Sir William Leishman's proposed syllabus and lectures (in preparation for acceptance of chair of Pathology at the Army Medical School?)

Wellcome Collection
183 Euston Road
London NW1 2BE UK
T +44 (0)20 7611 8722
E library@wellcomecollection.org
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Notebook of Sir William Leishman, Professor of Pathology 1903 – 1914 (Assistant Professor of Pathology 1899–1903)

J.B. Neal Major RAMC

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Proposed Syllabus of Junior Class in Pathology.

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Histology of Normal Blood.

1. Exam. of fresh unstained films & identification of the cellular elements normally present.
2. The preparation of blood films for staining.
3. General principles of staining.
4. Staining of blood films
5. The quantitative & qualitative enumeration of the cellular elements of the blood.
6. The use of the Haemocytometer and Haemoglobinometer
7. Examination of Bone Marrow
8. Demonstration of the Phagocytic power of the Leucocytes.
9. Method of obtaining serum for examination.
10. Estimation of the Alkalinity & Coagulability of the blood and their bearing on various patholog. conditions
11. The making and use of blood capsules and sedimentation tubes.

Pathology of Blood.

1. Inflammation.
2. Changes found in the blood in the following conditions
   Simple Anaemia – Post-haemorrhagic An. Pernicious A.

Chlorosis. Lymphatic Leuk. Splenic Med. Leucocyth.

3. Changes in the blood in acute disease and the relation of these changes to bacterial infection.

4. Widals reaction. Methods of carrying it out.

The collection of pathol. material for microscopic and bacterial investigation.

The principles & methods of sterilization employed in bacteriology

The preparation and sterilization of culture media.

Methods of preserving tissues &c for histolog. exam. hardening embedding & cutting of sections.

Bacteriology Technique.

General Morphology of Bact

Classification of Bact. and of Bact. Diseases

Microscop. and bacterial exam. of the Bacteria causative of the following diseases. The relation between these bacteria and the symptoms of the various diseases caused by them and their products. Further illustrated, where possible by the exam. of pathol. material from actual cases

Suppuration &c. Staph Pyog. Strep. Pyog. Micro. Tetrag.

Ulceration endocard. Erysipelas Acute Rheumatism.

Gonorrhoea. Syphilis. Soft Sore

Pneumonia Catarrhal pneumonia

Tuberculosis Nature of Tuberculin. The Diag reaction.
Leprosy.
Anthrax.
Actinomycosis Glanders &c.
Typhoid. Nature + use of Typh. Vaccine
Malta Fever.
Plague Nature + use of Plague Serum + Vaccine.
Spirillum fever.
Cholera. Nature + use of Cholera Vaccine.
Diphtheria. Nature + use of Antitoxin.
Tetanus. Anti-tetanus Serum.

Malaria. Cycles of Devel. in man + mosquito
Varieties of Mal. Inoc? expts. Diff. diag. of Anopheles
+ Culex. Value of prophylac. measures. Exam. of
films of mal. blood &c.
Dysentery Amoebic + bacillary.
Small pox + Vaccinia
Rabies.
Snake Venom and Antivenene.
Helminthology

Syllabus of Senior Course of Pathology.

The General scheme of the Junior Course will be followed with the following alteration.

1st It is proposed to omit much of the elementary work on the Path. of normal blood. the collection of path. material & the methods of preserving & cutting of sections. Also, the General Morphology of bacteria & Bact. technique will be less fully dwelt upon

2nd The officers will be encouraged to carry out for themselves many of the operations only demonstrated to the Junior Class.

3rd The following additions to the Junior Course are proposed.

Demonstration of the actual preparation and standardization of culture media and of the use of autoclaves and other sterilizing apparatus.

In the case of such diseases as Tuberculosis. Typhoid Cholera and Diphtheria the bacteria closely allied to the specific Genus will be studied and contrasted

The following additional subjects will be dealt with by Lecture and demonstration

1. Immunity

2. The preparation & Standardisation of Antitoxins
3. Anti Typhoid Anti Cholera & Anti plague Vaccines.
4. The pathology of some of the rarer forms of Tropical diseases, such as Yellow fever. Beri-beri Dengue. Filariasis. Sleeping sickness. Blackwater Fever &c.
5. Methods of estimating the Bactericidal and Phagocytic power of the blood.
6. Malaria. Contrast of human malaria with Laverania and Proteosoma of birds. The anatomy of the mosquito and the identification of the various species of Anopheles.
7. The Geographical Distribution of Disease.

Junior Class. Lecture. I.

Microscopy. General principles.

To obtain the best results it is necessary to understand the fundamental principles of microscopy. Certain steps to be taken when dealing with high powers & small objects which those unfamiliar with the reasons for these processes may leave out & thus get unsatisfactory or erroneous impressions. Hole practical application of these steps will come in the practical class but to understand their reasons, a lecture is necessary.

Description of microscope. illustrated by a Reichert & a Swift.

Satisfactory magnified images are result of cooperation of the microscopist and optician. Former duty is to prepare a specimen in the best way possible and to secure its being looked at under the highest optical conditions possible for the particular combination of lenses in use.

Microscopist must prepare a clear microscopic image properly illuminated by transmitted light.

Optician has to deliver to the observer at the eyepiece an accurately magnified image of the former and to provide the apparatus for illuminating & focussing the microscopic object.

Objects macro, or microscopical may be rendered visible to us in one of 3 ways.

1st Outline Image. a/ Dark margin bright background
b/ Bright margin dark

2nd Colour Image. simply defined by a difference in colour.

3rd/ Combined Colour and Outline Images

Analysis of the advantages and disadvantages of these methods.

Comparison of pure outline with pure Colour picture

In case of large objects which subtend a considerable angle of the retina there may be equally well defined by Colour or by outline. Very small objects on the contrary are much better defined by a difference of colour than a system of outlines. The reason of this, the Colour picture being a surface picture, it is visible until the whole diameter of the whole object ceases to subtend the sufficient angle on the retina, on the other hand an outline picture ceases to ~~subtend~~ be visible when the diameter of the outline ceases to subtend a sufficient angle of the retina. — Advantages — Bacteria. Combined outline & Colour picture not used in art.

Comparison of combined outline and Colour pict: with pure Colour pict:

1st/ When outlines appear in a colour picture, the brilliancy of the picture is reduced.

2nd/ " " the diameter is reduced

3rd/ " " the question arises as to whether in measuring, the width of the outline is to included or not

4th/ When dark outlines appear in a colour picture there is a possibility of confusing them with fragments &c. e.g. Cremation of R.B.Cs.

5th " " Subjective colouration may manifest itself as dark outlines & give rise to fallacy. — 'mottled malaria'

Thus out of the three forms of pictures only 2 are satisfactory to suit the same outline facts. and the focus colour picture this while true authentically is absent all times and most necessary to observe in microscopy.

The objects we have to deal with are chiefly unstained. blood films (except for haemoglobin yellow) bacteria almost universally colourless & sections ditto.

In the great majority of these cases to obtain our best results we must transform the unstained outline picture into a colour picture but in many instances we derive ~~more~~ some advantage by examining them unstained e.g. bacteria for motility, malaria parasites for movements of pigment &c.

In order then to render these pictures whether stained or unstained visible we must illuminate them in one of the three following ways, in one case to produce outlines, in the other to efface them.

1st Axial illumination. 2nd Oblique 3rd Combined.

Outlines are produced only by deflection of the light which is projected on to the object. This occurs only when object is mounted in a fluid of less refractive power.

Effects of combined axial & oblique light. in obliteration of images, if mustard, especially if mounted in equal refract. fluid

Description of course of rays in each of these kinds of illumination. (Illustrated by means of a glass ball, diagrams only practical class for small balls + paper.)

Summary. To render uncoloured objects visible they must be given artificial outlines either by being mounted in fluid of diff. refractive index to glass. or by using axial illumination. To examine coloured objects we must get rid of outlines by mounting in fluid of equal refractive index & using open condenser.

Mounting of objects in a suitable medium (equal index to glass) to get rid of outlines. All familiar with the use of Canada balsam & some with cedar oil but few know the whole reason of these agents. Such a fluid is necessary to avoid the refraction of rays of transmitted light & production of outlines. The principles only will be dealt with, the application in practical class.

1

Histology of Normal Blood.

Consists of the fluid = plasma & certain suspended bodies the corpuscles. red, white & blood-plates.

Plasma complicated constitution. Serum + fibrin. Contains many other substances of which only those concerned in problems of immunity and pathology will be dealt with. Alkalinity. Lime salts (coagulation lime.) Agglutinins. Alexines or complements. Immune body.

Formed Elements.

Description, Haemoglobin. Grams.

1/ Red Cells. 5,000,000. In considering variations in number Lorrain Smith + Haldanes work on the influence of an increase or shrinkage in the volume must be remembered. Val may vary from 18% Chlorosis – 6 or 7% in Pern. Anaemia

Size. 7.5 μ. (3.5 – 9 μ) Alterations according to concentration of fluid. effect of water – spherulation, salt sol. – crenation. Have no cell membrane + no contractile protoplasm. Rapid drying causes vacuolation or cleavage

Development. from nucleated reds (normoblasts). in bone marrow chiefly in varieties described later under bone marrow

Some say nucleus disappears. others that it separates + surrounds itself again with protoplasm. Evidence of origin from normoblasts, number of mitotic forms, appearance in blood after haemorrhage. However there they come from blood plates – haematoblasts. Function of R.B.C. Destruction in liver.

B/ White Cells Number 6–8000. Proportion to reds. 1–500. Description of the common varieties + percentage. Polynuclear. Mononuclear Lymphocytes. E.Y.C. Basophile. – Children have fewer. Number

Look up Main on Devel of Polymorphous in bone marrow.

Functions of WBC & adaptation for carrying out these functions

Motility. Chemiotaxis negative & positive. The property of moving to or from a particular point in response to a chemical stimulus.

Emigration power of passing out into the tissues through the capillary walls. Phagocytosis

in adults fairly constant. Ehrlich's classification by granules.
α Eosinophile as in C.G.C. β Amphophile – fine granules staining with both acid & basic dyes. only in marrow – myelocytes γ Coarse basophile – Mast cells. δ fine basophile granules ε Neutrophile fine granules staining with a mixt of acid & basic dyes — Polymuclears; really Eosinophile.
Development of W.B.C. chiefly in marrow & from Malpighian bodies of spleen & from Lymphatic glands. Ehrlich says Polymuclear are developed from Lymphocytes In Embryo no W.B.C are at first present
Lymphocytes appear earliest 2-3 μ in diam 250,000 per C.mm.
c/ Blood plates. Description. Number. Unstable nature. Views as to origin. Amphophile. High Sp Gr explain their most important function the formation of the white blood clot. Found in the circulating blood. In my opinion the detritus of nuclei probably of Nucleated reds chiefly: Diminished in fasting, cachexias, fevers &c. & increased after haemorrhage, leucocythaemia &c.

Bone Marrow. Important to study as chief seat of blood formation & as showing cells only found in pathology. Conditions of blood.
Marrow cells or Myelocytes. Large 12-14 μ large pale nucleus, fine granules amphophile or neutrophile or oxyphile. Mitotic or Karyokinetic figure common. C.G.C larger than in blood & mononuclear instead of polymuclear. Nucleated Reds Micro-normo & megaloblasts. Free nuclei may be found or double or budding ones. (often in Pern. An.)

Giant cells 60μ. Eosinophiles - Mast Cells. Also all the cells normally found in the blood.

2

Pathology of Blood.

Blood constitution may vary within certain limits consistent with health but many Path conditions produce marked changes both in the fluids + cells Often these changes are the only sign which gives a clue to the disease and in most diseases valuable information may be obtained as to causation treatment + prognosis by a methodical exam. Out of question to give anything like an exhaustive account but will run over the chief points of diseases, others will be dealt with as they come under discussion later.

A. Changes occurring in the formed elements – the red + white cells.

1. The red cells. Changes in number. Polycythaemia rare, due mostly to concentration from loss of liquid — Cholera &c. Oligocythaemia. Common most anaemias. almost certainly fatal if below 500,000.

Changes in size + shape microcytes, megalocytes. 3.5 – 14μ. The large cells most point to a severe anaemia as pernicious. Poikilocytes, most often in pernicious An. but also in other An^{s}. Importance of thoroughly familiarity with normal types. & with changes due to faulty technique. (Ill. mottled corpuscles of malaria.) Polychromatophile cells, often found, supposed by Ehrlich to be due to death of corp. Other changes due to death of corp. – diminution of haem in centre, apparent vacuole. Projections or points which break off & float in the plasma. Such changes found in many path. conditions.

Loss of elasticity, tendency to form in cylinders of liver.

Changes in Malaria — later.

Nucleated reds Nucleus, normo, megalo. Shape of nucleus. Protoplasm contains haemoglobin but may be polychromatophilic. Loss of elasticity denied by some. Met with in extreme anaemias & leucocythaemia as attempt at regeneration. Most authorities say very rare & soon disappear in healthy marrow after haemorrhages. Megaloblasts mostly in pernicious An.,

Normoblasts frequent in splenic medullary leucocyth. often absent in lymphatic. Megalob. mean a profound alteration probably degenerative of bon. marrow, normoblasts probably an increased activity of marrow.

Alterations in the Leucocytes. In number. Shape &. New forms.

1/ Number. Leucopenia, Very rare (recall normal number 8000 or 1–500 red) may be seen in extreme anaemias or long continued fevers, without inflammatory complication. Leucocytosis or increase common in path. conditions, especially acute inflammatory conditions 36.000. Also in many chronic diseases e.g. leukaemia, advanced cachectic conditions as syphilis, rickets (chiefly lymphocytes) malaria. The proportion of white to reds not so reliable as total number. In all septic cases an increase of Poly. is found, in the incubation period of most infectious fevers and throughout the course of croupous pneumonia (absence an unfavourable sign). No increase of bas.c in Typhoid or Malarial Fever. Increase of Polymucleus in inflammation very marked (after an initial fall) & may go on to Pus formation. Malignant diseases frequently accompanied by a marked leucocytosis Hayem says this is so with Sarcomas but not with Epitheliomata and so an aid to diagnosis.

Leucocytosis dependent on changes affecting the blood forming organs. Splenic medullary Leucocythaemia. condition of blood. Myelocytes coarse granular Eosinophiles. Nucleated reds. Lymphatic Leukaemia increase of lymphocytes. Chlorosis. chiefly due to a decrease of haemoglobin i.e the individual corpuscular value, but may be and as a rule is accompanied by Anaemia or reduction in number of cells. Poikilocytes frequent. Microcytes or small R.B.C. common. Nucleated reds are rare and one a sign of grave anaemia. Leucocytes little affected. Blood plates increased. Simple Anaemia. slight or great numerical decrease a proportional diminution of haemoglobin of reds reds may be small + poikilocytes. or megalocytes in severe forms. During regeneration nucleated reds may appear. No marked change in leucocytes Post. haemorrhagic Anaemia. rapid reconstruction of all elements; nucleated reds may appear. Pernicious Anaemia Blood very liquid, coagulation slow Very great numerical reduction of reds may be 350,000. (1 case of 143.000), oscillates + may again reach normal, Haemoglobin reduced but individual corpuscular value may be above normal 1 : 1.6 Red cells average diameter increased ('megalocytes', up to 12.5 μ), microcytes rarer. Poikilocytes common, (microcytes + broken off processes of poik[s] often motile) Nucleated reds of all varieties common., Coles says also free nuclei. Proportion of the various leucocytes not constant. Myelocytes may be found — Cause probably excessive blood destruction not defective formation. In bone marrow the fat is replaced by red marrow having a great increase of nucleated reds, chiefly megaloblasts.

3/

Introduction to Bacteriology & Sterilization

Omnipresence of Bacteria in Air. Water + Earth. Great vitality under unfavourable condition & rapid & enormous growth under favourable conditions as to food temp. reaction &c To study a particular bacteria it is necessary to isolate it from neighbours. Pure cultures: Growth under optimum conditions in artificial media. By behaviour in these media & animal experiments we are able to differentiate — not from morphological peculiarities alone.

At every stage we have to observe certain precautions as to sterility of all apparatus & culture material all such being covered with bacteria and spores which would contaminate. So at the very threshold we must understand the principles underlying this sterilisation and the various modes in which it may applied.

'Disinfection' means less than 'sterilization' as may only imply destruction of bacteria which have power of 'infecting'. 'Antiseptics' in addition to killing prevent the growth of bact:

Sterilisation may be brought about by chemical or thermal means. Unsuitability of former. Practically the only form of sterilization we use is heat though may combine this advantageously with chemicals.

Methods of applying Heat.

1/ Red heat. Platinum needles, point of forceps. glass &c always continuous, cool slowly

2/ Dry heat. Hot air chamber, description. Temp 150 - 180° for 1 hour

good for glass &c but little penetration & much inferior to steam

for materials & culture media.

3/ Moist Heat. Steam. most generally useful. Penetrating power of steam very high. Kills germs & spores at a much lower temp. & in a shorter time than dry heat. Not so destructive to material. Latex &c. Generally used intermittently & for a short time.

A/ Boiling. 5' kills germs. of no spores. Instruments may be boiled for ½ hour in water with some bicarb. of Soda (to prevent rusting) 1½ hour sterilizes anything

B/ Steam @ 100° called "Steaming or Live steam" most generally useful employed by means of 'Koch' or 'Arnold'. Description. No evaporation takes place 1½ hours will sterilize anything but fractional method is necessary for most culture media. Steam available for all media. Put in cold so that all the food mass may reach same temp.

C./ High pressure steam. Description of autoclave. 115°C = 1½ atmosphere 15 lbs + 8 lbs = 23 lbs on the square inch. 120°C = 2 atmosphere or 31 lbs. Latter temp. in 15 minutes will destroy practically all germs & spores. Time of exposure cannot however be regulated with so much nicety as it takes time to reach temp. required & also must be allowed to cool down before use. Precautions in using autoclave. Blow off air. Sufficient water; cool below boiling point. Most generally used method but all in due may be done though slower by B.

Intermittent or Fractional sterilization. Principles & destruction of spores. possibly may permit of spores of thermophiles bact. to live — initial heating low lowered vitality so that they do not develope at once. Another possibility

15 mins @ 100 on 3 successive days

tes in anaerobic genus when in shallow layers so that they are not sufficiently shut off from O. to grow in between the teatings.

Intermittent sterilization at low temps. sometimes necessary. Blood serum. 1 hour @ 57° for 8 days. will kill most non. sporing organisms.

Special methods. of applying heat. Hot oil. Sand. Mercury. Thermometers. Bread. Red lead of wax pencil. Charred paper.

4

Culture Media

General principles of making and necessity for variety.
Fluid, solid & special media

Preparation of meat extract. Beef (heart) veal, horse, (rather too much fermentable sugar) goat. Meat extracts as Liebig &c. (3 gms to the litre.)
500 = 1¼ lbs
1000 gms lean meat finely minced put in 1000 cc distilled? water. Digest 24 hours in cool place (or heated @ 40° for 20 mins. Eyre) Dissolves soluble albumin, extractives, salts & haemoglobin) Remove fat Squeeze through towel or muslin (At this stage add peptone & salt.) Boil (10 mins Eyre. 2 hours M & R) coag. albumen except a few & precip. earthy phosphates. Strain & heat for another half hour Filter through Chamberland & make up to 1000 cc with dist. water. Sterilise in Autoclave on 3 days @ 100°.

This contain very little alb. matter, Chiefly soluble salts of muscle. Extractives & sol proteids not coag by heat.

Nutrient Bouillon. add & dissolve by heat. 10 gms further peptone & 5 gms NaCl. Eyre makes an emulsion of this in 200 cc of meat ext. @ 60° adds this to 800 cc more extr. of meat. & steams for 45 mins to dissolve. Neutralises & Heats for ½ hour @ 100° to precip. phosphates) Filters through Chamberland & sterilises.

Neutralisation & Standardising. Importance of. Reaction of meat ext. acid: Best results are with faintly alkaline. Choice of an indicator. Litmus v. Phenol phthalein. When a medium reacts neutral to litmus

its reaction to Phen. Phthal. is acid + 25 (Eyre notation + = acid − = alkaline
& the number = number of cc of a normal acid or alk. solution necessary to
make a litre of the medium neutral to Phen. Phthal.) The optimum reaction
for bact. growth lies about midway between the neutral point indicated by P.P &
that ind. by litmus. When a bouillon is made neutral to P.P. the optimum point
is reached by adding 10 - 15 cc of normal HCl. i.e the opt. reaction is +10 or
+15 Eyre. —— For details of Eyres method see p 128. ——

Melting points &c. use of solid media

Nutrient Agar. 1.5 − 2% usually 15 - 20 gms of powdered agar. added at
same time as or after peptone & salt. (Eyre emulsifies this in 200
cc of meat extr. cold. & then adds both emulsions to 800 cc of meat ext.
making up the litre. Steam @ 100° for 1½ hours to dissolve agar.
Neutralise &c. Steam again 20 mins for phosphates.

Clearing after this with white of egg if necessary, boiling for ½ hour,
filter through Chardin. hot filter Tube & sterilise. Autoclave or 3 days @ 100

Glycerin Agar add 6 - 8% after filtration. Tubercle.
Glucose. " - 1 - 2% grape sugar. for anaerobes
Litmus Agar Blood Agar Neutral red &c Sterum Agar " membane before using

Nutrient Gelatine. Melting points, use &c. Gold. label French.
10 - 15%. Cut in small pieces, add to 1000 cc meat ext. & steam
at 100° for 1 hour. Estimate reaction &c Steam again for phosphates.
White of egg if necessary. Tube Sterilise 3 days @ 100° for 20'

Glucose Gelatin 2% Litmus &c

Peptone & Salt Solution 1-2% Pept. ½% Salt Filter. otherwise reaction usually sufficiently alkaline. Sugars may be added to test fermentation

Potatoes. Washed well scrubbed with stiff nail brush Peeled with sterile knife & eyes cut out. Cork borer & slice. Acid reaction ∴ Soak ½ a hour in 1% Sod. Carbonate Put in test tube with plug soaked in sterile water at bottom Steam 20 mins @ 100° for 5 consecutive days & reason.

Glycerin potatoes Soak in 25% Glycerin for 15 mins, plug moistened with same sol.

Blood Serum. Sterile serum inspissated @ 65° (an initial stage of coag-ulation) done very slowly in special hot water apparatus. Or may be coagulated by steam — for Diphtheria.

Loffler's Serum 3 parts calf serum. 1 neutral bouillon with 1% Glucose added

Lorain Smith's Alk. blood serum. 1cc of a 1% NaHC sol. added to 100 cc serum Naturally Alk. reaction

Milk & Whey. Free from cream. Fractional Sterilisation. For whey use rennet. Incubate before use

5.

Classification of Bacteria & General Morphology.

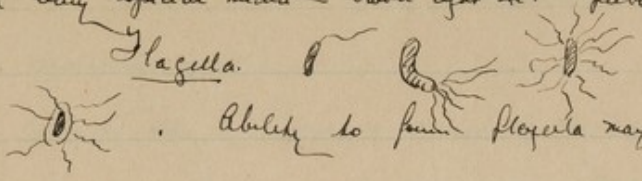
Difficulties of a good classification. Few authorities agree but certain general principles tending. Bact belong to the Vegetable Kingdom and form the lowest division. Causes of difficulty in accurate class: - Minute size, cultures dying out, insufficient description by discoverer, variability (effects of pathogenicity by spores, flagella, acid, gelatine liquefaction, colour, pigment formation, milk clotting &c.) close relationship of various species Coli group & typhoid, Staphylococcus, Diphtheria, Tubercle. Possibility of conversion of one into another Avian tubercle, bovine tubercle, coli into typhoid. Can only understand the pathogenic by the study of the non-pathogenic.

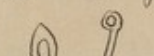
General Classification. A. Blastomycetes or budding fungi. Yeasts. Formula. B. Hyphomycetes (Mycelium fungi, moulds. Madura foot. C. Schizomycetes fission fungi, bacteria. Latter divided into. Lower Bacteria & Higher.

Lower:	Cocaceae. spheres	Staphylococci.	Higher	allied to hyphomycetes.
		Streptococci		Actinomyces.
		Diplococci.		Streptothrix.
		Tetra-cocci.		Cladothrix
	Bacteriaceae. rods.	Bacilli.		Leptothrix.
		Bacteria.		Beggiatoa
	Spirillaceae.	Spirilla.		Thiothrix.
		Vibriones.		

Morphology. Structure of bacterial cell. Cell membrane. Protoplasm. layer & central fluid. (by abstraction of water, strong saline sols, polarmolysis or retraction of the protoplasm may be seen) Nucleus not yet demonstrated. Babes. Ernst granules metachromatic granules. Capsules a thickening

of the cell membrane or its outer layers. Usually only found when germ is growing in the body or on very special media – blood agar &c. Feeble staining power requires separate means.

Flagella.  may be some distances from protoplasm. Ability to form flagella may be completely lost for generations.

Conditions of growth. Multiplication. A. Fission B Spores b2 Arthrospores b1 Endospores description of each process. Varieties of spores  . Germination. Involution forms. Composition (chemical) only state that very variable for same germ chiefly owing to food & conditions of life. Rapidity of Increase. – double in 20 mins. (17 million in 24 hours. @ ½ hour multl.) @ 1 hour multl.

Duration of Life.

Nutrient media. imitate natural food & natural habitat of germ as closely as possible. Must be soln in water, & have salts & sources for the supply of C & N. Most pathogenics prefer a medium containing albumin which is faintly alkaline. Reaction of media – refer to standardisation of media.

Relation to Oxygen. 1. Obligate aerobes 2. Obl. anaerobes 3. Facultative anaerobes Numerous inhabitants of mud & soil are in class 2 – Tetanus, Malig. Oedema &c. Presence of O. kills soon the vegetative forms but the spores are more resistant. Important to remember that aerobic varieties of anaerobes exist. Bacteria may alter in their capacity & become adapted to another condition of life. True anaerobes grow well without the exclusion of O if associated with aerobic varieties, act partly by consuming the O & partly by products favourable for the anaerobes.

Influence of Temperature Minimum Maximum & Optimum. Great range 0°-70°
Psychrophilic (cold) 0°-30° Mesophilic 10°-45° (includes most pathogenics) Thermophilic
40°-70° (soil bacilli & mesenteric group.)

Influence of Light. restricts all. Prolonged action of sunlight kills them
all. Ultra violet > blue. bad. Yellow red dont hurt. Method of testing

(27)

The Activities. Mechanical. Brownian. true movement. Chemotaxis positive
& negative. Optical. phosphorescence. only from living bact. Germ free filtrate
never luminious. Thermic can be measured. Chemical Chief is the
the secretion of ferments / enzymes intended to make the nutrient material in their
neighbourhood more suitable for assimilation. They are proteolytic or
albumin dissolving (liquifaction of gelatin) Diastatic change starch into
sugar. Inverting convert cane sugar into grape sugar. Rennet. clot milk
Pigment production. Formation of Ammonia. Poisonous Bodies or toxins
syn. toxalbumins metabolic products. . Sulphuretted Hydrogen
Reduction of nitrates to nitrites & ammonia. & many others, all L. & N.

6

Classification of Bacterial Diseases & Local Inflammatory Processes caused by Staph. Strept. &c

Having studied the general morphology of bacteria & principles employed in investigating them in the Lab. now come to study the mode in which those which are Pathogenic to man act. Enormous subject, daily expanding. Only place in a short course like this for a few of the commoner bacterial diseases which are most likely to be met with in the Service

Bacteria cause disease in man act in several different ways & before commencing the study of particular diseases must first understand these variations & learn to apply the principles of each to each separate disease

Bacteria may enter the tissues or blood of an animal & cause infection if 1st they can remain alive & increase in the host. 2nd if they produce substances which are injurious to the host. Many germs must get into body hourly fortunately few do harm they are either destroyed by phagocytes or bactericidal power of blood or lymph or they may pass out in urine or bile. Even pathogenic germs as pus organisms, tubercle & diph. may & do get in and whether they cause disease or no depends on the resistance of the host (immunity) or on increased virulence & other factors

Classification.

1. Local Inflammatory Processes. Blood stream not invaded Bac cultivate themselves in the tissues. May be primary or secondary. Malig. pustule in man post typhoid abscess

2. Septicaemias Bact. free in the blood stream at height of disease Primary. Anthrax in rodents sheep &c Splenic fever in man

Secondary. Ex. ?

3rd/ Intoxication Processes. Bact. cultivated themselves on external or internal surfaces of the body + destroyed the tissues producing toxins which are absorbed into the system + produce toxaemic effects. e.g. Cholera. Tetanus. Diphtheria

What determines the type of the disease ? One variety may give rise at one time to one form of disease at another to another Examples of change of type of diseases. Local Inf. Pro. to Septicaemia. Anthrax Tubercle. Gonorrhoea brought about by increasing or lowering virulence of germ or resistance of body.

The primary septicaemias is the most formidable, the local inflam. proc. the least The capacity of producing very poisonous toxins may coexist with the very small capacity for maintaining life in the interior of the organism.

Local Inflammatory processes. primary or secondary divided into acute + chronic. In accordance with the different types of inflammation produced, microorganisms concerned may be classified into Pyogenic or Granuloma producing organisms
General on Suppuration. M + R. 162.

Staphylococcus Pyogenes. 3 varieties Alb. Aur. Cit. Distributed everywhere in nature a frequently if not constantly present in skin, to not affected by the bactericidal substances in the blood, probably phagocytosis. Great variation in virulence of Staph. importance of this in Midwifery + other surgery Importance of antiseptic treatment + precautions much greater in case of Surgical + Midwifery hospitals than in ordinary conditions

Pathological effects that may be produced by an invasion of Staph. Acne Furuncle Lymphangitis (poisoned wound) blood poisoning, pyaemia endocarditis

Septic infection of joints . Inoculation against Staphylococcus.
Acute suppurative pneumonitis + osteomyelitis . Catarrh of Respir Mucous surfaces

Morphology of Staph. Pyogenes Aureus. Gram. Growth in various media
liquefaction of gelatine beaf broth . Requires higher temp to kill than
most spore free bacteria 80°C for ½ hour.

Morphology of Staph Pyog Albus. Same only white. Citreus rare.

Streptococcus. Characters of growth &c.

Other pus forming organisms.

Coli Bac. aerogenes capsulatus. Pyocyaneus. Tetragenus. Diplococcus
Intracellularis Meningitidis (decolourised by Gram) Pneumococcus. Gonococcus
with Staphylococcus depend on quantity, virulence + Exclusion of Air
Inoculation of Animals " does not always cause suppuration " Intraper. in dog
only causes fatal pneumonitis if intest. injured or a mechanical irritant present.
On other hand intravenous inject. of virulent cult. almost invariably produces
pyaemia, small abscesses in kidney especially, due to emboli of staphylococci
surrounded by necrotic cells + outside a ring of polynuclears. Effects
are produced by means of a Staphylotoxin which has a haemolytic effect on
R.B.C + leucocytic on W.B.C..

In case of Streptococcus great variations in virulence which produce different
effects from local redness to suppuration, erysipelatous state or general septi-
caemia. Varieties of Strept. producing pathogenic effects are doubtful, most
now think them all one, including Strept erysipelatis. Longus (most vir) or
Brevis. Found in normal mouth.

Lesions in Man. Staphylococci (see foot of last page.) Streptococci cause

diffuse phlegmonous & erysipelatous inflam^{n}, found in serous membranes suppuration, acute sup. periostitis, ulcerative endocarditis. Secondary abscesses in lymphatic glands. Produce sometimes fibrinous exudations on mucous surfaces, leading to false membranes (+ Diph.) Puerperal peritonitis & Septicaemia.

B. coli. Many inflam. & sup^{n} of in connection with alimentary tract, Bile ducts appendicitis &c. Also found in endocarditis & pleurisy. Bladder kidney ureters. (Virulence found to be exalted when taken from these situations)

Intragenus. Sup^{n} of mouth, resp. respiratory tract. Colitis mice susc^{y} to septicaem.

B. Pyocyaneus rarely found alone.

Mode of Entrance & Spread.

Omnipresence but only rarely affect man. Why? Surface lesion or loss of vitality - local or general - Paths of secondary affection. 1st lymphatics - glands & serous sacs. 2nd/ Natural channels, mucous bile duct. 3rd/ Blood vessels a/ directly from some infected point. b/ septic phlebitis, softening & secondary embolism. c/ direct extension along a vein. e.g. frontal vein to brain.

Special diseases caused by these organisms.

Ulcerative Endocarditis by Staph. Strept. Pneumococci. Coli Gonococcus infection as a rule is secondary.

Acute Suppurative Periostitis - Osteomyelitis

Erysipelas. Strept. virulent.

Meningitis. Chiefly pneumococcus. Cerebro spinal Meng. Dip. Intracell. Meningit.

Conjunctivitis. Koch-Weeks Bac. Morax diplo-bacillus.

Acute Ulceration. Pyocyaneus + Staph. small diplococcus. inoc^{n} experiments.

Anti-Streptococcus Serum. Staphylococcus Vaccine.

7.

Pneumonias & Pneumococcic Infections

Recent division of Pneumonias into.

1/ Croupous or lobar. Abund. fibrinous exudation affecting a lobe by continuity

2/ Catarrhal or lobular. Process spreads from bronchi to air vesicles, endothelial proliferation except in children, Commoner since influenza.

3/ 'Septic' pneumonias. 4/ Entrance into trachea of blood discharges &c. Unstable nodes

B/ Secondary pyogenic infection by blood stream

Bacilli causing the disease. Chiefly 2. Fraenkel's Diplococ. & Friedlander Pneumobacillus.

Description of Morphology, &c of each. Cultures. in practical.

Cultivation Rapid loss of virulence. Eyre & Washbourn's work.

Occurrence in Pneumonia In very variety they are found but Friedlander only in 5%. Pneumococci found throughout the lung chiefly in exudation in air cells. Rusty sputum.

Other bacilli found either with Pneumococci or alone causing pneumonias Influenza. Anthrax. (wool sorters disease?) Typhoid. Plague.

Other affections caused by Pneumococci. A. By direct extension to neighbouring parts — Empyema, pericarditis, mediastinal glands &c

B/ In distant parts either as secondary to pneumonia or as distinct affections. Subcutaneous tissue. Peritoneum. Joints. Kidneys. Liver.

Otitis media (per Eustachian tube.) Ulcerative Endocarditis. Meningitis.

As a primary affection Otitis Media caused by pneumococci is commoner than Pneumonia in Children.

Inoculation into Animals. Sputum pneumonic or healthy. In highly susceptible animals causes a General Septicaemia. Rabbit > mouse > guinea pig susceptible. C.P. dog sheep cat less. pigeon immune. Meaning of occurrence in healthy throats.

Toxins of the Pneumococcus. Death probably due in pneumonia rather to acute poisoning than to asphyxia from local intoxication. Toxins alone are fatal to susceptible animals. Cardiac failure from.

Antitoxins made by the Klempereus, neutralise toxins only no effect on bacteria. Crisis in pneum. may be due to point being reached at which Antitoxins formed in the body neutralise toxins.

Bac. Intra-cellularis Meningitidis. Already spoken up as causative of suppuration. Also causative of a special disease. – epidemic Cerebro-Spinal meningitis. Almost always found like Gonococci in Polymuclears. also a diplococcus but decolourised by Gram. Grows poorly, best on Löffler's serum. Not pathogenic to animals except intracranially in dogs - rabbits. Very low power of resistance to light, cold & drying. May be isolated by lumbar puncture for diagnostic purposes. Between 3rd - 4th lumbar vertebrae with Antitoxin needle 14 cm long 1 mm broad. Needle enters about 1 cent to right of middle line. At a depth of 3 - 4 cm in children, 7 - 8 in adults needle enters the subarachnoid space a fluid drops out of needle & is collected in a sterile test tube (see Mallory & Wright.)

Gonorrhoea (Neisser 1879)

Description of Diplococcus. Cultural characteristics. Blood agar.

Mostly found within cells but in early stages many are free or adherent to squamous epithelium. fewer in later stages - gleet.

Relations to disease. Invariably found in urethral discharge & other seats of gonorrhoeal infection. Disease cannot be reproduced in other animals. Injected in large numbers into joints of rabbits &c. dog causes an acute inflammation which however rapidly dies out, similar result with dead cultures. In the urethra the cocci penetrate the mucous membrane passing between the epithelial cells loosening & desquamation of these, inflammatory reaction below, great increase of secretion. Polymorphous serum & phagocyte, but cocci may extend deeper into lacunae or prostate. During chronic stages other organisms may appear. pyogenic cocci, coli &c, may extend along urethra to bladder & cause cystitis (aided by catheter importance of sterilizing)
In females cocci are in urethra & perhaps cervix uteri, seldom in lining epithelium of vagina. may pass into Fallopian tubes. even into peritoneum where they may cause a local peritonitis.

Gonorrhoeal Ophthalmia. Same relation to epithelium as in urethra.

Gonorrhoeal Arthritis. Gonococci often isolated. also from sheath of tendons. But in many cases none found (may have been in synovial membrane)

Gon^{al} Endocarditis has been found. Also a true Gonorrhoeal Septicaemia cultures many be obtained from the blood during life.

Soft Sore.

Ducrey 1889. Unna 1892. Confounded by many others

Minute oval rods 1.5 μ in the purulent discharge, mixed with other organisms in small groups or chains. Found in sections in superficial part of the floor of the ulcer but deeper than other organs + perhaps among the leucocytic infiltration. Stains readily but easily decolourised. Not been cultivated outside the body. Ducrey method of auto-inoculation for procuring it free from neighbours. Occasionally found in buboes, possibly these are caused by it and it is later killed off by other organisms.

Syphilis.

Lustgarten. 1884.

Somewhat resembles tubercle in size + shape. Slender rods straight or slightly bent. L. found them in the internal organs as well as in the sore but others have not. It has not been cultivated outside the body. Its relation to disease still problematical (M + R.)

6

Typhoid.

Cause. Bacillus of Eberth. 1880 Description & Cultural characteristics. (Differentiation from Coli. Gaertner &c dealt with by Hygiene Lab.) Motility flagella. Staining properties. Facult. anaerobe. Resistance read Horrocks & Gotti paper. May live very long in human body in urine, pleural exudate, pus of pleurisy &c - 10 months after fever. In course of urine has been found in Faeces + Coli. Pu. Occurrence in body. Spleen & lymph glands. Pepsin proteids. Blood from heart & veins during life. Rose spots. Sweat. Kidney. Liver & Bile. Urine. Also causes complications of typhoid. Serous & suppurative inflam[n] of spinal cord, brain & membranes Lungs (pneumonic form, danger of infection) Kidneys and in erysipelatous phlegmonous & suppurative processes in bones, skin, testicle, lymphatic glands, parotid, thyroid &c &c. Undoubted pyogenic action but usually + Staph. or Strept.

Experimental Inoc[n] Disease not imitated, but effects often fatal due to toxins & not infection. Best feeding young rabbits on veg[s] &c soaked in typh. Cult. Read M. & R.

Diagnosis of Typh. Bacilli may be obtained in cult. during life from Spleen Method of puncture. Urine in 25% of cases especially later (see Horton Smith & Urotropine.) Stools. Cannot isolated in first 10 days often that Coli swamp them as they grow so abundantly in any condition of lowered vitality of the intestines Pus. when abscesses &c present Blood. by venepuncture (11 out of 15 cases Coli.) Rose Spots.

Nature & Course of Infection proven. First thought to be an

Intoxication process, symptoms being due to absorption of toxins from intestinal canal. This seemed justified by A/ Presence of enormous number of short rods in faeces resembling Typhoid — really Coli. B/ The organism being apparently very rarely found anywhere in body except in spleen & mesent glands & these held to be accidental leakage from intest. C/ Peyers patches being ulcerated, it was held to be a 'surface invasion'. This led to idea that the treatment of the disease ought to consist in the disinfection of the intestinal canal by antiseptics - which now seems impracticable. Now held to be a septicaemia. Chief points leading to change of view being A/ Better methods of differentiating Coli from Typh. B/ Typh Bac often found in the blood. C/ Typhoid spots correspond to Typhoid colonies. D/ Excretion of bac. by urine.

Pathology of Course of disease. Channel of infection. Probable saprophytic growth in intestine. Invasion of the organism proper. Increase in size of spleen. Gradual onset of symptoms. Fever — due to absorption of toxins? from al. canal & development of ditto in organism. Typhoid spots. Intestinal rash? Conveyance of bact into kidneys & appearance in urine. Also lungs & epiglottis. Rash developed again & intest. lesions at each true relapse.

Changes in the blood which are associated with the disease.

Incubation period. Lobc. are diminished. Proportion of Polymuclear elements. Coagulability of the blood apparently diminished. Effects of the incubation period. Bactericidal & phagocytic power not yet studied.

Pyrexia period. Increase of agglutinins during early stages. Blood-cultures

remains the same few W.B.C. & polymorphs proportionally low. Coagulability often greatly reduced gives warning of possible supervention of severe haemorrhage. Alkalinity of blood generally diminished, due to fever or diet.

Period of convalescence. Agglutination falls, coagulability increases. Thrombosis of convalescents, treatment

Relapses. 3 theories. A/ Chantemesse & Widal. If immunising & bactericidal powers only slightly developed & absorption of toxic substances from other part of intestinal tract may give the few remaining bacteria a new lease of life. Confirmed by ex. on animals

B/ Wright & Lamb. Spleen colonies surrounded by non bacteriotropic ring or envelope, as a result less agglutinins present in spleen than blood, when anti-bacterial substances sufficiently developed in the blood to flood spleen & destroy these 'nidi' temp. falls. On other hand if a colony escapes as by the blocking of a capillary preventing flushing by blood bact may survive till blood loses its bactericidal power & then grow & cause a relapse.

C/ Denham. Regards infection as the result of the sum of a number of infecting agents similar but not identical in action the infection being brought about by a number of varieties & sub-varieties of the given microbes. He thinks therefore that in typhoid a particular variety being in excess the disease goes on till antibodies to this variety are sufficient to end it, but then others may come into action which have formed little or no antibody & cause a relapse.

Typhoid Serum.

Anti-typhoid inoculation. Describe Vaccine & quote summary of latest statistics.

Tuberculosis.

Cause of the disease: Koch's Bac. tuberculosis 1884. Morphology of the Involution forms. Actinomyces? motility? Bacillus .3μ × 2.5-3.5μ. young homogeneous old spotted — spores? Avian & Bovine Tubercle. Koch at first thought Bovine identical with human. Differs 1/ cultures - Avian moist & soft. 2/ Temperature Avian grows 41-43° Human not above 40° 3/ G.P. rabbit killed by human with gen: tuberculosis. by avian without known tubercular infiltration 4/ Dog easily takes human, very resistant to avian 5/ Fowls quite refractory to human. — Since then nearly all these points have been modified or contradicted by further exp. — Nocard & Roux with collodion sacs succeeded in changing human into avian in peritoneum cavity of fowls. Macé thinks all 3 same simply a question of adaptation to different media Products of all 3, same, can make tuberculin from avian with same effects as human.

Formation of Tubercle. "The tubercle is only the expression of the reaction of the organism against certain irritants." Macé i.e tubercles may result from other organisms e.g pseudo tub: protozoa, other bacteria, eggs of helminths even dust. In tuberculosis the process is: Entrance of Bacillus into a tissue, carried by a leucocyte through lymph or blood. Leucocyte fixes itself, becomes destroyed & bac. set free. Leucocytic agglomeration by diapedesis. Bac. multiply & form, Centre of a little nodule. The connective tissue cells (or leucocytes?) change to epithelioid Giant cells formed by nucleus division only, enclosing Bacilli. Then follow 1 of 2 paths, A/ fibrous capsulation (+ lime salts) an effort at recovery B/ colloid degeneration, necrosis & caseation caused by the toxins, bac. set free & may be carried elsewhere. Manuel thinks tubercles develop solely in

the blood vessels at the expense of the endothelial cells.

Another process may be general tubercular infiltration without formation of tubercles.

Inoculation of Animals. Method of isolating from sputum &c. by inoc: necessary on account of the other micro-organisms present. Kill G.P. in 2 or 3 weeks & cultivate from a nodule on liver or spleen pounding it up well in sterile water. Kitasato's rapid method from sputum by repeated washings after selecting a little granule.

Vitality & Virulence. Virulence may well maintained except after prolonged growth on glycerine agar. Sputum may remain active for months Bacilli very resistant after desiccation, 10 mins @ 71°. Great cold, dried fection. Virulence of various strains may vary but if low may always be recovered by a single passage through a G.P. The gastric juice has little effect. Chemicals & Antiseptics readily kill it Carbol. 1-20 in 30 secs. 1-100 in 1 minute.

Tuberculin. The effects of tubercle chiefly due to an intoxication from the products of the bacilli. Dead cultures contain these products as well. Koch's tuberculin. — see Macé 522. —

Habitat & Role (Ecological). Extensively distributed by sputa, bodies of animals. Frequent occurrence of virulent B. Tub. in nasal secretion of healthy people. — Spreading by flies. Infection by alimentary tract, tubercular meat & milk? Germs inhaled are always lodged in throat or bronchi &c expired air is germ free. Depends on predisposition whether infection takes place. Presence in lupus &c. Importance of boiling sputum or carbolising.

Leprosy.

Very wide geographical distribution but unequal in types. Two chief forms Tuberculer & Anaesthetic. Due to bacillus of Hansen 1871.

Pathological Changes. Chronic local inflam: process, toxic effects slight. Areas of fever occasionally accompanied by new formation of tubercles.

Tuberculer form. Erythematous patches, tubercles &c Chronic foci. Ulceration Internal organs may be affected secondarily. Appearances in sections, Lepra cells peri-arteritis, Granulation tissue. No caseation or giant cells

Anaesthetic form. Diffuse infiltration of nerves followed by destruction of the fibres great distortion Pain, patches on skin pale in centre. Trophic changes in skin, muscles bones. Skin atrophied, pale & anaesthetic, pemphigoid bullae. Necrosis & suppuration may follow changes in muscles & bones. Pus in bacilli

Bacilli Morphology as met with in tissues. Pure cultures, growth Agglutination positive. Notoriously fast in cultures very slow on glycerine media & closely resembles B Tuberculosis. Inoculation exp: very doubtful. Distinction of Bac. from Tubercle

Method of infection. Very slow development. Not readily inoculated in man. Extension of disease takes place through the lymphatics or blood. during febrile attacks? Bac. found in scrapings from ulcers &c. Transmitted by direct Contact but not certainly. Presence in nasal mucus. 128 times out of 153 cases (Dietrich. Münch. Med. Woch.) probably the most common source of Contamination of surroundings, & commonest site of the primary affection.

Plague.

Due to B. Pestis — Kitasato + Yersin 1894 simultaneously —

May manifest itself in 3 types. A/ Abortive B/ Bubonic type, culminating in Septicaemia C/ Pneumonic type also culminating in Septicaemia. The more virulent the type of the disease the more conflicting are the localised inflamatory processes. For cultures see Galli Valerio in B.M.J cuttings.

Morphology. Description. Behaviour in cultures. Steutzmis salt agar (2·0%) development of involution forms. Stalactitic growth in broth. Motility? Does not liquefy gelatin. Steadily over growth anaerobically. Readily killed by heat 58°C but resists cold well, cultures may live 1 year. 3 or 4 hours sunlight fatal, drying? More than 2 years. 66% Virulence outside body varies much. Animals. Mice G.Ps rats. rabbits all susceptible. Local inflam. reaction — glands — septicaemia — death. 1-7 days.

Epidemic occurrence of disease the result of a great virulence & great power of persevering that virulence in the conditions obtaining outside the body. (acclimatisation to the particular exterior environment.)

Channels of infection Epidemiological data and experiment point to the utmost variety of infection by channel of alimentary canal. The infection of plague pneumonia one case occurring after another — points to infection by the lungs. Skin Evidence of infection at P.M.s. Often no changes at site of inoculation (cf. exp. on monkeys with plague charged thorns) bacilli probably carried away by lymph stream before they propagate. Occasionally bubonic form. probably due to bacilli being introduced into loose layers of epidermis where they are held back temporarily — generally develope into a plague carbuncle.

the necrotic change in this is probably the result of the toxin locally produced. In either case bacilli are carried thence by lymphatics to lymph. glands, rarely producing lymphangitis — buboes. Great inflammatory swelling, haemorrhages, suppuration rare. Increase in size of gland may be due to immense number of bacilli present. In the case of a convalescing patient subsequent changes are in the direction of destruction of contained bacteria sloughing &c. The buboes constantly become secondarily infected with staphylococci, streptococci + pneumococci. Here the bac. are carried through the bacterial filter into blood stream and reach internal organs, enlarged spleen &c. They emerge into circulating blood at the culmination of the fever; then being generally rapidly followed by death. The emergence into the blood may be associated with the development of pulmonary symptoms — bacilli may escape into the sputum by development of a pologue sputum — rare. They may take a vesicular form, full of bacilli + may become haemorrhagic. or the so called cellulo-cutaneous form characterised by large ecchymosed pologue spots followed by necrosis of large areas of skin. The bacilli may escape into the kidneys or from intestines (haemorrhagic patches in mucous membrane)

Channels of infection skin, which part? in absence of local reaction difficult to determine. Mucous membrane of nose, mouth — practically never from surface of intestinal tract. Lungs probably something more than mere conveyance into the lungs is required. Plague pneumonia practically always supervenes upon infection by another case of pologue pneumonia + not on inhalation of dust pologue infected by discharges from a

Non-pneumonic case. Plague sputum essentially diverse as distinguished from P. Nuclear in bronchopneumonia + M.N. + neurons of tubercular pneumonia.

Bactericidal power. Absolutely none, on contrary bac. multiply.

Period of incubation very short 2-5 days.

Agglutination The blood possesses at best a feeble power, technique somewhat difficult + clinically valueless. May be useful in diagnosis the bacillus, does not appear before the 7th day.

Haffkine's Prophylaxis. Reduces both incidence + case mortality. Badly standardised. Tetanus accident. Question of modulation in the incubation period of plague. Dangers where resistance has been already reduced by inoculating bacteria or in large doses. Balfour Stewart says some protection exists both in bacterial bodies + supernatant fluid

Serum Therapy. Yersin's 1st dead then living cultures intravenously Lustig's nucleo-proteid derived from bodies of bacilli digested in caustic soda - acidified - precipitate collected + dried, doses dissolved in bicarbonate of soda + injected. Blood should be drawn during a pyrexia + should be very rich in protective substances. Commission said both were of some use.

Malta Fever.

General characters of disease Cause Mic. Melitensis of Bruce. Morphology. Cultural characteristics Resistance outside the organism very great. Old cultures.

Channel of infection Epidemiological data with regard to water supply & exp^ts feeding monkeys show that alimentary canal is not the channel Infection is very readily acquired by subcutaneous inoculation, minute quantities Malta fever hangs about particular houses quarters of town & particular localities. Dry barren rocky places seem to be the localities most affected

Reaction of organism to an infection or inoculation by M.M. Very little local reaction at site of inoc^n also slight constitutional symptoms this is in accordance with the low toxicity of M.M. as compared with Typhoid Polymuclear leucocytosis. Agglutination. Old cultures not trustworthy. Control by normal serum. Prognostic value. Bact. power. nil

The great tendency to relapse and the great infectivity of cultures probably stand in relation to the low bactericidal power.

Course of the disease & distribution of the bacteria Not been studied in detail probably proceeds on same lines as other septicaemias. No rash. Bac. not found in the blood till last stage. Not been found in the urine. The disease is almost uninfectious. The relapses and the local complications, neuralgia, orchitis, effusions into joints, cystitis, pleural & pericardial effusion would seem to be due to local cultivation of the organism. Not been found in spleen.

Protective inoculation. Serum therapy.

Diphtheria.

Infection proving Cause of the disease ∴ Klebs Loeffler Bac. 1882. Methods of isolating the Bac. from throat. Morphology. 3-4 μ long. Beading. Arrangement. Involution forms. Long, medium & short rods. Branching. Non motile. Gram. Neisser. Löffler's Methylene blue. Acid production. Good growth anaerobically. Pellicle in broth. Retains vitality when dried for 3 or 4 weeks. Killed 10 min. at 58°. Variations in virulence, mild cases & healthy throats, danger of epidemic spread from such. Ex. Miss Tomay's school. May persist in throat for many months. (15?) Antiseptic sprays combined with nasal douche 1-2000 Perchloride soon gets rid of them. Association with other germs especially streptococcus. Pseudo Diphtheria bacillus.

Inoc. of animals. Pathogenic for man, horse, ox, rabbit, guinea pig. cat chicken, pigeon — mice & rats immune. In man resp. tract usually but may also affect conjunctiva & other mucous membranes, vagina, wounds. Appearances in G.P. Rabbits ear &c.

Formation of membrane. Necrosis of epithelium, inflammatory reaction in the connective tissue beneath + fibrinous exudation. Epithelium raised by this fibrin and interstices filled, fibrin also round vessels deeper down so membrane adherent. Bacilli found in clumps in spaces between the fibrin in superficial region, the oldest part, but may be found deeper. May be on surface + other bact. Have been found in lymph. glands & internal organs due to entrance into the blood stream before death. — Streptococci often found lower than trachea — preparing the way for diphtheric germs? Prognosis of mixed infection some complications due to staph + strept.

Diphtheria Toxin. Production in broth favoured by plenty of Oxygen, plenty of peptone or albumin, absence of acid producing substances. Various media used. May be very strong .01cc killing a G.P. in 24 hrs. A high degree of immunity may be produced both against the bacilli & their toxins by gradually increasing doses.

Effects of the toxin in causing the various symptoms in man. Action on blood vessels, hyaline changes &c leading to haemorrhages & oedemas. On cells of kidney albuminuria. On muscle fibres of heart — heart failure. On central nervous system & peripheral nerves, disintegration of medullary sheaths. — post diphtheritic paralysis.

Pseudo Diphtheria Bacillus. A true species? or attenuated. Hoffmann's bacillus. Deficient in acid production from glucose. Short, one septum usually. Virulence in animals, not certain if no result as true Diph. may be attenuated. Necessis staining. Xerosis bacillus. from conjunctiva. does not produce acid in neutral media, non virulent

Antitoxin. Brief account of preparation & standardising of. by means of a standard antitoxin (containing 1 unit in a cc Ehrlich) & the minimal lethal dose of a strong toxin is found — just sufficient to kill a 250 gm G.P. on 4th day. The toxin to be used for testing is then standardised with the standard antitoxin. When its value is found, find out the number of units in the new antitoxin. A unit is the amount that will neutralize 100 min. lethal doses. Then a toxin being mixed, diluted to 4 cc & injected. Sera may go as high as 500 units per cc.

Curative & prophylactic dosage.

Yellow Fever

A disease peculiar to warm countries. Geographical distribution (Schenbe 51) Cause unknown. Many bacilli found & blamed. Sanarelli's best known, not confirmed by Yankee commission, found by S in blood & tissues 7 cases out of 13. Serum agglutinated the Bac Icteroides (healthy serum also at times). Certainly not propagated by water. Incubation period 1-5 days. Uric are not contagious. High temps. & moisture best for development. Very exceptional at high altitudes. Race. Affects whites most. Negroes very immune, if they do get it, it is mildly. Mongols slightly immune but not Red Indians or Hindoos. Of whites those born in Northern lands are more liable than Southerners. Acclimatisation and previous attack confer great immunity. Stegomyia. notes those who have had yellow fever, old residents, & natives are not stung by mosquitoes as much as new arrivals. Seldom affects children or old men. Strong persons predisposed. Infection takes place chiefly at night. Animals may get it - dogs & poultry. Gums spongy & tend to bleed. Contrast of pulse & temperature rates. After miscarriage foetus has been found affected. Ambulatory forms occur.

Pathology. Eruptions of many kinds. Cutaneous & internal icterus. Haemorhages of various organs. Parenchymatous degeneration of liver & fatty degeneration of the capillaries and heart.

July 1886 Prolonged inoculation by mosquitoes fed on patients less than 6 days ill, kept 2-5 days & allowed to bite men. Conferred some immunity & lowered death rate.

Recent discoveries of U.S. Army Commission. Journal of Hygiene Apr 1st 1902. Havana &

Cuba 1900-01. Sanarelli's work absolutely negatived: 1/ They found no bacteria or protozoon in blood or tissues, visible by 1/12 a present staining methods. 2/ The blood of Y.F. patients inoculated into healthy people reproduced the disease. taken during 1° 2° & 3d days of disease, successful in 6 out of 7 cases. 3/ Bacterium free serum filtrate injected in a non-immune person causes Y.F. Serum was diluted with sterile water & filtered slowly through a Berkefeld candle 4/ The specific agent is destroyed by 55° for 10 minutes ? attenuated, no spores? 5/ Exhaustive experiments proved fomites to be absolutely non-infective. 6/ Attendants &c never get it is non contagious.

Mosquito Infection. Stegomyia Fasciata. - a Culex with 16 synonyms. Among them the banded mosquito of Ross & tiger mosquito of Capt. James. Both male & female bite and in day time between 1-3 pm Distinguished by thoracic ornamentation & white last hind tarsal joint. Distribution (see B.M.J. cutting) Experiments. 10 out of 12 bitten volunteers contracted Y.F. Controls in same room but protected by mosquito netting all escaped. Incubation period in the mosquito 12 days is the soonest it can infect after biting a patient (contrary Finlay.) 57 days was extreme limit of successful transference but mosquitoes have survived 71 days after infection. Perhaps other mosquitoes may carry it.

Diseases allied to Y.F. Weils disease. much alike but a bacillus of the proteus group was found. Acute Yellow Atrophy of liver Bilious remittent. Bilious Typhoid. Blackwater fever. - haemoglobinuria pathognomonic Possibly some of these may belong to the groups of fevers called Y.F.

Cholera.

Cause Koch's comma Bac. 1884. found in stools. – Spirillum Chol. asiat.: – Morphology: .3 – 2μ long .3 – .4μ broad. Spirals & long forms. Involution & degeneration forms. Motility, flagella. No spores & Staining – Gram in stream in stools. Cultural characters Gelatine plates & stabs. Liquefaction of gelatine. Agar. Bouillon – film on surface. Peptone solution (Pept 2% Nacl 1% Koch) Indol & Nitrites produced Milk – acidity produced & clotting Potato. Vitality 65° for 10 min. Very sensitive to acid. .06% of HCl & HNO_3 inhibits. Maximum devel. soon reached. Growth with other organisms, at first outgrows them. (Schottelius' method – stools & double broth. 12 hrs at 37° & examine surface) Spores developed early.

Exp. to on animals. Only successful if gastric juice neutralized or avoided by tying bile duct & injecting into duodenum or by Na_2CO_3, cholera emulsion, opium. Pfeiffer's intra peritoneal injection & profound toxaemia & Continuous fall of temperature till death. Immunisation. "Pfeiffer's phenomenon" diagnostic value. Agglutinins.

Relation to disease Vib: found in stools in all cases, most early. Has also been found in vomit, bile duct, gall bladder, liver & blood (very rare). Found in water supplies by Koch & others. Duration of life in water great difference of results of experimenters. Generally, the higher the temp. of the water & the more organic matter the longer it may live. Dies rapidly when dried, but when cover-glass films or threads are kept in a moist condition they may live for months.

Bacteriolog. diagnosis of Cholera. Necessity for rapidity and importance of accuracy. By Koch's method 1893 this may be done in 18-24 hours.

1/ Microscopic exam. of small slimy particles from fresh stool. probably may Vibrio

2/ Prepare gelatin plates, & examine after 16, 22 & 36 hours.

3/ Inoc. peptone & salt 37° after 6-8 hours stain from upper layers. prepare a second peptone culture from it & gelatine plates & with what remains test for Indol.

If more time available go through other tests. Agar. potato Intraperitoneal inj. of G.P.s. Pfeiffer's phenomenon. Agglutination (Vibrio Metchnikovi. Other Vibrios) (cheese) (fowls)

Differentiation from other Vibrios. Gruber Pfeiffer. Deneke, Metchnikoff. Miller. Canon tooth

Haffkine's Vaccine. 1st Vaccine - weak. Attenuated by growing on Agar with a current of moist air passing over. (Causes only oedema instead of necrosis on G.P.s)

2nd Vaccine strong. Virulence increased by intraperitoneal passage through G.P.s 20-30 passages. peritoneal fluid incubated for 10 hours. Cultures only retain maximum virulence for 3-4 days. Vaccines made from surface agar cultivations. 1cc of both to a 'standard' tube. bacteriized or not. 1 c.c. dose. No 2 given 3-5 days after No 1.

Tetanus.

Cause. Bacillus of Nicolaier. Taken Kitasato in pure culture. Morphology. Rods, threads. Spores. Motility - flagella. Anaerobe, strict on first removal from host, later may grow to some extent aerobically — presence of other O. absorbing germs, glucose. Stains well by Gram. Method of isolating from a wound depends on resistance of spores. Boiling for 3 minutes in glucose agar or capillary tubes. Characters of cultures in Gelatin. Agar. Broth.

Clinical symptoms of the disease are due to the absorption of toxins into the system. The toxin is either introduced into the body along with the bacillus or is formed there by the bacillus. Effects of inoc^{n} of filtered toxin are identical with the clinical symptoms of the disease, inoc^{n} of deposit on filter also identical Effects of inoc^{n} of deposit after freeing it from toxin by washing or heating to 70° are for most part negative. The spores and bacteria are phagocyted and possibly destroyed by the bactericidal power of the blood. According to above it would seem that tetanus can only supervene upon the inoculation of a mixture of preformed toxin & tetanus bacilli but further expts show the following — a/ that if the spores freed from toxin are introduced in enormous numbers some escape destruction, produce toxin & cause the disease: b/ that if the spores as above are mixed with numbers of other bacilli the same result will supervene c/ that if spores as above are mixed with numbers of foreign particles as sand disease occurs d/ if spores enclosed in some foreign body - pieces of stick, pellet of agar - same result occurs. Vaillard also says lactic acid, effusion of blood, splinter of bone. The fact that tetanus occurs under these conditions has been ascribed to the interference with

phagocytosis. The conditions specified above would also however impede the access of lymph to the tetanus bacilli.

Nature of the Toxins. The crude toxin from filtered bouillon usually investigated Easily destroyed by heat — 65° Chemicals & sunlight, not by drying. The nature of tetanus toxins much involved & outside scope of lecture. One of the most powerful poisons known .0005 of a mgm for a mouse — proportionally about $\frac{1}{300}$ of a grain for a man. Nature of action Neurotropic excites reflex excitability of motor cells of cord, pons + medulla (less in cortex.) When absorbed probably proceeds along sheaths of nerves

Immunity. Tetanus Antitoxin Preparation & standardisation. Methods of employment in man. Subcutaneously, intravenously, intracerebral. Results not very good. unsatisfactory dosage.

Methods of examination of a case of Tetanus. Microscopical. Cultivation Inoculation of mice or G.P.s.

Other organisms which might be confused with Tetanus. Bacillus Issaeli. "Pseudotetanus" very similar, from intestine, feebly motile, not pathogenic for animals.

Bac. Botulinus. meat poisoning usually polar Spores, does not stain by Gram.

Bac. Oedematis maligni polar spores in semen. A destructive disease of cattle called Symptomatic Anthrax

Rabies.

Cause unknown. Reasons for imagining it to be a microorganism. Shall speak of it as the 'virus'. Rabies in man & animals. 2 forms.

Distribution of the Virus in the infected organism & mode of spread through organism. Present in saliva. Absent from blood and internal organs. Present in C.N. System. Lymphatic glands in connection with wound are free from the virus. Thus spread does not occur by same channels as in ordinary bacterial invasion. Not due to a toxin because of infinity of passages through animals.

Incubation Period in man & animals. Facts in connection with incubation period bearing on channels of spread. Very prolonged incubation periods in cases on the extremities, shorter on trunk or limbs near trunk, shorter still on head & neck, & shortest of all (Pasteur) intra-ocular inoc^{n} and finally or directly into nerve into Central nervous system. This suggests a creeping of the virus along nervous channels.

Experiments in connection with these facts. 1/ Nerves leading up from the wound contain the virus. 2/ Corresponding nerves on opposite side ditto. later. 3/ Vagus & other bulbar nerves. 4/ Section of nerve does not prevent spread. 5/ Section of lumbar cord after inoc^{n} of sciatic followed by spread of virus to opposite sciatic but not across gulf in cord. 6/ Virus does not appear in saliva until 24 hours after it has reached C.N.S.?

Pathological changes in C.N.S.

Pasteurs Anti-rabic inoc^{n}. Method & results.

Diagnosis of Rabies.

Snake Venom.

A classification may be made into Viperine & Colubrine venoms. The viperine venom is a haemotropic poison - an albumenous substance that is coagulable by heat. The colubrine contains a an albumenous substance haemotropic poison & a neurotropic element which will stand a short exposure to 100°. The haemotropic poison of snake venom produces a prostration followed by a negative phase of coagulability, most liable to occur when large doses are rapidly introduced into the blood. Attention has been drawn by Martin to the close resemblance of the intravascular clotting obtained after a viperine bite with that obtained after injection of nucleo albumins. It has been suggested that the R & B C & endothelial cells are broken up under the influence of the venom. The negative phase is associated with the local haemorrhagic & delayed convalescence. The neurotropic element in snake venom can be best studied by employing heated cobra venom.

Modes of preparation of Antivenene. The character of the serum obtained depends a/ on the character of the venom employed. b/ on the reaction of the organism, proper timing of injections & bleeding. Where a combination of different poisonous albumins are introduced an antitoxin may be produced to one of these & not to another.

Exp.ts with Calmettes serum. Doses inoc.t with a mixed venom deprived of its haemotropic elements by heating to 70° for 10'. Serum therefore does not contain any antibodies to haemotropic poison.

Testing of Antivenene. Multiples of lethal dose &c.

Malaria.

General as to causation. Prevalence. Geographical distribution

Relation to other Protozoa. Coccidia & Gregarines.

Human compared with Avian malaria.

Classification of Malaria.

Description of the cycle of development a/ in man. b/ in mosquito.

Detailed description - comparative of the three varieties.

1/ Quartan.

2/ Benign Tertian.

3/ Malignant Tertian

4/ Quotidian ?

Relation of the various stages of development of the parasites to the clinical signs in the 3 varieties.

Duration of the entry of the various kinds. Laveran. Billet.

Mixed infections. Double infections.

Increase of mononucleares.

Pigmented leucocytes & distribution of pigment in body.

Mosquitoes. General description of anatomy.

Eggs. Larvae Pupae & Imago of Culex & Anopheles.

Distinction of Culex from Anopheles

Life history and habits of Mosquitoes.

Geographical distribution

Chief varieties of Anopheles met with in stations occupied by British & Indian troops.

Points to be examined in classifying mosquitoes.

Culex & Yellow fever.

Filariasis & Mosquitoes.

Preventive measures to be adopted in view of our knowledge of above points. War on mosquitoes. Net protection. Isolation of sick. Quinine.

Points in connection with Malaria awaiting investigation.

Blackwater Fever.

Synonyms. Distribution. Short description of the disease.

Connection with Malaria.

Connection with Quinine.

Theories of causation. See Scheme.

Kala Azár

Distribution. Bengal, Assam Valley, athermic subnormal. Slow wasting, irregular fever, enlarged spleen, dyspepsia, affections. Darkening of the skin ("black" fever)

Relation to Ankylostoma. Bleri-beri. Malaria. M.M. Views of Rogers, Giles & Ross. Malaria.

Great mortality, whole districts depopulated. Sets in hot rainy season, Mar–Oct, mostly April – August. Duration 4–9 months may last 2 years, seldom kills under 3 months. Mortality very heavy. Infection carried from one place to another by patients who infect first their own family & then the village.

Causation not yet cleared up. Ankylostoma if anything more common in non infected natives on the spot. Rogers idea of transmission of Malaria direct from man to man improbable & his evidence of the parasites found so sketchy.

"Kala Dutch" of Northern Bengal probably identical with the above

Dengue.

An acute infectious disease. Initial & lenticular polymorphous eruption, accompanied by severe articular & muscular pains.

Geographical Distrib. Europe. Egypt. Asia. America N. & S. In warm countries only.

Cause. unknown allied to the acute exanthemata. Opinions on Contagion vary. Doctors & nurses often attacked. Incubation period (a few hours to 5 days) may short. Closely resembles Influenza. (identical?) Moonlight does not affect it. Spares neither age nor sex.

Symptomatology. Fever, character of pains. Eruption. No enlarg^t of spleen. Second eruption. Duration on average 6-7 days. Convalescence slow. Sequelae & Complications. Mortality very low, never exceeds 1%.

Path. Anatomy. Nothing.

Beri-beri

Epidemic & endemic in tropical & subtropical countries of Asia. Africa. America & Australia. Principle symptoms disturbance of motion & sensation, dropsy and an affection of the heart. Due to degenerative inflammatory affection of the peripheral nerves. History very ancient.

Geographical distribution. See Schembe 188.

Disease is infectious. 1/ Attacks strong healthy persons by preference. 2/ confined to certain sharply defined districts, principally a disease of large towns, hospitals jails &c. 3/ Season. great moisture & high temperature liable to many variations

Connection with food. Rice. Japanese Navy. Steamed rice exp.s Dried fish. Fat lacking food.

Somewhat resembles Malaria - but no connection. Endemic often where Mal. is rare & absent where M. common. Quinine no effect.

Not contagious. Ship outbreaks. Mechanical transmission of the disease through human intercourse. Cause not settled. Stanley says probably a toxin derived from an extraneous parasite of some article of food. Question of connection of the unknown germ with the soil still unsettled. Drinking water instance quoted by Roll. (Sch 196.) Possibility of causes being more than one in number.

Mostly a disease of prime of life. & less common in women. Europeans less affected than natives — better hygiene or food. An attack confers no immunity rather predisposes to a second.

Symptomatology. 1/ Incompletely developed or rudimentary form.

2/ The atrophic form. 3/ The dropsical. 4/ The acute pernicious or cardiac form. Description of cases. Dilatation of heart, right side. Terrible cardiac pain. Liability of milder forms to become suddenly grave or fatal from sudden involvement of heart.

Nature of the paralytic & nervous symptoms. Resemblance to peripheral neuritis due to Alcohol. Arsenical poisoning. Diphtheria. Influenza. — Hyperaesthesia. Anaesthesia. Reflexes. Reaction of degeneration. Atrophy of muscles, following tenderness.

Nothing found in blood. Urine. diminished usually, Albuminuria rare. Exanthems rare.

Oedema. locality. Fever. inconstant. Sequelae. Mortality.

Path. Anatomy. Oedemas. Heart. blood deficient in coagulability, due to excess of CO_2? Changes in the nerves. Degeneration inflam? Disintegration of medullary sheath & of axis cylinder. Increase of nuclei of endoneurium & beneath perineurium. especially in vicinity of vessels. finally in chronic cases, increase of connective tissue. Muscular branches most affected, little on trunks of nerves. Muscular degeneration, fatty.

Recent work on Beri-beri. See Discussion at B.M.A. /02. Worth of Stanley. Travers & Rost. Manson's last views.

Dysentery.

Aldershot Report.

In submitting the following report upon ~~the results of the investigations carried out to determine~~ upon the development of the protective substances in the blood after inoculation against Typhoid fever I would wish in the first place to emphasise the nature of the part played in this investigation by my colleagues Capt H. & Lieuts Small. & T. almost practically the whole of the Aldershot work, whose exacting nature must be evident to the Committee, was carried out by these Officers as in this I was personally only able to assist them to but a small extent and I am anxious that the Committee should not underestimate the large extent to which I am indebted to them Officers for the self devotion and skill with which the experiment has been carried through.

Nature of the Investigation.

It was the original intention of the Committee that if possible one half of the 2nd R. F. should be inoculated the remaining half serving as a control so that in this way valuable statistical evidence could be obtained as to the protective effect of the inoculations, by attaching Lieut S to the battalion for 3 years to be obtained however the 2nd R. F. the last regiment available this trooping season, was only taking out to India a little over 300 men and that it would complete its strength in India from men of the 1st battalion whom they were to relieve & who were probably older soldiers & to a large extent acclimatised. Partly on this account & partly because of the fact that ½ of the regiment was to be stationed at Lebong a healthy hill station near Darjeeling while the other half were to be quartered at Dinapore it was realised that little was to hoped from this particular regiment on the way of definite & convincing statistical evidence as to the protective effects of inoculation.

It was therefore decided by the Committee that as many volunteers as came forward should be inoculated and that at least one investigation of the development of protective substances in the blood which should be carried

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been Photographed.

Question of the development of a negative phase.

No evidence of this was found in any of the groups, either on first inoculation or on reinoculation.

It is possible that a negative phase of a very transient character may have existed but even with the largest dose employed no lowering of any of the protective substances could be detected although the blood was drawn 16 hours after inoculation and it may further be noted that in the case of one of two who was inoculated with 1cc of Vaccine A & in whom both the local & general reactions were far more severe than in any of the men no trace of a negative phase was found.

~~It is seen therefore that~~
The system of testing the pooled blood of the groups makes it impossible to say that some individuals may not

have shown a negative phase. Had it been marked or even sensual evidence of this would certainly have been forthcoming in our results.

It seems probable therefore that, up to the limits of the dosage employed, if a negative phase is developed it is so slight or so transient as to be negligeable.

Interspacing of the inoculations & reinoculations.

The interval selected — 10 days — would appear to be a very suitable one. At that date the protective substances formed in response to the first inoculation were on the rise. And the efforts of reinoculation appear to have further stimulated their development & certainly to have been followed by no decline.

Value of the Agglutinin curve as a measure of the other protective substances.

The amount of the Agglutinins in the remain groups appear to afford a fair estimate of the development of the other protective substances a fact which (perhaps to be taken advantage of in future investigations in which it might not be practicable to carry out the other and more delicate technical processes.

Results of inoculation of group D.
(previously inoculated 5 years ago.)

The very small dose employed as a first dose .01 cc failed to elicit any marked response in the elaboration of protective substances. The reinoculating dose was accordingly raised to .1 cc but in this case also, so far as the experiment went, no unusual development followed.

It is possible that the interval of 5 years was too great to expect any increased response in the group.

In conclusion, I may remark the Committee that some of the most important points in connection with this investigation of the blood changes following Typhoid inoculation remain to be worked out by Lieut Smallman, in accordance with the programme laid down for him, and that as soon as these come to hand they will be communicated to the Committee.

reduced dose for boys?

Brief General Conclusions.

The following ~~summary~~ ~~very briefly~~ Conclusions

In ~~summarising~~ of the main ~~points~~ which appear to emerge from the analytical work detailed in the report and protocols, and illustrated graphically in the form of curves, it must be borne in mind that these conclusions only represent my own individual opinions ~~and it is not~~ than likely that other ~~conclusions may be drawn~~ which may or may not coincide with those which may be drawn from the facts given others. ~~And further~~ and the perhaps excessive detail of the report has been adopted mainly to assist those who may study it to draw their own conclusions.

1. The elaboration of protective substances.

There can be no question

It must in the first place be borne in mind that the duration of the investigation was only long enough to suffered trace the origin and development of the protective substances and the immediate effects of the 1st and 2nd inoculations with different doses of Vaccine The further results in the recording of

Wednesday Further experiments on the same lines are to be carried on by Lieut Smaelman in India as soon as he can get to work to record the later fluctuations in quantity of the various Prohetic substances in the blood of the inoculated. His results will be communicated by me to the Committee from time to time.

The facts brought out in the Report show a remarkable development of Prohetic substances in the blood of the inoculated but nothing can at present be said as to the length of time these high levels will be maintained.

1/ Towards The local and general reactions following on inoculations. Even with the highest doses employed In no case did these reactions give rise to much disturbance at the end of 48 hours almost all symptoms had disappeared in a few instances slight pain & tenderness except for slight local tenderness at the site of inoculation for a day or two later.

The symptoms on inoculation with doses in groups A & B were as slight as those employed on the

Speaking generally the severity of the symptoms were proportionate to the dose employed.

first inoculations were more marked in most cases that

A contrast was obtained in the case of groups A & B as to the effects of the same dose of Vaccine - .6 cc - employed in the case of A as a first dose, in the case of B as a second dose following a first inoculation of .3 cc.; in three cases No marked differences in the reactions were recorded.

Although the reactions were severe in not would be well if further with any of the doses it seems research should lead to a modification of the possible that the vaccine may be acceptable of improvement in the way of diminishing the effects of inoculation immediate without detriment to the subsequent elaboration of Prohetic substances.

Such a modification would I feel sure greatly simplify the task of the advantage in obtaining volunteers. Getting soldiers to volunteer for inoculation.

2/ Effects of dosage on the development of Prohetic substances.

This was most marked in the case of the largest doses. Groups A who received the largest doses. A. and the quantity of protective substances developed in the other groups in general was more a general relation to the dose employed than the order of their doses.

The differences recorded were not however proportionate to the differences in dosage added. for instance the values in those groups B were only slightly lower than in groups A. which received a total dosage of bacilli double that of B. and again the development in B groups which received only 1/6 of the total number of bacilli inoculated in A groups was remarkably high. considering the small dose employed.

In future experiments to determine the final disappearance of the protective substances of these substances in the blood of the groups will form a more reliable basis on which to form conclusions as to the amount of protection likely to be afforded by the different doses as it is possible that the height of the initial rise is not a true indication of the length of time during which these substances remain above their normal limits.

Intention to let Committee form own conclusions from facts.

~~Only mention points which seem to be clearly~~ The chief points in connection with each separate investigation have been already commented on. So will only give general conclusions.

What is proved by the exp^t.?

That there is with a moderate dose of 100 Vaccine a remarkable development of protective substances.

Duration of substances. — Appear transitory. Not brought ~~out~~ ~~traken~~ but will be Smallman.

Effects of dosage.

Advantage appears to rest with A. next with B. but C though lower quite remarkable.

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1 dose v. 2. Could not be done but S. will test in India.

Effects of reinoc^n followed by further rise.

Negative phase. Possible in individuals but no evidence in group.

Agglutinin as a measure — advantages.

Failure of D. prob. reason.

Local + Gen. reaction. possible modifications of Vaccine may improve

Lines of improvement

Mod. Vaccine to lessen reaction.

Imp. Standardization.

Multiple moderations. small dose.

Owing to the small numbers of the

Natives of the Forest.

The Commissioner having decided that the number of men of the 2nd R.F. proceeding to India was too small to utilize the inoculations as a test ~~experiment~~ of the measure of protection the

Hon [illegible]

Charts

Aggl. 1 – 5

Bact al. 6

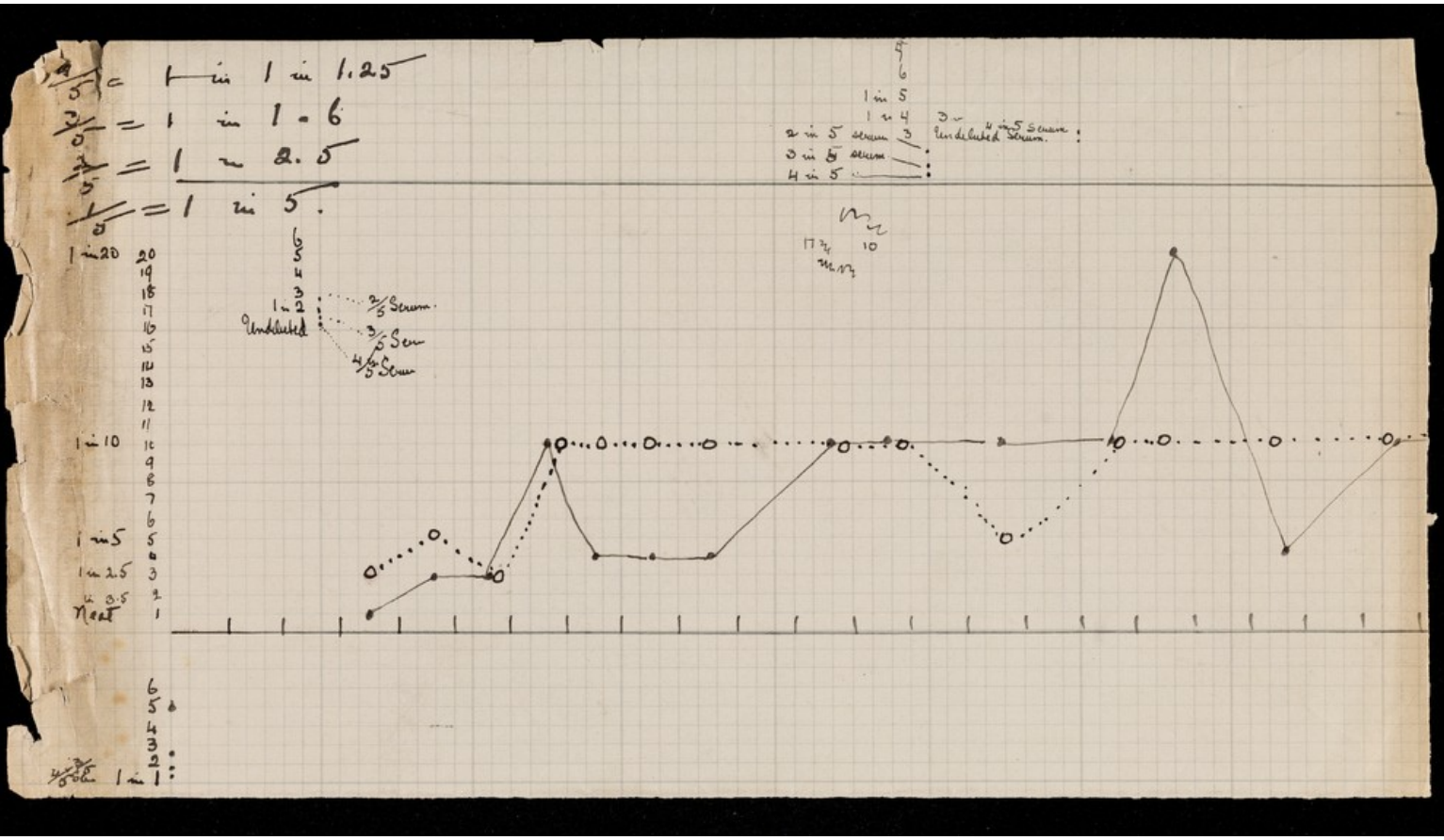
Bact typis 7.

Ops. 8

Stim. 9.

Protocols

Bacteri'cidal.	Table.	1–4
Vir do	"	5.
Bact typic		6–9
Ops.	"	10
Stims	"	11


4/5 = 1 in 1 in 1.25
3/5 = 1 in 1.6
2/5 = 1 in 2.5
1/5 = 1 in 5.
1 in 20
1 in 10
1 in 5
1 in 2.5
1 in 2
Neat
1 in 5
1 in 4
2 in 5 serum
3 in 5 serum
4 in 5
Undiluted
2/5 Serum
3/5 Ser
4/5 Serum