University College

Gower St.

May 1, '24.

Hospital

Dr. Harington - Pathological Chemist.

Disagrees with Kendall on formula of thyroxin. Working on own interpretation. Lunch.

Dr. A.V. Hill .... Prof. of Physiology

Hill and Brown - glass electrode for pH determ., modification of Haber's original idea. No H used.

Interior soln. of known pH. PO_4 soln. of almost any concn. will do. Dip in beaker of soln. to be measured. Very sensitive quadrant electrometer must be used, which is a disadvantage.

Dr. Frederick G. Donnan,

Prof. of Physical Chemistry.

Was most kind – showed me all over his laboratories. Has many research students. Some of problems: Effects of vapors on surface tension of Hg, using drop method; cmpsn. of vapor phase of mixets. of H_2O and $C_3H_5(OH)_3$; vapor pressure of $Na_2SO_4 \cdot 10H_2O$ under > 1 atm. pressure; phys. chem. of silicate solns.; mother-of-pearl and Liesegang's rings; effects of silent discharge on various substances, including solid formed from dry CO,

for student labs., or anywhere where noisy, instead of using telephone for conductivity detns, uses double rotating commutator, supplied acc. to specification by Sigma Instrument Co., Pixmore Ave. Letchworth, Eng. 1 side connected to source of current, other to galvanometer.

Tea.

St. Mary's Hospital,
Praed St., Paddington.

May 8, '24

Institute of Pathology and Research.

Sir Almroth Wright.

Showed various methods used in lab. in diagnosis of blood infections and control of condition of patient.

Hemolysis of rabbit blood by certain ~~staphylococci~~ staphylococci inhibited by horse serum.

"Emigration Discs" – Thimbleful of blood stood on glass slide deposits its leucocytes on the slide – leucocytes fasten to any solid surface. If these deposited on plasma clot (or plasma clot deposited on these – any bacteria in plasma will either grow or be killed by leucocytes. If grow, colonies will show, sometimes to naked eye. Had one beautiful prepn. in which colonies on 1 side, leucocytes on other – "no-man's land" in between. Believes it shows that leucocytes actually secrete substance that

~~destroys~~ kills the bacteria.

Tea.

Dr. Freeman.

Working on anaphylaxis & hay fever. Very small injections during attacks often helpful. Does not believe in polyvalent pollen treatment. ~~Desensitization to tim~~ Timothy desensitizes to all grasses, just as Mackenzie found.

Lecture by A.V. Hill on "Function of Hemoglobin in the Blood"

Excellent summary of knowledge to-date, except that more of our own work mentioned.

Informal discussion afterwards. Dr. Wright thought many men lying chilled in trenches, afterwards dying of developing gangrene, might have met their end owing to sudden liberation of lactic acid into blood from tissues in which circulation had stopped. Also in prolonged anesthesia.

Royal Institution
21 Albemarle St.
Davy-Faraday Laboratories

Sir William Bragg.... Director.

He and Mr. Shearer now working on higher fatty acids, etc., which are ca. 50 μμ long. Uses old-fashioned gas tubes with Cu anticathodes for this work, and thus can use wave length of 1.7 μμ, also put specimen much closer than in Gen. Elec. app. Exposures of 15 min. to 1 hr. usually enough. Very good crystallograms w. stearic, palmitic, etc. acids.

Also working on Na in form of long single crystals in specially thin capillary tubes.

Mr. Shearer showed some of Faraday relics, also a Cavendish thermometer, R.I. lecture room where Faraday gave his lectures,

room in basement in which Faraday did his work, with his little cupboard still in recess in wall, Kelvin's (?) soap-bubble film app., Dewar's original liquid-air plant, with its huge belts and enormous pumps and compressors.

In organic lab. using ThO_2 catalytic method for prepn. of higher ketones such as PrCOPalm. Mixt. of acids passed over heated ThO_2, repeatedly, at rate of 1 drop per sec. On fract distn. PrCOPr 1st, then mixed ketone, PalmCOPalm in residue. No charring.

Cambridge University
Institute of Biochemistry

May 24, '24.

Prof. Hopkins out.

Dr. Heald (?) showed labs.
Working on mercapturic acids.
Others using new Barcroft app.,
attached to clove-oil manometers,
for measuring O consumption of
bacteria, tissues, etc. Also on
problem of origin and fate of ~~inulin~~
inositol in polyuria conditions.

May 26.

Long talk with Prof. Hopkins.

Dr. Haldane, Jr. working on
effect of NH_4Cl on blood chemistry.

Dr. Tunnicliffe - thinks synth. of
glutathione worked out. Glutamic acid
+ PBr_3 gives omega-Bromide, with Br on
the proper (far) OOOH. This unites readily

w. systems give product app. identical w. natural pigt.

Mr. Hill. - Has succeeded in putting many different metals into hematoporphyrin. All come out relatively easily except Al. Fe^{++} will not go in, but Ni, Co, Ag, Mg, Fe^{+++} prepd. So far only characterized spectroscopically. Co compd. only one to take up & give off a gas (NO?)

Copenhagen University

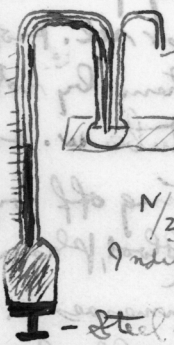
Sept. 2, '24.

Inst. of Hygiene.

Prof. A. Krogh.. Prof. of Physiology

Dr. Marie Krogh

With Dr. Rehberg, working out micro-method for urea and NH_3 in blood. Uses micro-buret made from long 1 cc. pipette:



Claim accuracy of rdgs. to .001 cc.

NH_3 driven out of sample by air freed from NH_3 1st by conc. H_2SO_4, then dil. H_2SO_4. NH_3 caught in titrating vessels as above, using 2 in series, or having tip of tube just

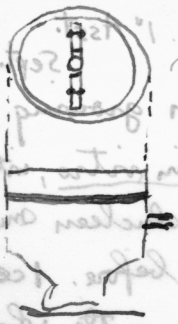
touching acid to avoid spattering.

Showed basal metabolism wk. Expts. on fat & carb. ly. diet showed wk. better performed on latter, while former resulted in extreme fatigue.

With Mr. Rasmussen, working on detn. of colloid osmotic pressure in blood. Makes colloid sacs of varying permeability by varying thickness & rel. proportions alc. & Et_2O. Makes them by rotating on outside of glass tube w. small hole at end, & getting off by H_2O pressure. Puts (blood, plasma, serum (?)) in sac, immerses in Ringer's soln. with ~~small~~ slightly larger tube around bag, so that equil. very quickly established.

Has small centrifuge with H_2O-pump attached, with tubes and motor working in vac. Speeds

of 10 000 R.P.M. attained.



Sliding screw clamps on revolving part.

Sept. 3

Have done physiol. wk. on digitalis, strophanthin, ouabain, squill. Rana succulenta heart shows no cumulative effect w. strophanthin.

Says we should have some competent botanist grow seeds from which we got - idnt, so as to identify species.

Sept. 6.

Showed movies of capillary circulation, circulation in sm. veins & arteries of frog, also in peculiar frog lung, in which inguinal surface is bathed with blood.

Copenhagen Univ.

Institute of General Pathology.

Dr. Albert Fischer.... 1° Asst.

Sept. 3, '24

Has succeeded in growing Rous chicken tumor cells 10 mos. in vitro, with aid of dead or alive chicken muscle. Still as virulent as before. 1 cell suffices to produce growth, whereas with non-malignant cells many cells necessary to initiate growth. Has simple incubator with slides on trays which can be removed & carried to microscope.

Sept. 8

For detn. that single cells can start growth used

Rous chicken sarcoma

Flexner Jobling rat carcinoma

Mouse sarcoma

Human brain sarcoma

Copenhagen Univ.

Prof. Einar Biilmann ..... Chemistry

Has developed the quinhydrone electrode so that now very rapid pH detns. possible. As many as 200 soil pH detns. can be run in 1 day by single person. Lewis of Liverpool has used a capillary form of electrode successfully for pH of blood.

Hydraulic device for dark shade, or curtains for lantern work, also for raising or lowering blackboard.

Also studied $Ph_2N:NPh_2 \rightleftharpoons PhNH-NHPh$ reaction. Found that in acid necessary part of latter transf. into $p(C_6H_4NH_2)_2$, with lowering of potential. Used this for deting. velocity const. of benzidine rearr. at diff. concns. acid.

Copenhagen Univ.

Polytekniske Laeranstalt.

Prof. Brönsted ... Phys. Chem.

Tried quinhydrone method for Ph_2NH_2 and complex $MeNH_2$ derivs, unsuccessfully.

Inst. for Theoretiske Physik.

Prof. Niels Bohr

Prof. Hansen

Prof. Bohr does not believe time is ripe to "reconcile" phys. & chem. theories of the atom. Too little known of each. Final theory must borrow what it needs from both sides & not necessarily be a compromise. Showed labs, incl. that of Prof. Hevesy, where hafnium work is being done.

Haldane, Prof. J. S. Jun 12, '24
Tea, Jun. 15.
Dr & Mrs.

Does little work now in own laboratory. Much travelling on acct. of interest in mining problems. With chemist, working on why SiO_2 dust causes miner's phthisis, while other dust, such as coal, or shale with 70% SiO_2, is harmless. Lung epithelium takes up latter type and cells are desquamated; while SiO_2 taken up but remains. Believes still in O_2-secretion theory, against mechanistic conception of life, but, like Dr. Loeb, has turned now to physical chemistry for deeper understanding of biological phenomena, and will shortly publish a book on osmosis, based on kinetic theory, as did Waterson in a paper which Royal Society refused to publish, and was for-

gotten 50 years. Believes
Carnot cycle, used to prove
2nd law of thermodynamics,
incorrect. Can't Hoff's all
wrong on osmosis.

Kaiser Wilhelm Institut

~~Jir. Ch~~ Dahlem, Berlin

Jul. 26, '24

Prof. Hahn ... Asst. Director

Prof. Lise Meitner ... Radioactivity

Prof. Kurt Hess ... Organic Chem.

Has isolated in crystn. form the $C_6H_{10}O_5$ unit which, by polymerization association, makes up cellulose.

Cellulose, diss. in NH_4'l Cu soln. gives very high rotation, measurable w. Hg lamp, and by using this & calcd. degree of assocn. from formula, ( )x found to be 1. Ppted. as much cellulose on acidf. Cu method permits detection of mixtures, since if curves obtd. by varying concn. of subst. & concn. of Cu do not coincide, mixt. present. Used this to show lichenin a mixt. While polysaccharide chem. moves in state of flux.

Showed labs.

Usual acetyl no. detn. gives results 1% too high. Showed app. for detn. within 0.1%, using vac., at 80°, running steam through to carry off HOAc, liberated by H_3PO_4 (?)

For acetylating polysaccharides SO_2 & Cl method best (Barnett's?) Subst. + HOAc. SO_2 ½ min. Warm ½ hr. Ac_2O, then Cl ½ min., warm again.

Dr. Otto Warburg....

Thinks he, Meyerhof, and Barcroft are the only physiologists, now that Dr. Loeb is dead, who know chemistry and physics. Does not believe that one should go at a subject from the "chem." or "phys." or "pH" pt. of view, but that one should have grasp of the subject as a whole and be fam-

ilar enough with any other science necessary for soln. of a problem to use it as a tool.

Now working on retinas, on reaction they show of splitting relatively enormous amts. of sugar into lactic acid. Action "catalytic" means no more to call it "enzymic." Measures lactic acid formed by liberation of CO_2 from $NaHCO_3$ containing medium. Cell shaken in H_2O bath, connected w. a manometer, arrangement much like Barcroft's. Does not think Donnan equilibrium applies to colloids. Where's membrane?

Dr. Otto Meyerhof

Had just come over from Kiel. Showed his new lab. which were just being equipped

Prof. Carl Neuberg

Very cordial. He and asst., Dr. Gottschalk, showed labs. Have a water blower in one lab. for compressing air. All steam chests, baths, etc. out of use because coal too expensive. Very few animals available because of expense. Showed how, in presence of $CaSO_3$, yeast forms AcOH from sugar, giving blue color w. Na nitroprusside & piperidine (few drops weak aq. soln.), while control without sulfite showed no color. With much yeast in H_2O bath only took a few min.

Dr. London of Petrograd also there & at lunch at Prof. Neuberg's house.

Munich

Chem. Lab. of the State -

(Academy of Sciences)

Arcis Str. 1. Jul. 29, '24.

Prof. Richard Willstätter...

Showed labs.

For rapid distn. of H_2O, uses brine cooling system to condense distillate, high vacuum so as to speed up concn.

Very long, intimate, and satisfactory talk in evening about work and other matters.

Dr. Sobotka finished showing labs. and fine lecture hall, helped with micro. weighings. Important 1° to open side or front doors to equalize temp. Weighings should be taken as nearly as possible within same time after ~~opening~~ taking off caps. Only small weights used —

place of large ones taken by little flask of short balancing tube weighed. If all precautions taken, accurate result possible to 5 mgr. sensitiv. Rider reading to tenths, diff. bet. R & L wings = hundredths & thousandths of mg.

Some very good light duty shakers running by H_2O-turbine.

National Institute for Medical Research.

Mt. Vernon, Hampstead.

Dr. H.H. Dale, Director.

Sat. aft., Apr. 26, '24.

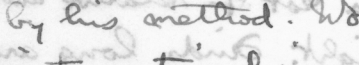
Visited Dr. Dale, saw the labs, met Drs. Marks, Laidlaw, Andrus, Mrs. Dale and Misses Dale.

Fri. A.M., May 9, '24.

Saw Dr. Dale again.

Dr. Dudley showed insulin picrate and hydrochloride obtained by his method. Working on an international insulin standard.

Also working on Spermin. Finds it is $C_5H_8(NH_2)_2$, but is not the usual straight chain or



Forms a crystl. picrate and a very insol., beautifully crystl. phosphate $S.H_3PO_4$, when pH is just right.

Dr. Harold King —

Stopped work on muscarine. Now working on As derivs. of type of Bayer 205.

May 19, '24.

Dr. Leonard Hill —

Action of ultraviolet light on t. b., rickets, effect in causing injury. Uses frog mesentery as test object, dilns. of methylene blue in aq. acetone as test of relative amts. of U.V. light. Finds long arc rich in U.V. rays.

Dr. Purdie — Working on tissue culture, using mouse embryos. Says Dr. Carrel's papers would be much more impressive if used drawings instead of photos.

Dr. Dobell — Protozoölogist.

Natl. Inst. for Med. Res. cont'd.

Mr. Smiles — Ultraviolet light app. for taking photomicrographs. Has specially delicate fine adjustment so calibrated that can be focussed in light of any wave length, then adjusted for U.V., making trial exposures unnecessary. Advantage — Greater resolving power makes staining unnecessary. Showed very striking transparences of anthrax and yeasts.

Also showed special DARK Field Illuminator, permitting use of lens at full aperture (light at full intensity) but requiring slide not > 0.5 mm. Shows S. pallida without staining.

Dr. Dudley.. Showed Kuhlmann "Schnellwage" — very quick, sensitive, accurate. 4" place detd. by diff. in scale on 2 sides.

May 24th

Dr. Laidlaw — At Physiological Society meeting at Cambridge: Substance in t.b., distinct from tuberculin, reacts w. immune serum, shows redg. sugars on hydrolysis.

Institut Pasteur, Brussels

Jul. 23, '24

Prof. Jules Bordet.....

Believes the two main problems of immunity now that of specificity and that of filterable viruses. Said he had a Pn strain that suddenly gave rapy, viscous cultures, a filtrate gave exceedingly heavy ppt. w. immune serum. Thinks anthrax not phagocyted because of capsule, believing action physical rather than chem. Anthrax culture & body fluids of animals dying of it contain sol. sp. sub. Thinks should perform following expt:

1 animal S alone + Pn

1 " ppt from S + immune serum then Pn

1 " immune serum then Pn

Does S carry down the protecting antibodies?

Dr. André Gratia....

Disagrees with Besredka's theory of local immunity. Finds that if anthrax strains virulent enough to grow capsule in blood stream before being phagocyted animal will die even if skin intact. Further antibodies do appear in blood after skin immunization — agglutinins & perhaps anti aggressins. Has gotten a "rough" & "smooth" anthrax modification & can detect agglutinins at very high dilns. by growing "smooth." In normal broth + normal serum stays ~~smooth~~ diffuse, but agglutinins make it grow clumpy even at 1:200,000

Institut Pasteur, Paris.

Jun. 23, '24.

Dr. Macheboeuf .... Asst. to Prof. Bertrand.

Showed biochemical laboratories. Some of large-scale app., in huge, factory-like, glass-covered enclosure. Hydraulic presses, large-scale vacuum & other stills, also a vacuum apparatus of 4 cylindrical units into which anaerobic culture vessels could be placed & evacuated. Could also be used as vac. desicc. when connected w. Aq-lined H_2SO_4 tank containing a stirring device.

Institut Pasteur, Paris.

Jun 24, '24.

Dr. Besredka - much interested in S.S.S.

Dr. Plotz - told of how guinea pigs will tolerate many lethal doses of anthrax b. if inserted under skin in capillaries & not liberated until skin entirely healed.

Dr. Nicolle ... working on syphilis problems w.

Dr. Levaditi. - Very enthusiastic about his Bi compds., & writing a book on them. "Bismoxyl", Dr. Nicolle says, is a compd. formed by digestion of $Bi(OH)_3$ (?) w. lives tissue. Single course of treatment often makes Wassermann -.

Dr. Levaditi also working on herpes, encephalitis, showed a rabbit with herpes lesions in eye and on

skin scarified w. virus.

Jun 25.

Dr. Besredka – Believes that in certain diseases at least immunity is not due to anti-bodies, but to a sol. subst. in the culture filtrate which stimulates a local organ to exert its protective action. E.g., in typhoid, if digestive tract is immunized, animal is immune. (Dr. Grinsberg says this is the only method used now in France, Greece, etc. to immunize agst. typhoid. 1" a bile pill is swallowed, then later, tablet of killed typh. b. Repeated twice. No reactions. Results excellent). If anthrax injected into g. pig in ordinary way, animal dies, but if done so

that skin left intact, the skin, the organ of immunity concerned in this case, protects the animal & the bacilli disappear. If strep. cultures fluid rubbed into skin & this then inoc. w. strep., do not grow, whereas control infect the animal. This taken to indicate a sol. sp. subst. with protective power. Wants reprints

Dr. Plotz - showed Pasteur's tomb, library, etc.

Dr. Weinberg .... Gas gangrene

Dr. Guinsberg.

Jun. 28.

Dr. Weinberg

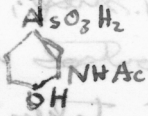
Dr. Guinsberg .... Says gas-gangrene serum (polyvalent) much used in industrial accident, also very valuable in gangrene of the appendix.

Pasteur Institute, Paris.

Jun 25 26.

Prof. Ernest Fourneau ... Prof. of Medical Chemistry.

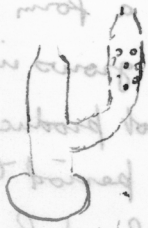
Believes tryparsamide not strong enough. "Stovarsol" is



. Can be given per os: often w. excellent results, & can also be used as a preventive. Gets very discouraged about chemotherapy sometimes, but believes certain lines, such as investigation of quinoline derivs., acridines, promising. Also working on perfumes, question of where the chicken gets its lines. Has private laboratory, large genl. lab., and smaller research rooms. Finds Vigreux column very useful, also devised a modification of

Erlenmeyer flasks, now being made in numerous sizes.

Larger capacity, less likely to be over



Vac. distg. flasks w. ✓ grease column fused in.

Had a shaker (in plane) of the type used by Grignard in his synthesis, app. for ~~lbg~~ 6 flasks in H_2O bath & keeping contents stirred. Want reprint

Dr. Calmette

Finds that a small amt. snake venom, added to lecithin (egg yolk), gives a powerful hemolysin. A small amt. of this, transferred to another tube of egg-yolk, produces an equally strong hemolysin

after a period of incubation; and so on, for an indefinite no. of transfers.

By growing t.b. in bile (for 13 years — Gunsberg) a form is produced which grows in animals but does not produce tubercles. After a period these animals (incl. monkeys) become immune to virulent t.b. Preventive innoculation of new-born infants is now being tried, esp. those of tuberculous mothers, 65% of which ordinarily die before the age of 2.

Jul. 2

Drs. Nicolle & Cotteny (?)

Dr. Nicolle partially paralyzed, makes self understood

w. difficulty. He and Dr. Cottony asked many questions about our Pn work & Dr. Avery's. Wanted to know if rabbits immunized with Pn NP gave serum which protected mice agst. Pn. Said virulence of Pn can be maintained by keeping in ice-box in gelatin-broth (Nicolle's method). Working on production of active sera. Sometimes get sera active agst. type III. To get good serum, necessary to work w. very virulent organisms. Cottony wants reprints

Jul. 8

Dr. Bertrand ... Prof. of Biochemistry

Jul. 17.

Dr. Levaditi .... Showed sample of Treponarsyl, an illegal trypparsamide mfgd. by Merrice of

Brussels. Wants a small sample of our tryparsamide.

Dr. Weinberg ... Working on "cataxie" — sort of symbiosis of bacteria exerting its pathogenic effect through several factors. If serum destroys one link in the chain, all that is necessary to pave way for cure. Believes that chem., much the same sort of thing happens when an antitoxin is rendered non-toxic by heat, toxic group being altered, but antigenic properties remain same. Wants reprints.