodies	Glycoproteins
Ehrlich's side chain theory	Certain cells had specific receptor for antigen Antigen will select the cell w/ proper receptor
Template theory (by Felix Haurowitz)	Antibody-producing cells produce generalized type of antibody Antigen serves as a mold/template
Clonal Selection (by Neils Jerne & Macfarlane Burnet)	Most acceptable theory Individual lymphocyte produces 1 type of Ig Antigen finds cells capable of responding to that Ig → proliferate
Reduction of a polymer	Ex. IgM 1. 2-mercaptoethanol (2-ME) 2. Dithiothreitol (DTT)
Fab	Ag binding 1 LC + ½ HC
Fc	Confer biologic activities of C' fixation Skin fixation Placental transfer
Papain	3 fragments = 2 Fab + 1 Fc Above the hinge region
Pepsin	2 fragments = 1 $F(ab)_2$ + 1 Fc' Below the hinge region

	$F(ab)_2$ = major fragment Fc' = (-) disulfide bond
κ:λ ratio	2:1 (65%: 35%)
Disulfide bonds	N = H-H, H-L Abn = L-L (identical) = Bence-Jones protein (Multiple myeloma)
Hinge region	Proline Between CH1 and CH2
Fab	NH_3
Fc	COOH
Domains	Regions/sections in an immunoglobulin molecule
+1 CH (CH4)	IgM and IgE
Isotype	HC that determine Ig chain
Allotype	Variations in the constant region of HC and LC (Km, Gm)
Idiotype	Variations in the variable region of HC and LC
J-chain	IgM and IgA
Secretory component	Prevents enzymatic degradation of IgA
Starlike	Ab (IgM) ≠ Ag
Crablike	Ab (IgM) = Ag
IgA	Monomer (serum/IgA_1) Dimer (secretory/IgA_2) Fix C' (alternative pathway)
IgG	↑↑↑ concentration (80%) > IgA > IgM > IgD > IgE ↑↑↑ half-life (23 days)
IgG 4 subclasses	Differ in # and arrangement of disulfide bonds
IgG_1	↑↑↑% Best to cross the placenta
IgG_3	15 HH (-) bind to protein A Best to fix C' > IgG_1 > IgG_2
IgG_2	(-) Cross placenta
IgG_4	(-) C' fixation
IgM	Largest (900 kDa) Heaviest (19s) Best to fix C' (classical pathway)
Agglutination	IgM (large)
Precipitation	IgG (fine particles)
ADCC	NK cells (Fc γ receptor) = release perforins w/c are toxic to the virus (Ag)
IgD	Immunoregulation Found on unstimulated but immunocompetent B cell
IgE	Regain Allergic reactions Against parasites
Atopy	IgE-mediated allergic reaction
RAST	Patient allergic to Rye grass
Eosinophil	Release MBP and ECP
RIST	Total IgE
RAST/FAST	Allergen-specific IgE
Complement	β-globulin (electrophoresis) 3 anaphylatoxins: C3a, C4a, C5a C5a: chemotaxin and anaphylatoxin C3b: opsonin

	Produced by the liver except: - C1 = intestinal epithelial cell - Factor D = adipose cell
Anaphylatoxin	Release of vasoactive amines ↑ smooth muscle contractions ↑ vascular permeability
Classical pathway	Activated by Ag-Ab complexes C3 convertase: C4b2a/C4b2b C5 convertase: C4b2a3b/C4b2a3b C1q, 1r, 1s = bound by Ca^{2+} C1q = 6 globular structures (at least 2 globes must attach to Fc of CH2 of IgG/ CH3 of IgM)
Alternative pathway	Initiated by: 1. Aggregates of IgA 2. Yeast cell wall or zymosan 3. LPS 4. Cobra venom factor C3 convertase: C3bBb (stabilized by Properdin and Mg^{2+}) C5 convertase: C3bBb3b
Lectin pathway	Initiated by microorganisms w/ mannose in their cell wall Lectins: proteins that attach to CHO MASP-1 & 2: MBL associated serine proteases 1 and 2 MBL = C1q MASP-1 = C1r MASP-2 = C1s
C8	Starts pore formation (cell lysis)
C9	↑ cell lysis
C1 INH	Dissociates C1r and C1s from C1q
Factor I	Cleaves C3b and C4b
Factor H	Inactivates C3b Prevents binding of B to C3b
C4-binding protein	Inactivates C4b
Vitronectin/S protein	Prevents attachment of C5b67 complex to cell membrane
DAF	Dissociates C3 convertase
HRF & MIRL (CD59)	Inhibit MAC
C1, C4, C2 deficiency	LE-like syndrome
C3 deficiency	Severe and recurrent infections (most severe)
C2 deficiency	Most common C' deficiency
C56789 deficiency	Neisserial infections (gonococcemia/meningococcemia)
C1 INH deficiency	HANE
DAF/HRF deficiency	PNH

Hypersensitivity Reactions

	Type I	**Type II**	**Type III**	**Type IV**
Other name	Immediate Anaphylactic	Cytotoxic	Immune-complex	Delayed Cell-mediated
Immune mediator	IgE	IgG and IgM	IgG and IgM	T cells
Complement involvement	No	Yes	Yes	No
Effector cells	Basophils Mast cells	RBCs WBCs Platelets	Host tissue cells	T cells Macrophages

	Type I	Type II	Type III	Type IV
Mechanism	Release of mediators	Cytolysis due to Ab and C'	Deposits of Ag-Ab complexes	Release of lymphokines
Examples	Anaphylaxis Hay fever Food allergies Asthma Bee sting	HTRs AIHA HDN	Serum sickness Arthus reaction SLE RA	Low MW compounds (ex. Ni) Cosmetics Rubber Poison ivy/oak

Myasthenia gravis	Acetylcholine receptor blocking antibody
Multiple sclerosis	Anti-myelin antibody
Pernicious anemia	Anti-intrinsic factor antibody Anti-parietal cell antibody
Goodpasture's syndrome	Anti-glomerular basement membrane antibody
Primary biliary cirrhosis	Anti-mitochondrial antibody
Chronic active hepatitis	Anti-smooth muscle antibody
Hashimoto's thyroiditis	Anti-microsomal antibody Anti-thyroglobulin antibody
Graves' disease	Anti-TSH receptor antibody
Bence-Jones protein	Multiple myeloma
AFP	Hepatocellular carcinoma
hCG	Choriocarcinoma
Calcitonin	Familial medullary thyroid carcinoma
PSA	Prostate cancer
CEA	Colorectal cancer
CA 19-9	Pancreatic and colonic adenocarcinoma
CA 15-3	Breast cancer
CA 125	Ovarian cancer
SEROLOGY	
1' immune response	Long lag period ↓ Ab IgM
2' immune response (anamnestic/booster)	Short lag period ↑ Ab IgG
Affinity	Attraction between 1 Fab and 1 epitope
Weak bonds	Dissociation can easily occur 1. ionic bond 2. hydrogen bond 3. hydrophobic bond 4. Van der Waals forces
Avidity	Sum of all attractive forces between multivalent Ag and multivalent Ab ↑ avidity = ↓ tendency of complex to dissociate
Precipitation	Soluble antigen == soluble antibody Noted by Kraus
Zone of equivalence	Max precipitation occurs (Ag = Ab)
Prozone	Antibody excess False (-) Remedy: Serum dilution
Postzone	Antigen excess False (-) Remedy: repeat the test after a week to give time for antibody production
Passive immunodiffusion	Passive: no electrical current is used

	Immunodiffusion: Ag and Ab reaction occurs by diffusion
Radial immunodiffusion	Ab → Gel Ag → Well
Mancini/Endpoint method (RID)	Ag is allowed to diffuse completely IgG = 24 hrs IgM = 50-72 hrs $\underline{d^2 = \text{Ag concentration}}$ Ex. C3 determination
Fahey and McKelvey/ Kinetic method (RID)	Measurement is taken before the point of equivalence Time: 18 hrs $\underline{d = \log \text{Ag concentration}}$
Oudin single diffusion	Ab → Gel Ag → Diffuse (+) precipitin band
Ouchterlony double diffusion	Both Ag and Ab diffuse through semisolid media Serological identity = smooth curve Nonidentity = 2 crossed-lines Partial identity = spur formation
Laurell rocket immunoelectrophoresis	RID + electrophoresis Height/apex of rocket α Ag concentration
Countercurrent immunoelectrophoresis	Ag and Ab are on apoosite sides Ag ---(electrophoresis)---> (+) Precipitin lines ↑ migration = ↑ Ag concentration
Immunoelectrophoresis	Detect Bence-Jones protein Serum (source of Ag) = electrophoresed to separate protein fractions Trough = add antiserum Change in shape, etc (arcs) = abnormality
Immunofixation electrophoresis	Similar to IEP except antiserum is layered on the medium
Agglutination	Reaction between cellular or particulate antigen
Direct agglutination	Ag found naturally on surface of particle Ex. Kauffman and White (*Salmonella*)
Hemagglutination	Ag is naturally found on RBC Ex. ABO blood typing
Passive agglutination	Ag == carrier (latex, Bentonite, red cell, charcoal) (+) Agglutination when (+) Ab
Reverse passive agglutination	Ab == carrier (+) Agglutination when (+) Ag
Coagglutination	Uses bacteria as inert particles Ex. *S. aureus* = most frequently used
Agglutination-inhibition	(+) No agglutination Ex. β-hCG = classic example (↑1st trimester)
Hemagglutination-inhibition	Red cells: indicator particles Classic serologic test for viral Ab (Rubella and Influenza Ab)
Grading (agglutination)	0 = No agglutination 1+ = 25% Agglutination 2+ = 50% Agglutination 3+ = 75% Agglutination 4+ = 100% Agglutination
DAT	In vivo sensitization Specimen: EDTA/citrated RBC Investigation of:

	-HDN -HTR -AIHA -DIHA
IgG	Nonagglutinating Ab Can sensitize cells w/o causing visible agglutination
AHG reagent	Spans the distance between 2 IgG's
Mechanisms of DIHA	1. Drug absorption = Penicillin 2. Membrane modification = Cephalosporin 3. Immune complex formation = Stibophen, Phenacetin, Rifampin 4. Autoantibody formation (Gen. to Rh) = Methyldopa (Aldomet: Ab to Kidd), Mefenamic acid (Ponstel)
HTR	(+) DAT (-) DAT (mf) DAT = some are lysed and some are not lysed by C'
IAT	In vitro sensitization Specimen: Patient serum (common) Uses: -Cross-matching -Ab detection -Ab identification -RBC Ag phenotyping (weak D) = Specimen: RBC
Wash 3x	To remove unbound globulins
Inadequate washing	False (-) antiglobulin test Unbound globulins can neutralize AHG reagent
If (-) AHG	Confirm by adding Check or Coomb's cells (O+ RBCs sensitized w/ IgG) -Valid: Agglutination -To ensure AHG was added or not neutralized
Types of AHG reagent	1. Polyspecific AHG = contain anti-IgG and anti-C3d (C' degradation products) 2. Monospecific AHG = contain anti-IgG or anti-C3d
Radioimmunoassay (RIA)	Uses radioactive substances as label -Tritiated Hydrogen -^{125}I
Scintillation counter	Measure radioactivity β = liquid scintillation counter γ = crystal scintillation counter
Competitive binding assays (RIA)	Bound radiolabeled Ag is 1/α to patient Ag present
Noncompetitive immunoradiometric assays (IRMA)	Bound radiolabeled Ab is α to patient Ag present in supernatant fluid
RIST	Measure total IgE
RAST	Measure Allergen-specific IgE
Wastes container (DOH)	1. Red = sharps, needles 2. Yellow = infectious 3. Yellow w/ black band = chemical wastes 4. Green = non-infectious wet waste 5. Black = infectious dry waste 6. Orange = radioactive waste
Enzyme immunoassay (EIA)	Similar to IRMA except that it uses enzymes 1. Horseradish peroxidase = most common 2. ALP

	3. β-galactosidase 4. Glucose oxidase 5. G-6-PD
Capture/Sandwich EIA	Ab == Ag == enzyme labeled Ab Enzyme activity is α to the amount of Ag
Fluorescent immunoassay	Uses fluorophores/fluorochromes 1. Fluorescein Isothiocyanate (FITC) = Green 2. Tetramethylrhodamine Isothiocyanate (TRITC) = Red
Direct immunofluorescent assay	Histopathology Unknown Ag + FITC/TRITC labeled Ab = (+) Fluorescence
Indirect immunofluorescent assay	Serology (Ex. FANA, FTA-ABS) Known Ag + unknown Ab + FITC/TRITC labeled AHG = (+) Fluorescence
Fluorescence polarization immunoassay (FPIA)	Change in polarization of fluorescent light emitted from a labeled molecule
PACIA	Measures the number of nonagglutinating particles left
Syphilis	A.k.a. Great pox/Evil Pox/French/Italian/Spanish disease Caused by *T. pallidum* subsp. *pallidum* = RIP: Refrigerate blood for 3 days
Congenital syphilis	Hutchinsonian triad: Keratitis, Notched teeth, Deafness
Treatment	1st: Heavy metals (Ex. Arsenic: Arsphenamine, Salvarsan, 606) Penicillin: Drug of choice (crosses the placenta – Tx: Neurosyphilis)
1' syphilis	Lesion: Hard chancre Lab: Darkfield microscopy = (+) coiled organisms w/ corkscrew motility
2' syphilis	Highly infectious Systemic dissemination of organisms Wart-like lesions: Condylomata lata Lab: Darkfield microscopy, serologic tests
Latent syphilis	(-) Signs and symptoms (+) Serologic tests
3' syphilis	Granulomatous lesions: Gummas (Dead treponemes) CSF: Neurosyphilis Lab: Serologic tests
Jarisch-Herxheimer phenomenon	Large quantities of toxins are released as the bacterial dies during treatment
Serologic Tests for Syphilis (STS)	♫ 1st: Wasserman test = Principle: C' fixation ♫ Nontreponemal serologic tests = nonspecific = Subjected to biologic false (+) = Principle: Flocculation (special type of precipitation involving fine particles) = Detects Reagin (Ab to cardiolipin) = Ex. VDRL, RPR, TRUST, USR, RST ♫ Treponemal Serologic tests = specific = Detect Treponemal antibodies = Ex. TPI, FTA-ABS, HATTS, TPHA, MHA-TP
Biologic False (+) - Syphilis	"TRIPLSM$_2$" TB RA IM Pregnancy Leprosy SLE Measles Malaria

VDRL	Specimen: Serum (common) or CSF Reagent: VDRL Ag (C-L-C): 1. Cardiolipin: Main reacting component 2. Lecithin: Removes anticomplementary activity of cardiolipin 3. Cholesterol: Enhances reacting surface of cardiolipin Serum: Δ 56'C for 30mins (Inactivate C') [Reinactivation of C': After 4 hrs, Δ 56'C for 10mins] Examine for flocculation microscopically (100x) = Nonreactive: No clumps = Weakly reactive: Small clumps = Reactive: Medium to Large clumps
Qualitative serum VDRL (Ag delivery needle)	Slide = 14mm diameter (ceramic ring) Needle = Gauge 18: delivers 60 drops per mL of Ag (1/60)
Quantitative serum VDRL (Ag delivery needle)	Slide = 14mm diameter (ceramic ring) Needle: = Gauge 19: delivers 75 drops per mL of Ag (1/75) = Gauge 23: delivers 100 drops per mL of saline (1/100)
CSF VDRL (Ag delivery needle)	Slide =16mm (diameter) =1.75mm (depth) Needle: Gauge 21/22: delivers 100 drops per mL of Ag
Rotation (VDRL)	Serum = 180 RPM for 4 mins CSF = 180 RPM for 8 mins
RPR	Specimen: Serum Reagent: Modified VDRL Ag 1. C-L-C 2. Charcoal: makes the reaction easy to read 3. EDTA: prevents lipid oxidation 4. Choline chloride: inactivates C' 5. Thimerosal: preservative Examine macroscopically
RPR Antigen delivery needle	Ring (plastic card) = 18mm Needle = Gauge 20: delivers 60 drops per mL of Ag
Rotation (RPR)	100 RPM for 8 mins
Treponema pallidum immobilization test (TPI)	Standard test to which other tests are evaluated Live organisms (from testicular chancre of rabbit) + Patient serum (anti-Trep) Positive = ≥50% immobilized Doubtful = 20-50% immobilized Negative = <20% immobilized
FTA-ABS	Gold standard 1. Patient serum (Δ 56'C for 30mins) + Reiter strain (nonpathogenic strain) ♫ Reiter strain = Sorbent (removes cross-reactivity w/ other treponemes) 2. Indirect immunofluorescence Nichol's strain (known Ag, virulent) + Patient serum (anti-Trep) + FITC AHG (+) Fluorescence
Hemagglutination tests	Ag: RBCs sensitized w/ Nichol's strain HATTS, TPHA, MHA-TP
Congenital infections	"ToRCHeS" a. Toxoplasmosis b. Rubella c. CMV = common d. Herpes

	e. Syphilis
ASO Tube test	Titer: reported as Todd unit Neutralization of the hemolytic activity of Streptolysin O (+) No hemolysis (-) Hemolysis
Serum preparation	Serum ÷ TV
Titer	Reciprocal of the highest dilution in w/c a positive reaction occurs
RBC control	No hemolysis
SLO reagent control	Complete hemolysis
ASO Titer	NV = 0-166 Todd (Tube test) Significant = >200 IU/mL (Slide test)
DNase B Ab testing	Anti-DNase B sometimes appear earlier than ASO ↑ Sensitivity for detection of glomerulonephritis Measured by neutralization DNA == methyl green → Green DNase == DNA ≠≠ methyl green → (-) Colorless Anti-DNase == DNase ≠≠ DNA == methyl green → (+) Green [no color change]
Streptozyme	Slide agglutination screening test for detection of Ab's to several Streptococcal Ag's
1' Hepatitis viruses	Hepatitis A, B, C, D, E
2' Hepatitis viruses	EBV, CMV, etc.
Hepatitis A	Infectious hepatitis PicoRNAviridae (RNA) MOT: fecal-oral Short incubation period = 15-40 days
Hepatitis B	Serum hepatitis HepaDNAviridae (DNA) MOT: sexual, parenteral, perinatal Dane particle = infectious
Hepatitis C	Non-A, non-B hepatitis Flaviviridae (RNA) MOT: sexual, parenteral, perinatal Major cause of post-transfusion hepatitis (80% HCV || <10% HBV)
Hepatitis D	Viroid like (RNA) Require infection w/ HBV (coinfection or superinfection)
Hepatitis E	Caliciviridae/HepEviridae (RNA) MOT: fecal-oral, contaminated H_2O ↑ fatality: pregnant
HBsAg	A.k.a. Australia antigen 1st marker to appear in HBV infection Screen blood donors Acute or chronic infection
HBeAg	High vertical transmission risk (Mother → Child) High degree of infectivity
HBcAg	NOT a serologic marker Detected only by liver biopsy
IgM anti-HBc	1st antibody to be produced Only marker detectable during "core window" period Acute infection
Total anti-HBc	Acute or chronic IgG: lifelong marker of HBV
Anti-HBs	Marker of past infection and immune state

	Tested for vaccination and follow up		
Anti-HBe	Marker of convalescence (recovery)		
	HBsAg	**Anti-HBc**	**Anti-HBs**
No HBV infection	-	-	-
Early infection	+	-	-
Acute HBV	+	+	-
Window period	-	+	-
Past infection	-	+	+
Immunization	-	-	+
HCV	Surrogate test: ↑ALT, (+) anti-HBc Specific test: (+) Anti-HCV = ELISA, RIBA		
IgM anti-HDV	Detected by ELISA		
IgM anti-HEV	Detected by ELISA, WB, Fluorescent antibody blocking assay		
HEV RNA	ID by PCR		
PCR	D>A>E: Denaturation > Annealing > Extension		
1st generation test (HBsAg)	Ouchterlony double diffusion		
2nd generation test (HBsAg)	Counterelectrophoresis Rheophoresis Complement fixation		
3rd generation test (HBsAg)	RIA ELISA RPHA RPLA		
HIV-1	A.k.a. HTLV-III, LAV, ARV RNA virus (ssRNA, icosahedral, enveloped) Retroviridae (Lentiviridae) AIDS in US, Europe		
HIV-2	West Africa Less pathogenic, ↓ transmission		
HIV	Retains infectivity for: 3 days (dried specimen) >A week (aqueous environment)		
Main structural genes (HIV)	Env Gag Pol		
Env (envelope) gene	gp160 = gp120: knobs/spikes = gp41: spans the inner and outer membrane Attachment and fusion to CD4+ cells		
Gag (Group Ag) gene	p55 = p15 = p17 = <u>p24</u> Located in nucleocapsid		
Pol (polymerase) gene	Located in the core near the nucleic acid = Reverse transcriptase: transcribes RNA → DNA = Integrase: inserts viral DNA to host DNA		
Ab to p24	1st Ab to appear in HIV infection		
Screening tests (HIV)	1. <u>ELISA</u> = standard screening test 2. Agglutination tests = gel/latex particles 3. Dot-Blot testing		
Confirmatory tests (HIV)	1. <u>Western Blot</u> = standard confirmatory test		

	- CDC Criteria: 2 out of 3 Ab bands to p24, gp41 and gp120/160 = (+) WB 2. Immunofluorescence assay
SLE	Lupus = "wolf" Connective tissue disorder
LE factor	7s IgG
LE cell (buffy coat)	Neutrophil w/ homogeneous round body
ANA test	Nonspecific 1. FANA = immunofluorescence 2. Visible ANA = light microscopy
FANA	Mouse liver (Ag) +Patient serum (ANA) + FITC labeled AHG (+) Green gold fluorescence
Visible ANA	Hep 2 cells (Ag) + Patient serum (ANA) + HRP labeled AHG + Diaminobenzidine (+) Dark brown stain
Hep 2 cells	Human epithelial cells
Homogeneous/Diffuse/ Solid	Anti-DNP = Rheumatoid disorder
Peripheral/Ring/Rim/ Membranous	Anti-dsDNA = most specific for SLE Active stage of SLE
Speckled/Mottled/ Pepperdot	Require another test Anti-ENA: a. anti-Smith = SLE b. anti-RNP = MCTD, SLE, RA
Nucleolar	Anti-nucleolar RNA = Scleroderma
Anti-centromere	CREST syndrome ♫ Calcinosis ♫ Reynaud's phenomenon ♫ Esophageal dysmotility ♫ Sclerodactyly ♫ Telangiectasia
RA	Inflammatory disease involving joints
RF	IgM reacting against Fc portion of IgG (HC) Specimen: Serum, synovial fluid
Tests (RA)	1. Rose-Waaler test = sheep cell agglutination 2. Singer-Plotz test = latex fixation
Titer (RA)	Positive = >80 Weakly positive = 20-40 Negative = <20
CRP	Nonspecific indicator of inflammation Thought to be an antibody to the C-polysaccharide of pneumococci ↑ 4-6 hrs | Peak: 24-72 hrs (48 hrs) Similar to antibody Ca^{2+} dependent Tests: 1. RPLA = latex w/ anti-CRP 2. Precipitation test 3. RIA 4. C' fixation = (+) No hemolysis | (-) Hemolysis
C' fixation (CRP)	Specimen: Serum (Ag) Positive reaction: Ag == Ab + C' → Ag == Ab == C' + Amboceptor (indicator) → No hemolysis Negative reaction: Ag ≠≠ Ab + C' → Ag ≠≠ Ab, free C' + Amboceptor (indicator) → Hemolysis

Amboceptor (hemolysin)	Indicator Sheep RBCs coated w/ anti-sRBC
IM	Caused by EBV = Target cells: B cells (CD21) Hema: Lymphocytosis Atypical lymphocytes = T cells reacting to B cells infected w/ EBV
Paul-Bunnell screening test	General/screening test for heterophile Ab's Reagent: sheep RBC (+) Agglutination
Davidsohn differential test (Tube)	1. Adsorption (removal of Ab in serum) w/ Guinea pig kidney cells and beef/ox erythrocytes 2. Addition of indicator cells (sRBCs) 3. Agglutination
Antibodies to IM	(+) Adsorption w/ beef/ox erythrocytes (+) Agglutination after adsorption w/ GPK cells
Antibodies to Forssman Ag	(+) Adsorption w/ GPK cells (+) Agglutination after adsorption w/ beef/ox erythrocytes
Antibodies to Serum sickness	(+) Adsorption w/ beef/ox erythrocytes and GPK cells (-) Agglutination after adsorption w/ beef/ox erythrocytes and GPK cells
EBV Ag's	1. VCA = Viral Capsid Ag (cytoplasm) 2. EA = Early Ag a. EA-D = Diffuse early Ag (nucleus and cytoplasm) b. EA-R = Restricted early Ag (cytoplasm) 3. EBNA = Epstein-Barr nuclear Ag (nucleus)
Monospot/Spot/Rapid differential slide test	Horse RBCs (indicator cells) = more sensitive indicators of Ab's found in IM
Additional Topics	
H. capsulatum	Cross reacts w/ *B. dermatitidis*
SREHP	Serine-rich *E. histolytica* protein
Optimal	pLDH (parasitic LDH) Malarial organisms
Malaquick	HRP-2/HRP II Ag: Histidine Rich Protein Ag *P. falciparum*
Streptococcus MG	Primary atypical pneumonia
OspC	Outer membrane associated protein Lyme disease
Latex agglutination	Cryptococcal Ag in CSF
Seroconversion	(+) specific Ab → previously undetectable
Transient Hypogammaglobulinemia of infancy	5-6 months of age IgG = most affected
Selective IgA deficiency	Most common congenital immunodeficiency
Severe combined immunodeficiency	Most serious congenital immunodeficiency Affects T and B cells Children → Enclosed in a plastic bubble ("Bubble boy")
DiGeorge's syndrome	Congenital thymic aplasia
X-linked hypogammaglobulinemia	Bruton's agammaglobulinemia ↓↓↓ All Ig (-) B cells
Common variable immunodeficiency	Recurrent bacterial infection and sinusitis Selective IgG deficiency may occur
PNP deficiency	Metabolism of purines is affected

WAS	Triad of immunodeficiency, eczema and thrombocytopenia Inability to mount IgM response to the capsular polysaccharide of bacteria
A-T	↓↓↓ IgG_2, IgA, IgE Uncoordinated muscle movements (ataxia) Dilatation of blood vessels (telangiectasia)
Waldenström's macroglobulinemia	↑↑↑ IgM ↓↓↓ other antibodies
Leukocyte adhesion deficiency syndrome	Defective adhesion protein (CD18) on the surface of phagocytes
S. typhi (Widal)	Titer of >1:160 (clinically significant)
R. rickettsii (Weil-Felix)	Titer of >1:320 (clinically significant)
Tolerance	Refers to the specific immunological non-reactivity to an antigen resulting from a previous exposure to the same antigen
Tolerogen	Antigens that induce tolerance
Self-tolerance	No immune response against self-antigens
Clonal detection	Involves killing of T cells (negative selection) that reacts against antigens present in the fetus at that time
Central tolerance	Tolerance to self acquired w/in the thymus
Peripheral tolerance	Tolerance acquired outside the thymus
Clonal anergy	Functional inactivation of certain T cells
Clonal ignorance	State in which certain autoantigens are undetected by the immune system under normal circumstances
Autoimmunity	Result of breakdown of mechanisms responsible for tolerance Induction of immune response against components of the self
Molecular mimicry	Invading pathogen expresses antigens that resemble "self". These activate T and B cells. When the infection is under control, these cells may now turn against self-antigens Ex. Rheumatic heart disease
Sjögren's syndrome	Chronic inflammatory disease that affects the exocrine glands (lacrimal and salivary glands)
Reiter syndrome	Triad of arthritis, conjunctivitis and urethritis
HLA-DR3	SLE Addison's disease Graves' disease IDDM Myasthenia gravis Sjogren's syndrome Atrophic thyroiditis
HLA-DR4	RA (HLA-Dw4) IDDM
HLA-B27	Ankylosing spondylitis Reiter syndrome
HLA-Dw5	Pernicious anemia
HLA-DR5	Goitrous thyroiditis

Autoimmune Diseases			
Specificity	**Disease**	**Organ**	**Autoantibody to**
Organ specific	Hashimoto's thyroiditis	Thyroid	Thyroglobulin TPO (microsomal)
|	Primary myxedema	Thyroid	Cytoplasmic TSH receptor
|	Graves' disease	Thyroid	TSH receptor
|	Pernicious anemia	Red cells	Intrinsic factor Parietal cell
|	Addison's disease	Adrenal	Adrenal cells
|	Premature onset menopause	Ovary	Steroid producing cells
|	Male infertility	Sperm	Spermatozoa
|	IDDM	Pancreas	Pancreatic islet β-cells
|	NIDDM	Systemic	Insulin receptor
|	Atopic allergy	Systemic	β-adrenergic receptor
|	Myasthenia gravis	Muscle	Acetylcholine receptor Muscle
|	Goodpasture's syndrome	Kidney Lung	Renal and lung basement membrane
|	Pemphigus	Skin	Desmosomes
|	Pemphigoid	Skin	Skin basement membrane
|	Phacogenic uveitis	Lens	Lens protein
|	AIHA	Red cells Platelets	Red cells
|	Idiopathic thrombocytopenia	Platelets	Platelets
|	Primary biliary cirrhosis	Liver	Mitochondria
|	Idiopathic neutropenia	Neutrophils	Neutrophils
|	Ulcerative colitis	Colon	Colon
|	Sjögren's syndrome	Secretory glands	Duct mitochondria
|	Vitiligo	Skin Joints	Melanocytes
|	RA	Skin, kidney, joints, etc	IgG
Non-organ specific	SLE	Joints, etc.	DNA, RNA nucleoproteins