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MUSEUM CATALOGUE

DEPARTMENT OF PATHOLOGY.

The University, Hong Kong.

PREFATORY NOTE.

A word of explanation on the system of cataloguing in this Museum is necessary. The scheme adopted is arranged on a modified decimal system of museum classification, a plan first suggested by the late Professor Wyatt Johnson and later applied by Dr. Maude Abbot of McGill University.

A descriptive number is used, in which the number representing the anatomical condition precedes, and that representing the pathological follows the first decimal point, the individual specimen being indicated by another figure placed to the right of and after the second decimal point of the descriptive number. Take for example a specimen labelled 43.26.4. Reference to the scheme of anatomical classification shows that the number 43 indicates the spleen. Likewise the number .26 in the scheme of pathological classification signifies infarction. The last figure 4 represents our serial museum number for the individual specimen of this condition.

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KEY TO THE CLASSIFICATION.

Part I. ANATOMICAL CLASSIFICATION.

1. Circulatory Sysem.

11. Pericardium.
12. Myocardium.
13. Endocardium.

14. Heart as a whole.
15. Arteries.
16. Veins.

2. Respiratory System.

21. Nares.
22. Larynx.
23. Trachea and Bronchi.
24. Lungs.
25. Pleura.

3. Digestive System.

31. Teeth.
32. Mouth. Tongue. Pharynx.
33. Oesophagus.
34. Stomach.
35. Intestines.
36. Peritoneum and Mesentery.
37. Liver.
38. Gall-bladder and Bile Ducts.
39. Pancreas.

4. Haemopoietic Organs and Ductless Glands.

41. Bone-marrow.
42. Lymph-nodes.
43. Spleen.
44. Thymus Gland.
45. Thyroid.
46. Parathyroids.
47. Adrenal.
48. Carotid and Coccygeal Glands.
49. Pituitary Body.

5. Urogenital System.

51. Kidney.
52. Ureter.
53. Bladder.
54. Prostate.
55. Urethra.
56. Penis.
57. Seminal Vesicles, Vas Deferens, and Cord.
58. Testis, Epididymis, Tunica Vaginalis.
59. Perineum.

6. Female Genitalia.

61. External Genitalia.
62. Vagina.
63. Uterus.

64. Fallopian Tube.
65. Ovary and Parovarium.
66. Pelvic Peritoneum and Connective Tissue.
67. Breast.
68. Generative System in Pregnancy.

7. Nervous System.

71. Membranes.
72. Cerebral Vascular System.
73. Cerebrum.
74. Cerebellum.
75. Spinal Cord.
76. Nerves.
77. Nerve Ganglia.
78. Eye.
79. Ear.

8. Musculo-Cutaneous System.

81. Skin.
82. Hair.
83. Nails.
84. Muscle.
85. Fascia.

9. Osseous and Articular System.

91. Bones of Cranium.
92. Bones of Face.
93. Vertebrae.
94. Sternum.
95. Ribs.
96. Bones of Upper Extremity.
97. Pelvic Girdle.
98. Bones of Lower Extremity.

0. Regional.

01. Head.
02. Face.
03. Neck.
04. Back.
05. Thorax.
06. Abdomen.
07. Pelvis.
08. Upper Extremity.
09. Lower Extremity.

Part II. PATHOLOGICAL CLASSIFICATION.

.1 Antenatal Structures and Abnormalities of Development.

.11 Foetal Structures (Normal Anatomy).

.12 Malformations of Incomplete Development.
.13 Reduction in Size (Hypoplasia).
.14 Reduction in Number (Syndactylism, &c.).
.15 Persistent Foetal Structures.
.16 Excess in Size.
.17 Excess in Number.
.18 Malposition or Heterotaxis; Aberrant Structures.
.19 Anomalies due to Foetal Disease.

.2 Circulatory Disturbances.

.21 Anaemia.
.22 Congestion or Hyperaemia.
.23 Haemorrhage.
.24 Thrombosis.
.25 Embolism.
.26 Infarction.
.27 Oedema.

.3 Inflammatory Processes.

.31 Catarrhal or Desquamative.
.32 Exudative.
.33 Destructive.
.34 Specific Inflammations due to Cocci.
.35 Specific Inflammations due to Bacilli.
.36 Specific Inflammations due to Tubercle Bacillus.
.37 Specific Inflammations due to Treponema pallidum.
.38 Specific Inflammations, Causative Agents still undermined.
.39 Productive or Proliferative Processes.

.4 Infections and Parasites.

.44 Higher Bacteria. Also Yeasts and Moulds.
.46 Protozoa. Malaria.
.47 Flat Worms.
.48 Round Worms.
.49 Insecta and Arachnida.

.5 Disorders of Metabolism and Intoxications.

.51 Diseases Associated with Changes in the Blood and Blood-forming Organs.
.52 Intoxications Associated with Disorders of Ductless Glands.
.53 Diseases due to Autochthonous or Heterochthonous Poisons of Organic Nature.
.54 Diseases due to Heterochthonous Poisons of Inorganic or Plant Nature
.55 Arterio-sclerosis.
.56 Diseases due to Defects of Nutrition.
.57 Diseases of Disordered Metabolism.
.58 Organic Nervous Disorders.

.6 Retrogressive Changes.

.61 Atrophy.
.62 Degenerations.
.63 Infiltrations.
.64 Concretion. Calculus Formation.
.65 The Necroses.
.66 Stenosis due to Disease.
.67 Dilatation due to Disease.

.7 Progressive Changes.

.71 Regeneration.
.72 Hypertrophy.
.73 Benign Tumours (of one of the modifications of fully formed connective tissue).
.74 Benign Tumours (of Epithelial Origin).
.75 Indeterminate Group (Tumours of Uncertain Histology or Malignancy).
.76 Endotheliomata.
.77 Cystoma.
.78 Malignant Tumours. Sarcoma.
.79 Malignant Tumours of Epithelial Origin.

.8 Traumata (from Mechanical, Chemical or Physical Causes).

.81 Wounds.
.82 Fractures.
.83 Dislocations and Sprains.
.84 Displacements.
  .841 Hernia.
  .842 Intussusception.
  .843 Volvulus.
  .844 Prolapse.
.85 Impaction of Foreign Bodies.
.86 Thermal Injuries.
.87 Chemical Lesions.
.88 Pressure Effects produced by compression or traction from without, or distension from within.
.89 Birth Processes.

.9 Operative Procedures.

.91 Amputations.
.92 Excision.
.93 Plastic.
.94 Ligature.
.95 Incision.

.96 Union and Replacement.
.97 Fixation.
.98 Experimental Surgery.
.99 Miscellaneous Operations.

0. Teratology.

1. CIRCULATORY SYSTEM.

11. PERICARDIUM.

.3 Inflammatory Processes.

11.32.1. Acute pericarditis, cor villosum.
11.32.2. Acute pericarditis, cor villosum.
11.32.3. Acute pericarditis, cor villosum.
11.32.4. Acute pericarditis, cor villosum.
11.32.5. Chronic pericarditis, thickened and adherent pericardium.
11.32.6. Chronic pericarditis, adherent pericardium and milk spots; pneumonic lung in situ.
11.32.7. Chronic pericarditis.
11.32.8. Chronic pericarditis with pneumonic lung and suppurative pleurisy.

11.36.1. Tuberculous pericarditis.

12. MYOCARDIUM

.2 Circulatory Disturbances.

12.23.1. Petechial haemorrhages from case of leukaemia.

.3 Inflammatory Processes.

12.36.1. Tuberculosis. Tubercles on epicardium.

12.37.1. Syphilitic myocarditis and sacculation at aorta.

.7 Progressive Changes.

12.72.1. Hypertrophy of left ventricle and aortitis.
12.72.2. Hypertrophy of left ventricle.
12.72.3. Concentric hypertrophy of left ventricle.

13. ENDOCARDIUM.

.3 Inflammatory Processes.

13.3.1. Acute endocarditis, large cauliflower vegetation aortic valve.
13.3.2. Acute endocarditis, recent vegetation aortic valve.
13.3.3. Chronic endocarditis, mitral orifice rigid and oval.
13.3.4. Chronic endocarditis, sclerosis of aortic cusps and vegetation.
13.3.5. Friable, detachable, vegetation on aortic cusps.
13.3.6. Subacute bacterial endocarditis, thrombi on aortic and mitral cusps with destruction.
13.3.7. Thickened aorta, vegetation and destruction of aortic cusps.
13.3.8. Chronic endocarditis, small vegetations in pulmonary valve.
13.3.9. Chronic endocarditis, thickening of aortic cusps and stenosed mitral.
13.3.10. Chronic syphilitic sclerosis and dilatation of aorta with incompetence. Hypertrophy left ventricle.
13.3.11. Thickened aortic cusps. Hypertrophy left ventricle.
13.3.12. Dilated, thickened, puckered aorta. Hypertrophy left ventricle.
13.3.13. Acute endocarditis, diffuse vegetation over aorta with destruction. Thrombi at apex and over chordae tendinae.
13.3.14. Chronic endocarditis, funnel shaped stenosis of mitral valve.

14. HEART AS A WHOLE.

.2 Circulatory Disturbances.

14.2.1. Aneurysmal dilatation of coronary artery.

.3 Inflammatory Processes.

14.37.1. Gumma.

.6 Retrogressive Changes.

14.61.1. Brown atrophy.
14.61.2. Brown atrophy.
14.61.3. Brown atrophy.
14.61.4. Brown atrophy.
14.61.5. Brown atrophy.
14.62.1. Fatty degeneration.
14.62.2. Fatty degeneration.
14.62.3. Fatty degeneration.
14.62.4. Fatty degeneration and hypertrophy. Atheroma and sacculation of aorta.
14.62.5. Fatty degeneration and atheroma.
14.62.6. Fatty degeneration and atheroma.

15. ARTERIES.

.3 Inflammatory Processes.

15.37.1. Double saccular aneurysms, arch of aorta.
15.37.2. Large saccular aneurysm, first part of aorta.
15.37.3. Saccular aneurysm of innominate artery.
15.37.4. Aortic aneurysm with laminated clot.
13.37.5. Large aneurysm compressing lung and eroding vertebrae.
15.37.6. Very large aneurysm of first part of aorta with calcareous plates.
15.37.7 Aneurysmal dilatation of the arch.
15.37.8. Atheroma thoracic aorta.
15.37.9. Fusiform aneurysm of abdominal aorta.
15.37.10. False aneurysm of gluteal region with laminated clot.
15.37.11. Popliteal aneurysm eroding femur.

.5 Disorders of Metabolism and intoxications.

15.55.1. Arteries—arterio-sclerosis.

.8 Traumata (from Mechanical, Chemical or Physical Causes).

15.81.1. False popliteal aneurysm secondary to knife wound.

.6 Retrogressive Changes.

15.62.1. Calcification of coronary artery.

2. RESPIRATORY SYSTEM.

22. LARYNX.

.3 Inflammatory Processes.

22.35.1. Diphtheria, false membrane over vocal cords and mucous membrane of larynx.

22.36.1. Tuberculosis, ulceration of vocal cords, epiglottis and mucous membrane of larynx.

22.36.2. Tuberculosis, deep ulceration.

22.36.3. Tuberculosis, extensive ulceration of epiglottis, and vocal cords.

23. TRACHEA AND BRONCHI.

.6 Retrogressive Changes.

23.67.1. Bronchiectasis and fibrosis.

23.67.2. Bronchiectatic cavities at base filled with purulent exudate.

24. LUNGS.

.2 Circulatory Disturbances.

24.22.1. Chronic venous congestion.

.3 Inflammatory Processes.

24.32.1. Lobar pneumonia, red hepatization.

24.32.2. Lobar pneumonia and suppurative pleurisy.

24.32.3. Lobar pneumonia, grey hepatization and fibrinous pleurisy.

24.32.4. Lobar pneumonia and thickened pleura.

24.32.1. Large abscess cavity of right lobe.

24.35.1. Pneumonic plague, haemorrhagic consolidation.

24.35.2. Pneumonic plague, haemorrhagic consolidation.
24.36.1. Tuberculous pneumonia with thickened pleura.
24.36.2. Chronic tuberculosis, large hollowed cavity at apex with smaller ones elsewhere.
24.36.3. Miliary tubercles, consolidation and pleurisy.
24.36.4. Chronic tuberculosis, caseation and cavitation.
24.36.5. Large cavities at upper and middle lobes, and recent tubercles at base.
24.36.6. Caseous pneumonia with old cavities at apex.
24.36.7. Caseous pneumonia with cavities at apex and pleurisy.
24.36.8. Extensive caseation of upper and middle lobes, consolidation of base.
24.36.9. Miliary tuberculosis.
24.36.10. Acute miliary tuberculosis of one lung and empyema and collapse of the other.
24.36.11. Tuberculosis with widespread cavitation, definite fibrous wall.
24.36.12. Multiple ragged cavities at apex.
24.36.13. Acute miliary tuberculosis.
24.36.14. Miliary tuberculosis with old foci in apex.
24.36.15. Miliary tuberculosis.

.6 *Retrogressive Changes.*

24.637.1. Anthracosis.
24.67.1. Emphysema.

.7 *Progressive Changes.*

24.78.1. Sarcoma.
24.78.2. Sarcoma.
24.78.3. Lymphosarcoma, secondary.

24.79.1. Secondary carcinoma.
24.79.2. Secondary carcinoma.
24.79.3. Secondary carcinoma.
24.79.5. Secondary carcinoma.
24.79.6. Secondary carcinoma.
24.79.7. Secondary carcinoma.
24.79.8. Neuroblastoma.
24.79.9. Oat-celled carcinoma, primary.

25. PLEURA.

.3 Inflammatory Processes.

25.32.1. Suppurative pleurisy and septic pneumonia.
25.32.2. Chronic thickened pleura.

3. DIGESTIVE SYSTEM.

31. TEETH.

.7 Progressive Changes.

31.74.1. Odontome.
31.74.2. Odontome.
31.74.3. Odontome.

32. MOUTH. TONGUE. PHARYNX.

.1 Antenatal Structures and Abnormalities of Development.

32.12.1. Hare-lip and cleft palate.
32.12.2. Hare-lip and cleft palate.
32.12.3. Hare-lip and cleft palate.
32.12.4. Hare-lip and cleft palate.

.7 Progressive Changes.

32.75.1. Mixed parotid tumour.
32.75.2. Mixed parotid tumour.
32.75.3. Mixed tumour of palate.
32.75.4. Mixed tumour of palate.

32.78.1. Myxo-fibro-sarcoma of jaw.
32.78.2. Sarcoma of jaw.

32.79.1. Basal-celled carcinoma of jaw.
32.79.2. Epithelioma of lip.
32.79.3. Nasopharyngeal carcinoma.

33. OESOPHAGUS.

.8 Traumata (from Mechanical, Chemical or Physical Causes.).

32.87.1. Caustic poisoning.

34. STOMACH.

.6 Retrogressive Changes.

34.65.1. Chronic gastric ulcer, pyloric stenosis.
34.65.2. Chronic gastric ulcer, pyloric portion.
34.65.3. Perforated gastric ulcer.
34.65.4. Multiple gastric ulcers; one in lesser curvature and several in pylorus.
34.65.5. Perforated pyloric ulcer.
34.65.6. Stomach, multiple minute ulcers.

.7 Progressive Changes.

34.79.1. Carcinoma associated with peptic ulcer.
34.79.2. Adenocarcinoma, pyloric portion.
34.79.3. Infiltrative carcinoma, pylorus.
34.79.4. Carcinoma, pyloric portion.

35. INTESTINES.

.1 Antenatal Structures and Abnormalities of Development.

35.12.1. Intestine—diverticula.
35.12.2. Congenital of colon dilatation.
35.15.1. Meckel's Diverticulum.

.3 Inflammatory Processes.

35.32.1. Acute appendicitis.

35.35.1. Ulceration in typhoid fever.
35.35.2. Ulceration in typhoid fever.
35.35.3. Ulceration in typhoid fever.

35.36.1. Tuberculous ulcers, colon.
35.36.2. Tuberculous ulcers and tubercles, small intestine.
35.36.3. Tuberculous ulcers and tubercles on peritoneal surface ileum.
35.36.4. Tuberculous ulcers, large confluent caecum.
35.36.5. Tuberculous ulcers, small intestine, thinning of wall.
35.36.6. Tuberculous ulcers, small intestines and great thinning of wall.
35.36.7. Tuberculous ulcers, ileo-caecal valve.
35.36.8. Tuberculous ulcers, large intestine.
35.36.9. Tuberculous ulcers, small intestine, thinning of wall.
35.36.10. Tuberculous ulcers, large intestine.
35.36.11. Tuberculous intestines and caseating mesenteric glands.
35.36.12. Tuberculous ulcer with enlarged mesenteric glands.

.4 *Infections and Parasites.*

35.46.1. Amoebiasis, colon, small multiple ulcers.
35.46.2. Amoebiasis, colon, confluent and discreet ulcers with undermined edges.
35.46.3. Amoebiasis, colon, multiple ulcers with undermined edges.
35.46.4. Amoebiasis, large intestine, hypertrophied walls.
35.46.5. Amoebiasis, colon.

.6 *Retrogressive Changes.*

35.64.1. Appendix with stercolith.
35.65.1. Perforated duodenal ulcer.

.7 *Progressive Changes.*

35.73.1. Multiple lipomata.
35.74.1. Submucous polyp.

35.78.1. Lymphosarcoma.

35.79.1. Carcinoma rectum, infiltrative growth.
35.79.2. Carcinoma rectum, ulcerating annular growth.

.8. *Traumata* (from Mechanical, Chemical or Physical Causes).

35.84.1. Intussusception.
35.84.2. Volvulus.

36. PERITONEUM AND MESENTERY.

.3 *Inflammatory Processes.*

36.36.1. Tuberculosis omentum.

.7 *Progressive Changes.*

36.73.1. Retroperitoneal myxo-lipoma.
36.78.1. Retroperitoneal fibro-sarcoma.

37. LIVER.

.2 *Circulatory Disturbances.*

37.22.1. Chronic venous congestion, nutmeg liver.
37.22.2. Chronic venous congestion, nutmeg liver.
37.22.3. Chronic venous congestion, extensive fatty change.
37.22.4. Chronic venoue congestion, extensive fatty change.

.3 *Inflammatory Processes.*

37.33.1. Amoebic abscess liver, large abscess right lobe.
37.33.2. Amoebic abscess liver, communicating abscess right base of lung.
37.33.3. Amoebic abscess liver, communicating abscess right base of lung.
37.33.4. Amoebic abscess liver, necrotic areas right lobe.
37.33.5. Amoebic abscess liver, multiple necrotic foci and medium large cavity.

37.35.1. Plague. Necrotic stippling of surface.
37.36.1. Tuberculosis. Multiple tubercles on surface.
37.36.2. Tuberculosis. Multiple tubercles on surface.

37.37.1. Syphilis. Gumma.
37.37.2. Syphilis. Gumma.
37.37.3. Syphilis. Globular circumscribed gumma.
37.37.4. Syphilis. Gumma, irregular in outline.
37.37.5. Syphilis. Small gumma.
37.37.6. Syphilis. Diffuse gummatous infiltration.
37.37.7. Syphilis. Gumma.
37.37.8. Syphilis. Monocellular cirrhosis.

37.39.1. Multilobular cirrhosis.
37.39.2. Multilobular cirrhosis.
37.39.3. Atrophic multilobular cirrhosis, hobnail liver.
37.39.4. Multilobular cirrhosis.
37.39.5. Obstructive biliary cirrhosis.
37.39.6. Obstructive biliary cirrhosis.
37.39.7. Biliary cirrhosis.
37.39.8. Biliary cirrhosis.
37.39.9. Multilobular cirrhosis. Case of Banti's disease. (See 43.51.2)

.4 *Infections and Parasites.*

37.44.1. Actinomycosis. Honeycombed parenchyma.
37.47.1. Clonorchis sinensis in bile ducts.
37.47.2. Clonorchis sinensis in bile ducts.
37.48.1. Ascaris lumbricoides.
37.48.2. Ascaris lumbricoides.

.6 *Retrogressive Changes.*

37.62.1. Fatty degeneration.
37.62.2. Cystic formation (Cat).
37.64.1. Intrahepatic stone formation.
37.64.2. Intrahepatic stone formation.

.7 *Progressive Changes.*

37.76.1. Cavernous haemangioma.
37.76.2. Cavernous hàemangioma.

37·78.1. Spindle-celled sarcoma.
37·78.2. Sarcoma.
37·78.3. Melanotic sarcoma, secondary deposits.
37·78.4. Melanotic sarcoma, secondary deposits.

37·79.1. Primary carcinoma, hepatoma.
37·79.2. Primary carcinoma, hepatoma.
37·79.3. Primary carcinoma, hepatoma.
37·79.4. Primary carcinoma, hepatoma.
37·79.5. Primary carcinoma, hepatoma.
37·79.6. Primary carcinoma, hepatoma.
37·79.7. Carcinoma, secondary deposits, primary naso-pharynx.
37·79.8. Primary carcinoma, hepatoma.
37·79.9. Carcinoma.
37·79.10. Primary carcinoma, hepatoma.
37·79.11. Primary carcinoma.

38. GALL BLADDER AND BILE DUCTS.

.3 Inflammatory Processes.

38.31.1. Chronic cholangitis.
38.31.2. Hydrops of Gall Bladder.
38.31.3. Large distended gall bladder with calculus.
38.31.4. Chronic Cholecystitis.
38.31.5. Thickened, fibrotic gall-bladder with calculus.
38.31.6. Chronic cholecystitis.

.6 Retrogressing Changes.

38.64.1. Thickened gall bladder with calculi.

4. HAEMOPOIETIC AND DUCTLESS GLANDS.

41. BONE MARROW.

41.51.1. Erythroblastic reaction.

42. LYMPH NODES.

.3 *Inflammatory Processes.*

42.36.1. Tuberculous mesenteric glands.
42.36.2. Tuberculous mesenteric glands.
42.36.3. Tuberculous mesenteric glands with intestines.
42.36.4. Tuberculous mesenteric glands with intestines.
42.36.5. Tuberculous mesenteric glands.

.5 *Disorders of Metabolism and intoxication.*

42.51.1. Lymphatic glands, Hodgkin's disease.

.7 *Progressive Changes.*

42.73.1. Lymphoma.
42.78.1. Lymphosarcoma, glands and intestines.

42.79.1. Carcinoma, secondary to nasopharyngeal growth.
42.79.2. Carcinoma, secondary to nasopharyngeal growth.

43. SPLEEN.

.2 *Circulatory Disturbances.*

43.26.1. Red infarct.
43.26.2. White infarct.
43.26.3. White infarct.
43.26.4. Red infarct and acute congestion.

.3 *Inflammatory Processes.*

43.36.1. Tuberculosis, miliary tubercles.
43.36.2. Tuberculosis, miliary caseating tubercles.
43.36.3. Tuberculosis, miliary caseating tubercles.
43.36.4. Tuberculosis, small tubercles.
43.36.5. Tuberculosis, small miliary tubercles.
43.36.6. Tuberculosis, large caseous masses and infarct.
43.36.7. Tuberculosis, miliary tubercles.

.4 Infections and Parasites.

43.46.1. Malaria.

.5 Disorders of Metabolism and Intoxications.

43.51.1. Banti's disease and cirrhotic liver.
43.51.2. Banti's disease and cirrhotic liver. (See 37.39.9)
43.51.3. Myeloid leukaemia.
43.51.4. Banti's disease with marked peri-splenitis.

.7 Progressive Changes.

43.78.1. Spindle celled sarcoma, secondary.

45. THYROID.

.5 Disorders of Metabolism and Intoxications.

45.52.1. Exophthalmic goitre.

.7 Progressive Changes.

45.72.1. Simple goitre.
45.72.2. Simple goitre.
45.75.1. Adenoma.
45.79.1. Adeno-carcinoma.
45.79.2. Adeno-carcinoma.

47. ADRENAL.

.2 Circulatory Disturbances.

47.22.1. Congestion of medulla.

5. UROGENITAL SYSTEM.

51. KIDNEYS.

.1 *Antenatal Structures and Abnormalities of Development.*

51.12.1. Congenital atrophied kidney, hypertrophied other kidney.
51.12.2. Congenital polycystic kidney.
51.12.3. Congenital polycystic kidney.
51.12.4. Horseshoe kidney.
51.12.5. Horseshoe kidney with dendritic calculus.
51.15.1. Cyst of Gaertner's duct.

.2 *Circulatory Disturbances.*

51.22.1. Chronic venous congestion.
51.22.2. Chronic venous congestion.

51.26.1. Haemorrhagic infarct.
51.26.2. Haemorrhagic infarct.
51.26.3. Haemorrhagic infarct.

.3 *Inflammatory Processes.*

51.31.1. Acute glomerulo nephritis.
51.31.2. Acute glomerulo nephritis.

51.32.1. Diffuse suppurative nephritis, pyaemia.
51.32.2. Diffuse suppurative nephritis, pyaemia.
51.32.3. Diffuse suppurative nephritis, pyaemia.

51.36.1. Tuberculosis, multiple ragged cavities.
51.36.2. Tuberculosis, caseating miliary tubercles, destruction of pelvis.
51.36.3. Tuberculosis, cavitation and extensive caseation.
51.36.4. Tuberculosis, enlarged kidney and caseation.
51.36.5. Tuberculosis, large caseating cavities.

51.37.1. Syphilis, gumma.
51.39.1. Chronic parenchymatous nephritis.

.5 Disorders of Metabolism and Intoxications.

51.55.1. Granular kidney, one atrophied with cyst.
51.55.2. Arteriosclerotic kidney.
51.55.3. Early chronic interstitial nephritis.
51.55.4. Arteriosclerotic kidney.
51.55.5. Arteriosclerotic kidney.
51.55.6. Arteriosclerotic kidney.
51.55.7. Granular kidney, one atrophied, other hypertrophied.

.6 Retrogressive Changes.

51.64.1. Nephrolithiasis with hypernephroma.
51.64.2. Calculus in calyx and pelvis.
51.64.3. Multiple calculi in calyces.
51.64.4. Large dentritic calculus in pelvis.
51.64.5. Calculus in pelvis and pyonephrosis.
51.64.6. Calculi in calyx.

51.67.1. Calculus blocking ureter, hydronephrosis.
51.67.2. Calculus in ureter, dilated with hydronephosis.
51.67.3. Calculus in ureter—dilatation of pelvis.

.7 Progressive Changes.

51.78.1. Sarcoma.
51.78.2. Sarcoma.

51.79.1. Hypernephroma with calculus.
51.79.2. Hypernephroma.
51.79.3. Embryonal carcinoma.
51.79.4. Embryonal carcinoma.
51.79.5. Neuroblastoma.
51.79.6. Hypernephroma.
51.79.7. Hypernephroma.

53. BLADDER.

.3 Inflammatory Processes.

53.36.1. Tuberculosis.

54—9 MALE GENITALIA.

.3 Inflammatory Processes.

58.37.1. Gumma of testis.

.7 Progressive Changes.

54.72.1. Enlarged prostate—hypertrophy.
56.79.1. Epithelioma of penis.
56.79.2. Epithelioma of penis, cauliflower growth.
56.79.3. Epitheliomatous ulcer of penis.
56.79.4. Epithelioma of penis, large warty growth.
56.79.5. Epithelioma of penis, large friable growth.

58.79.1. Testis, large solid globular tumour, carcinoma.
58.79.2. Testis, embryonal carcinoma (seminoma).

.0 Teratology.

58.0.1. Testis, teratoma.

.8 Traumata (from Mechanical, Chemical or Physical Causes).

58.84.1. Inguinal scrotal hernia.

6. FEMALE GENITALIA.

61. EXTERNAL GENITALIA.

61.72.1. Clitoris—hypertrophy.

63. UTERUS.

.7 Progressive Changes.

63.73.1. Multiple interstitial fibroids.

63.73.2. Multiple interstitial and sub-serous fibroids.
63.73.3. Sub-mucous fibro-myoma.
63.73.4. Single fibroid undergoing degeneration.
63.73.5. Large multiple fibroid.
63.73.6. Intramural fibro-myoma.
63.73.7. Single sub-mucous polyp.
63.73.8. Large single hard fibroid.

63.79.1. Adeno-carcinoma, body of uterus.
63.79.2. Adeno-carcinoma, body of uterus.
63.79.3. Chorion epithelioma.

64. FALLOPIAN TUBES.

.1 Antenatal Structures and Abnormalities of Development.

64.18.1. Extra-uterine pregnancy.
64.18.2. Extra-uterine pregnancy.

65. OVARY AND PAROVARIUM.

.7 Progressive Changes.

65.74.1. Papilliferous cyst adenoma.

65.77.1. Large, thick-walled unilocular cyst.
65.77.2. Corpus luteum.

65.78.1. Sarcoma of ovary.

65.79.1. Malignant adenoma.
65.79.2. Solid carcinoma.
65.79.3. Malignant papilliferous cyst adenoma.
65.79.4. Adeno-carcinoma of ovary.

.0 Teratology.

65.0.1. Teratoma of ovary. (Dermoid).
65.0.2. Teratoma of ovary. (Dermoid).

67. BREAST.

.7 Progressive Changes.

67.73.1. Lipoma.

67.74.1. Fibro-adenoma.
67.74.2. Fibro-adenoma.
67.74.3. Fibro-adenoma.
67.74.4. Fibro-adenoma.

67.78.1. Mixed-celled sarcoma.
67.78.2. Sarcoma.
67.78.3. Mixed-celled sarcoma.
67.78.4. Mixed-celled sarcoma.
67.78.5. Sarcoma.

67.79.1. Speroidal-celled carcinoma.
67.79.2. Adeno-carcinoma.
67.79.3. Encephaloid carcinoma.
67.79.4. Adeno-carcinoma.
67.79.5. Carcinoma simplex.
67.79.6. Encephaloid carcinoma.
67.79.7. Carcinoma.
67.79.8. Duct carcinoma.
67.79.9. Carcinoma.
65.79.11. Fungating carcinoma.
65.79.12. Fungating carcinoma.
65.79.13. Carcinoma, chronic mastitis.
65.79.14. Paget's disease.
65.79.15. Encephaloid carcinoma.
65.79.16. Adeno-carcinoma.
65.79.17. Encephaloid carcinoma.

68. GENERATIVE SYSTEM IN PREGNANCY.

.1 Antenatal Structures and Abnormalities of Development.

68.11.1. Foetus at 2 months in amniotic sac.
68.11.2. Foetus at 4 months with placenta.
68.11.3. Foetus at 4 months.
68.11.4. Foetus at 6 months.
68.11.5. Foetus at 7 months with placenta and membranes.
68.11.6. Foetus at 3 months.
68.12.1. Monster at 5 months.
68.17.1. Dichotomous twins fused at thorax.
68.17.2. Twins, fused heads, single face.

.8 Traumata (from Mechanical, Chemical and Physical Causes).

68.84.1. Foetus with herniated liver.

7. NERVOUS SYSTEM.

71. MEMBRANES.

.12 Malformations of Incomplete Development.

71.12.1. Meningocele.
71.12.2. Meningocele.

.3 Inflammatory Processes.

71.34.1. Acute meningitis, purulent exudate on cortex, pneumococcal.
71.34.2. Acute meningitis, meningococcal.
71.35.1. Meningitis, due to Friedlander's bacillus.
71.36.1. Tuberculous meningitis.
71.36.2. Tuberculous meningitis.
71.36.3. Dura mater, tuberculosis.

.7 Progressive Changes.

71.76.1. Meningioma of the psammomatous type.

73. CEREBRUM.

.5 Disorders of Metabolism and Intoxications.

73.55.1. Haemorrhage in left ventricle.
73.55.2. Haemorrhage in ventricle.
73.55.3. Extensive haemorrhage in ventricle.
73.55.4. Large blood cyst.

.6 Retrogressive Changes.

73.61.1. Atrophy of hemispheres.

.8 Traumata (from Mechanical, Chemical or Physical Causes).

73.81.1. Sub-dural haemorrhage and laceration, contrecoup.

.7 Progeessive Changes.

73.73.1. Astrocytoma.
73.73.2. Astrocytoma.

74. CEREBELLUM.

.3 Inflammatory Processes.

74.36.1. Tuberculoma.
74.36.2. Tuberculoma.

.7 Progressive Changes.

74.73.1. Astrocytoma.

76. NERVES.

.7 Progressive Changes.

76.73.1. Neurofibroma.

78. EYE.

.7 Progressive Changes.

78.73.1. Glioma.

.8 Traumata (from Mechanical, Chemical or Physical Causes).

78.83.1. Detachment of retina.

8. MUSCULO-CUTANEOUS SYSTEM.

81. SKIN.

.12 Malformations of Incomplete Development.

81.12.1 Imperforate anus.

.3 Inflammatory Processes.

81.36.1. Tuberculous dactylitis.
81.36.2. Granuloma of hand.

.4 Infections and Parasites.

81.44.1. Mycetoma of foot.
81.44.2. Mycetoma of foot.
81.44.3. Mycetoma of foot.

.6 Retrogressive Changes.

81.65.1. Gangrene of leg.
81.65.2. Skin, chronic ulcer.

.7 Progressive Changes.

81.73.1. Soft fibroma with degenerative changes, of inguinal scrotal region.
81.73.2. Fibroma.
81.74.1. Papilloma.
81.78.1. Malignant melanoma, dorsum of foot.
81.78.2. Osteosarcoma, dorsum of hand.

.7 Progressive Changes.

81.79.1. Epithelioma of hand.
81.79.2. Epithelioma of abdominal wall.

84. MUSCLE.

.3 Inflammatory Processes.

84.36.1. Tuberculosis of diaphragm.

85. FASCIA.

.7 Progressive Changes.

85.73.1. Lipoma.
85.73.2. Lipoma.
85.73.3. Lipoma of arm.

85.78.1. Myxo-sarcoma.

9. OSSEOUS AND ARTICULAR SYSTEM.

91. BONES OF CRANIUM.

.3 Inflammatory Processes.

91.37.1. Gumma.
91.37.2. Gummatous periostitis and caries of frontal bone.
91.37.3. Syphilitic caries of skull.

.8 Traumata (from Mechanical, Chemical or Physical Causes).

91.82.1. Extensive fracture vault of skull.

92. BONES OF FACE.

.4 Infections and Parasites.

92.44.1. Actinomycosis, jaw of ox.

.7 Progressive Changes.

92.78.1. Myxo-fibro-sarcoma of jaw.

93. VERTEBRAE.

.3 Inflammatory Processes.

93.36.1. Tuberculous spinal caries with pronounced deformity.

95. RIBS.

.7 Progressive Changes.

95.79.1. Secondary adeno-carcinoma.

96. BONES OF UPPER EXTREMITY.

.6 Retrogressive Changes.

96.65.1. Necrosis and calcification of finger.

.7 Progressive Changes.

96.78.1. Sarcoma of scapula.
96.78.2. Periosteal sarcoma of humerus.
96.78.3. Periosteal sarcoma of humerus.
96.78.4. Myeloma of radius.
96.78.5. Large round-celled sarcoma of metacarpals.

96.79.1. Epithelioma of hand.

97. PELVIC GIRDLE.

.6 Retrogressive Changes.

97.62.1. Ankylosis of hip-joint.

98. BONES OF LOWER EXTREMITY.

.3 Inflammatory Processes.

98.33.1. Septic osteomyelitis of femur.

.6 Retrogressive Changes.

98.62.1. Tibia and fibula—osteoporosis.

.7 Progressive Changes .

98.78.1. Myeloma of lower end of femur.

.8 Traumata (from Mechanical, Chemical or Physical Causes).

98.82.1. Tibia, healed fracture.
98.82.2. Femur, showing fracture and callus formation.

.0 REGIONAL.

.01 HEAD.

.1 Antenatal Structures and Abnormalities of Development.

01.12.1. Anencephalus.
01.12.2. Anencephalus.
01.16.1. Hydrocephalus.
01.16.2. Hydrocephalus.
01.18.1. Cyclops.
01.18.2. Cyclops.

05. THORAX.

.1 Antenatal Structures and Abnormalities of Development.

05.18.1. Heterotaxis.
05.18.2. Heterotaxis.
05.18.3. Transposition of viscera.

09. UPPER EXTREMITY.

.1 Antenatal Structures and Abnormalities of Development.

08.14.1. Syndactylism.

HUMAN GENETICS AND ITS RELATION TO MEDICAL PROBLEMS.

(Continued)

by

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CHAPTER IV.

GENETICAL RATIOS REVEALED BY THE LAWS OF MORGAN.

Linkage.

Mendel's second law introduced us to the idea of free and independent assortment of factors, and with our chromosomal knowledge we can now talk of free assortment of genes. But the genes themselves are carried on the chromosomes, and as we have seen these latter are so constant in shape, size and number in the cells of each species, it is reasonable to suppose that this constancy goes even further so that allelmorphs always occupy the same loci on homologous chromosomes. This is no longer an hypothesis but an established fact as we shall show later. But if the same chromosome is always made up of the same gene loci, then that chromosome must always hand on this number of genes *as a group* to the zygote. For example, if we have two factors B & P present at loci on one chromosome, and their recessive allelomorphs *b* & *p* present at corresponding loci in the other member of the chromosome pair, then on gamete formation, one germ cell will receive the chromosome carrying *B* & *P* while the other germ cell will receive the other carrying *b* & *p*. *B* & *P* will always be handed on together, and so will *b* & *p*. It will not be possible to get a germ cell with both *B* & *p*, nor one with both *b* & *P* unless the chromosomes had broken and joined up again, so that the corresponding pieces of the chromosomes had changed places. This constant grouping of certain factors together was noted by Bateson and is known as *LINKAGE*, but as it was first scientifically explained by Morgan, it is often referred to as Morgan's first law. It naturally follows on from the application of the chromosome theory of heredity to Mendel's second law of free assortment, not disproving the latter, but modifying it and limiting its application. Mendel's second law we now understand to apply only to factors whose genes are carried on different chromosomes (or, as we shall see later, to genes which are situated far apart on the same chromosome). If two factors are carried on two different chromosomes, they will behave absolutely independently; if they are on the same chromosome they will be linked in a group which will contain all the factors on that chromosome. We should therefore have as many groups of factors as we have chromosome pairs, or, as some chromosomes may conceivably carry factors which do not

cause visible characters, it would be better stated that the number of factor groups should never exceed the number of pairs of chromosomes, and this has so far always proved to be the case. *Drosophila melanogaster* has four pairs, and all the factors thus far examined fall into one of four groups, each member of each group exhibiting linkage with the other factors of its group. We can thus make a sort of chromosome ledger, entering in each page all the factors that occur together on the same chromosome, and if we should discover a method of distinguishing which chromosome carried which group, we would have made the first step towards mapping the chromosomes. In the fruit fly all this has been done by Morgan and his school, an immense work which has more than justified the faith placed in the veracity of the laws on which it was founded.

Let us see how the law of linkage affects the ratios in the various experimental generations. Two characters that have appeared in races of fruit flies are black bodies and vestigial wings. These characters are both recessive to those exhibited by the normal or wild type, and therefore the pairs of factors may be represented by *B* & *b*, *V* & *v*, a fly with black body colour and vestigial wings being recessive for both pairs of factors, and having the genetical formula *bbvv*. A wild type fly homozygous for both pairs would be genotype *BBVV*. The gametes formed by these two types would be *bv* in the former case and *BV* in the latter, and hence we can understand the F_1's are all wild type, *bBvV*. Now let us backcross an F_1 female to a vestigial black body male. The latter as we have seen produces only *bv* gametes, but if the genes are on different chromosomes the former can produce *bv*, *bV*, *Bv* & *BV*, and therefore the results of this backcross will be *bbvv* (black body with vestigial wings), *bbvV* (black body with normal wings), *bBvv* (normal body with vestigial wings) and *bBvV* (normal body with normal wings), all four phenotypes being produced in equal proportions.

This result is not what one gets experimentally: the second and third phenotypes in the above diagram do not appear. (For modification of this statement see p. 137. We only get from the backcross the combination of characters that went into the parental cross viz., black body with vestigial wings, and normal body and wings, both in equal proportions. Morgan explained this by linkage. If the characters are on the same chromosome they do not comply with the law of independent assortment, for on gamete formation the genes on the same chromosome must go to the same germ cell, and therefore the only possible F_1 gametes are *bv* & *BV* and these when combined with *bv* give *bbvv* (black body and vestigial wings) and *bBvV* (normal body and wings) in equal proportions. To represent this diagramatically, the second part of Figure 8 would therefore have to be changed as shown in Figure 9.

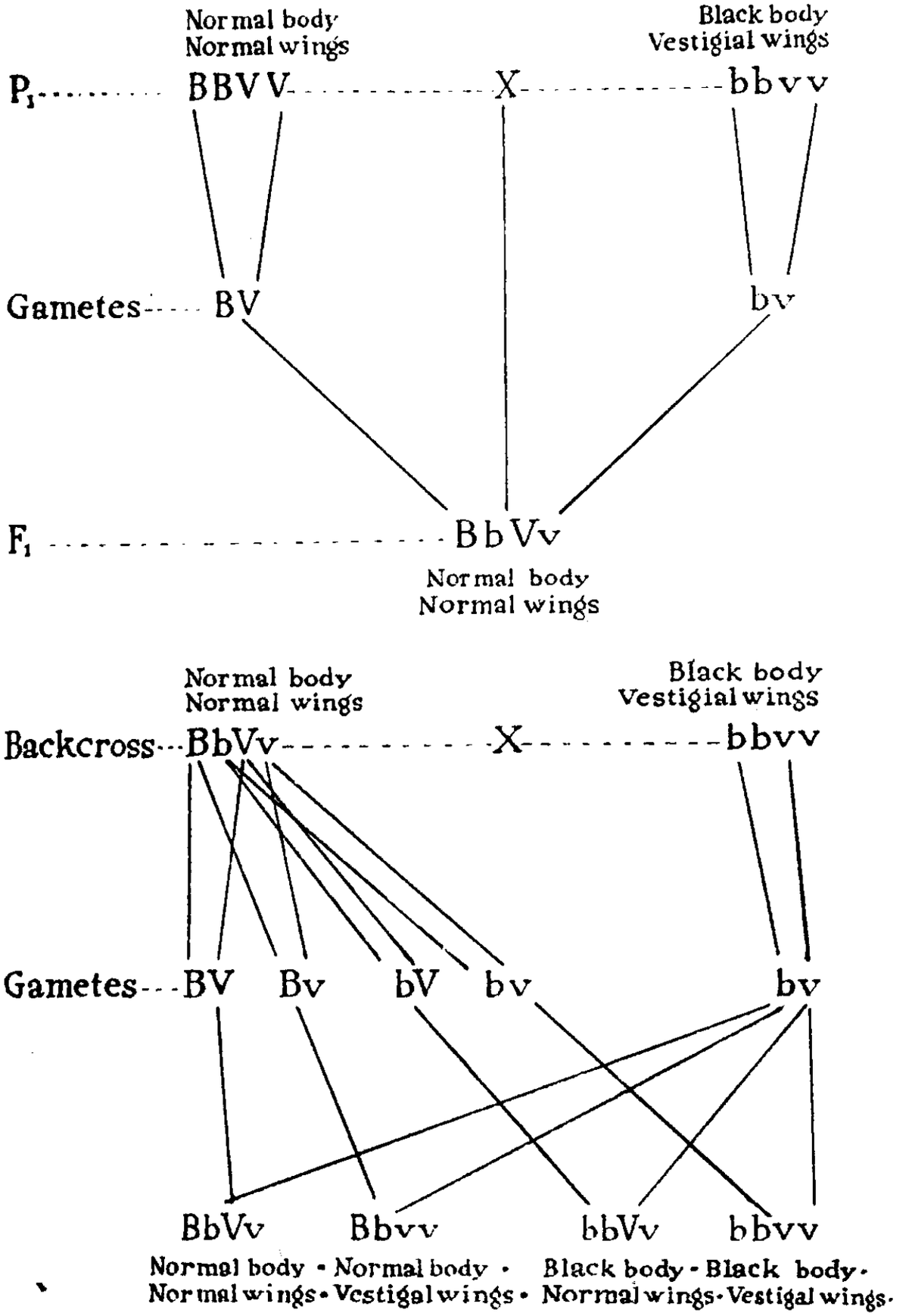


Figure 8.—A diagram, the upper part of which shows the result of crossing fruit flies homozygous for normal body and normal wings with those homozygous for black body and vestigial wings. In the lower half is shown the result of back crossing an F_1 female with the vestigial male parent, if the allemorphic pairs are carried on separate chromosomes. The result would be equal proportions of the four phenotypes as shown in the last line.

It might be argued that the same result would be obtained by considering only one pair of factors to be involved, e.g., *P* & *p* which factors in the homozygous recessive condition *pp* cause the appearance of two characters (1) black body and (2) vestigial wings. This is quite true. The result would be the same, but other experiments have proved that there *are* two pairs of factors involved, the pairs being independent except for the fact that their genes are on the same chromosome.

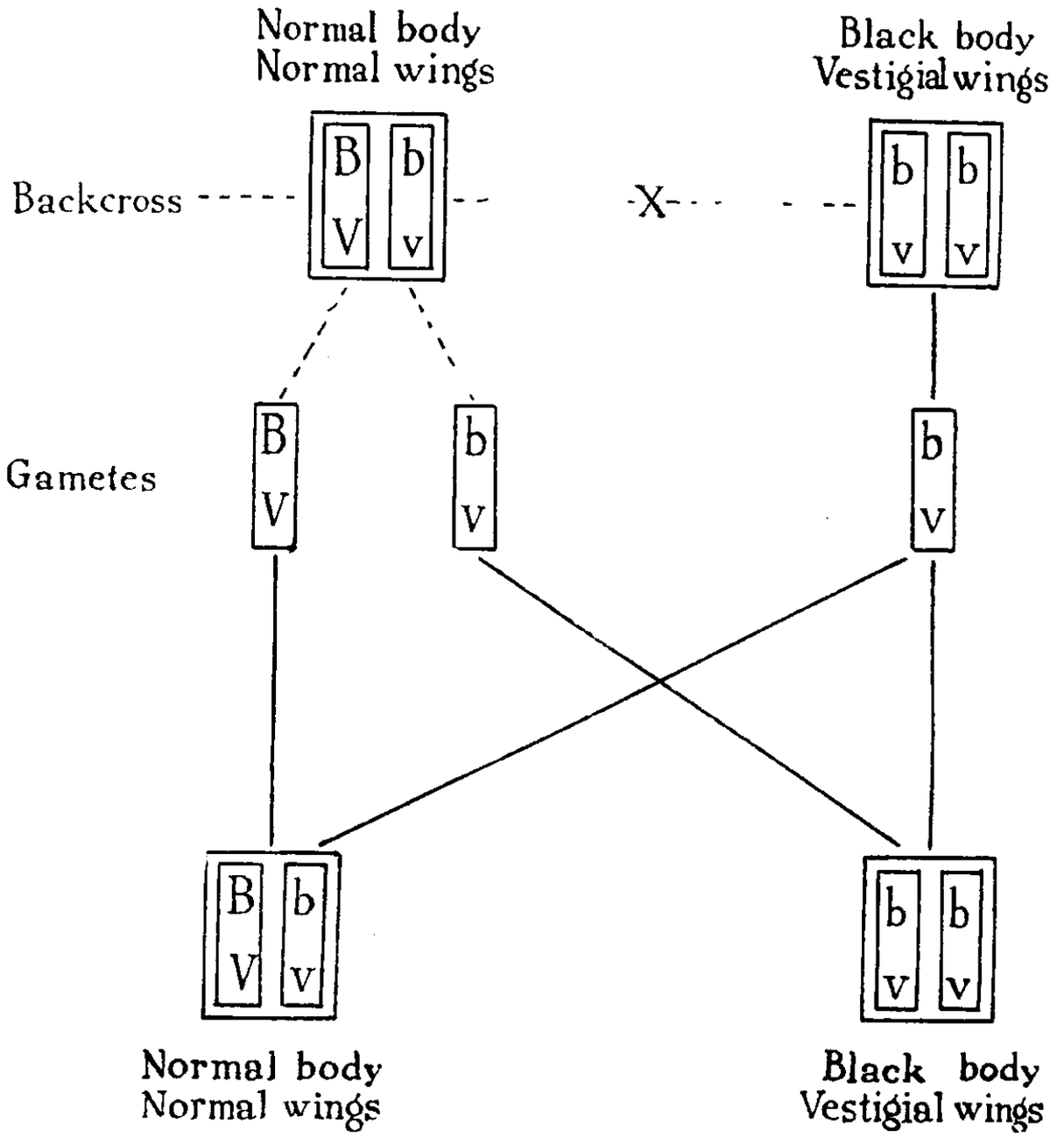


Figure 9.—In this diagram the lower half of Figure 8 is modified showing how only two phenotypes result from the back crossing if the two pairs of factors are considered as being completely linked on the same chromosome pairs.

Linkage is fairly common in the *Drosophila* because there are only four pairs of chromosomes; in the human there are 24 pairs, and thus far we have been able to demonstrate only one type of linkage there which we shall now discuss.

Sex Linkage.

Above we stated that being able to recognise different chromosome pairs would help us in mapping them, i.e., in allocating certain genes to definite positions on certain chromosomes. The first step in this direction was the recognition of the pair known as the sex chromosomes. We have said that each pair is made up of identical chromosomes; this is true in every species of all the chromosome pairs excepting one pair in each case; in this pair a difference *may* be noticed, depending on the sex of the cell, and since, as we shall see, they have something to do with the determination of sex, they are known as the *sex chromosomes* in contra-distinction to the others which are known collectively as *autosomes*. In the female *Drosophila* the two sex chromosomes are indistinguishable form one another, and each is called an *X-chromosome*, and to signify this state of affairs the female sex-chromosome formula is often briefly written *XX*. In the male however, one chromosome is indistinguishable from those seen to be present in the female, and therefore designated *X*, but the other differs both in function and shape. As far as we can ascertain it carries no genetical factors, and in view of its shape as sometimes seen under the microscope it is called a *Y-chromosome*. The male sex-chromosome formula is therefore *XY*. On gamete formation the female produces eggs containing only *X*-chromosomes, but the male produces sperm 50% of which contain an *X*-chromosome, and 50% a *Y*-chromosome. The sex of a zygote depends therefore on whether the egg is fertilised by an *X*-carrying sperm, in which case a female will result, or by a *Y*-carrying sperm in which case an *XY* or male zygote will result.

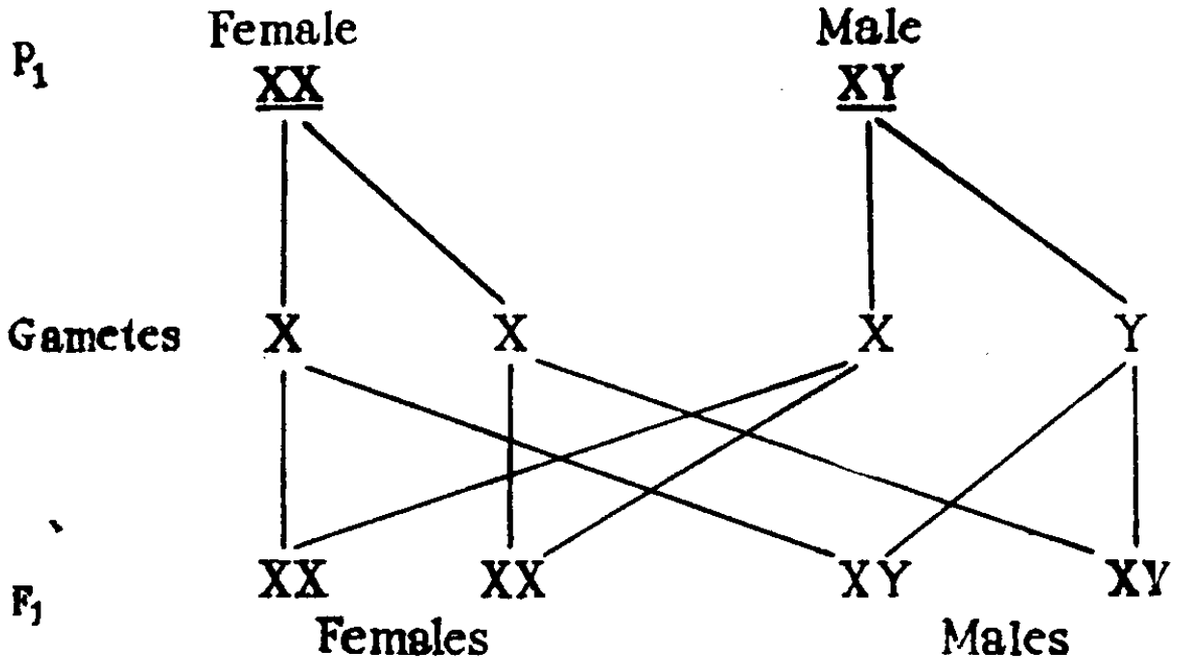
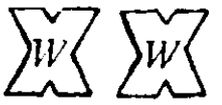
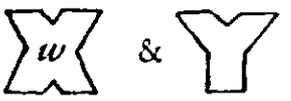
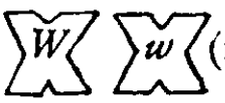
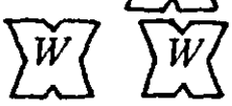
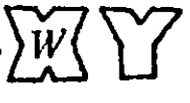


Figure 10.—A chart showing the gamete arrangement of the sex chromosomes, indicating the chromosomal theory of sex determination.

This is the genetical explanation of sex determination and although it explains the approximate equality of the sex ratio, it does not explain why the actual M/F ratio is not exactly equal to 1.

This *XX* and *XY* plan is not followed by all plants and animals. In some cases the male is *XX* and the female *XY*, and in yet others the sex chromosome pair is not a pair; it is only half a pair, *Y* being absent altogether. In such cases the formulae are *XX* & *XO*. For some time it was thought that this was the case with man, but the evidence of Painter seems to have established the existance of a small *Y*-chromosome in the male, and therefore the human sex formulae are the same as for *Drosophila*, female $=XX$ and male $=XY$.

If all this be true and if some of the sex chromosomes carry ordinary body characters as well, we should be able to demonstrate the linkage of the characters with sex. This has been done over and over again and two or three examples will suffice to make the mechanism clear. In *Drosophila* the normal eye colour is red and this character is dominant to the recessive white condition. The former character is caused by a factor represented by *w* and the latter is found in the homozygous *ww* condition or where the *w* factor is present in the absence of *W*. This pair of allelomorphic genes *W* & *w* is carried on the sex chromosomes. A homozygous red-eyed female is thus represented  and a white-eyed male thus  (Note the Y-chomosome carries no genes.) The gametes formed from the female are all  , and from the male, both  The F_1's are therefore 50%  (red-eyed females, phenotypically the same as their mother but genotypically heterozygous) and 50%  , (red-eyed males.) All the F_1's are thus red-eyed. The gametes formed from these are  &  from the females, and  &  from the males, hence the F_2 possibilities are  (red-eyed female, homozygous)  (red-eyed female, heterozygous),  (red-eyed male), and  (white-eyed male). The white-eyed condition went into the cross on the male side and came out again in the grandchildren in the male sex and not at all in the females.

It is this type of illustration (which is really only half the story) that has given rise to the confusion between the terms *sex-linked* and *sex-limited*. In the previous experiment it happened that the character came out of the cross in the same sex as it entered it, and not at all in the other sex. But that is not the essential feature of sex-linkage at all.

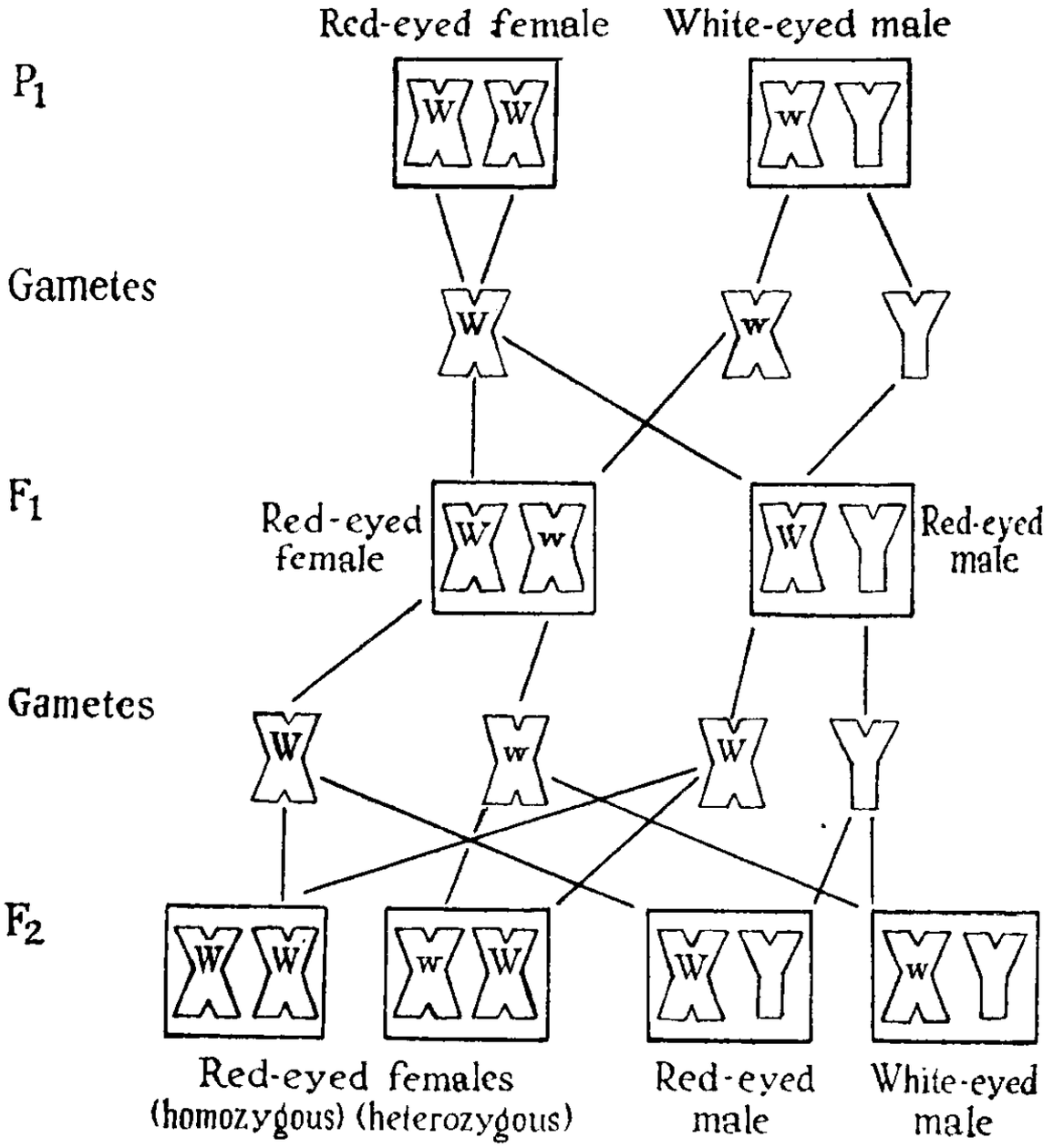


Figure 11.—A chart showing the behaviour of characters whose genes are situated on the sex chromosomes. Here the recessive condition of the F_1 male reappears in only half of the F_2 males and not at all in the females.

That a character is sex-linked does not mean it is linked with one or other of the sexes; it means that it is the expression of a factor whose gene is carried by the sex-chromosome pair. To illustrate this point, let us consider the crossing of a white-eyed female with a red-eyed male.

Here note the F_1's are of two phenotypes, red-eyed and white-eyed, all the males being white-eyed like their mothers and the females red-eyed like their fathers. In the F_2 the sexes no longer separate the phenotypes,

for half the males are white-eyed as are also half the females. The white-eyed character went into the cross on the female side, came out in the F_1 on the male side, and in the F_2 on both sides. Figure 12 shows clearly that though this factor is sex-linked it is not sex-limited.

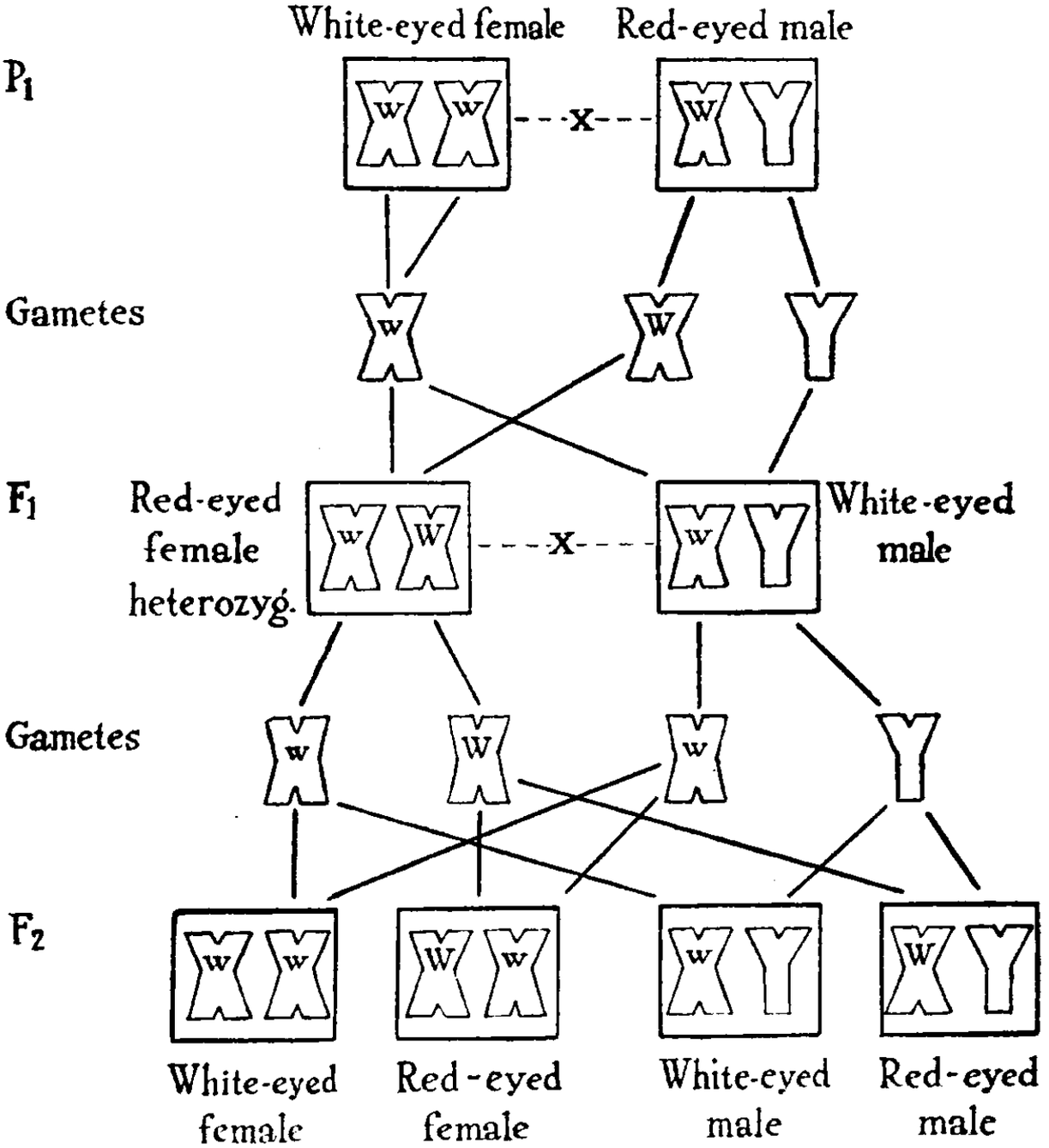


Figure 12.—Another chart showing the behaviour of sex-linked characters, the recessive condition appearing in both sexes of the F_2 generation.

Of the small number of human characters accurately investigated, some such as haemophilia, certain types of colour blindness etc., have proved to be the result of the homozygous recessive condition, the factors being carried on the sex-chromosomes. If the factor causing the normal dominant condition be represented by '*N*' and its allelomorph by '*n*', the result of a mating of a homozygous normal female with an affected male would be represented as in Figure 13.

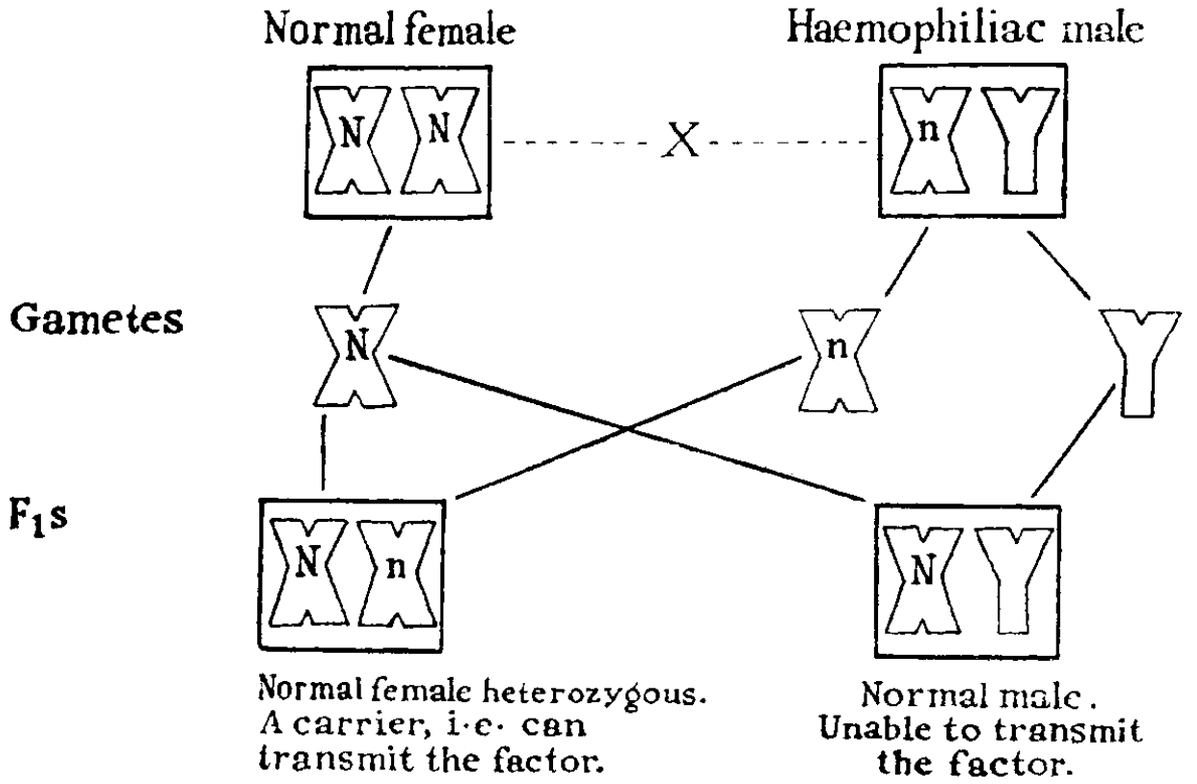


Figure 13.—A chart showing the F_1 resulting from crossing a normal female with a haemophiliac male.

In a mating such as this all the children will be phenotypically normal; they will not show the abnormal condition, but the females all carry one recessive gene which, if it be left unopposed in any later generation by its dominant allelomorph, will allow the abnormality to become evident. Such cases are depicted in Figure 14.

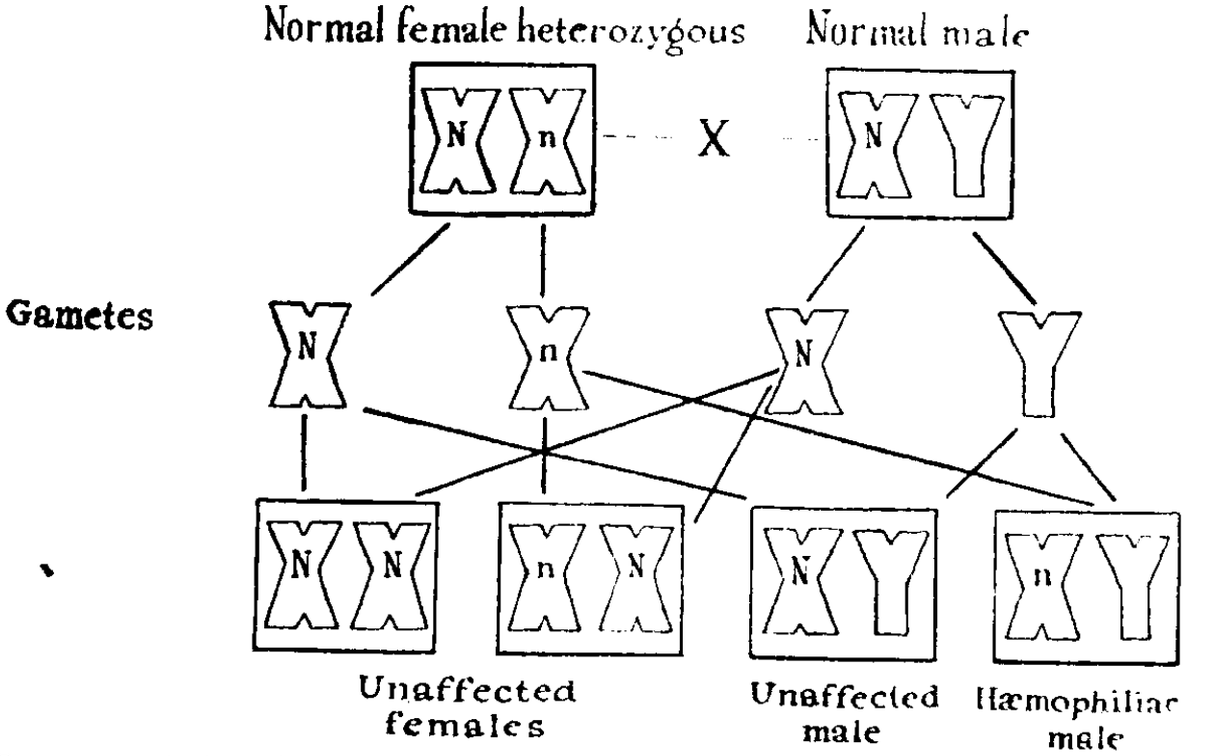


Figure 14.—A chart showing the result of mating a normal male with a normal F_1 female from Figure 13.

The result of mating a heterozygous female with an unaffected male is thus healthy females (half of whom are carriers of the recessive gene), and males, 50% of whom are haemophiliacs. The pathological condition of the grandfather has thus reappeared in half of the grandsons, the recessive factor passing by way of the female member of the intervening generation. It has skipped her generation, reappearing in her sons. Figure 14 represents the state of affairs which generally appertains in practice. But if a female carries one recessive factor she is unaware of the fact (for the phenotype of the homozygote and heterozygote are indistinguishable) until mating gives the opportunity for the unmasking of this recessive factor. If by any chance, or mis-chance, such a female married a haemophiliac, half the daughters as well as half the sons would be affected by the disease, as shown in Figure 15.

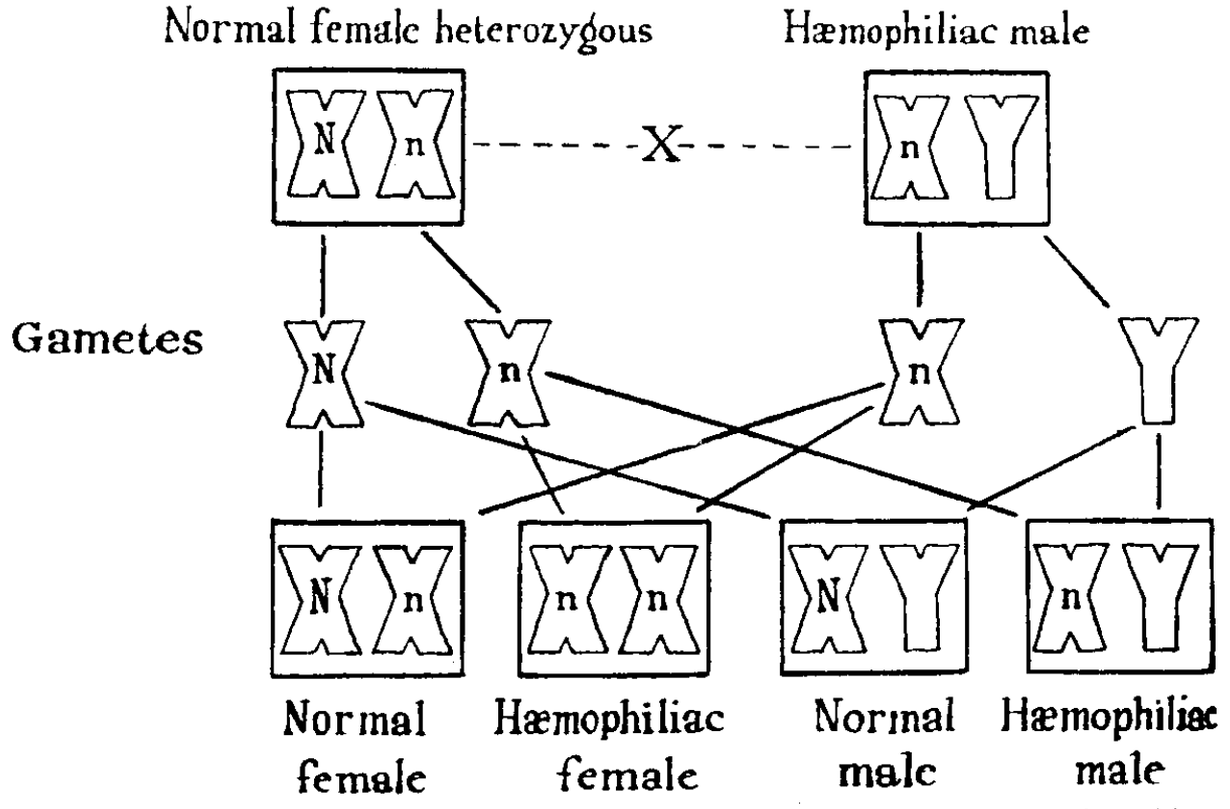


Figure 15.—A chart showing the result of mating a heterozygous female with a haemophiliac male.

Such a mating as depicted in Figure 15 is very rare in practice firstly because haemophiliacs are less likely to survive and mate successfully and secondly, the condition being so rare, the chance of a haemophiliac mating with a heterozygous female is very remote; and when one remembers that then only half the females of such a union would be homozygous for the factor, one realises why female haemophiliacs are so very rare indeed. Yet theoretically it can occur because the factors are sex-linked and not sex-limited.

Morgan's law of Linkage has explained not only a number of cases where the phenotype ratios deviated markedly from the original 3 : 1, but also a number of cases where the phenotype was in some way intimately involved with the sex mechanism.

Crossing over.

The next step is to consider the phenomenon of crossing over. Just as linkage shows that the law of independent assortment does not apply to all the genes in the cell, so the phenomenon of crossing over shows that the law of linkage does not apply exactly to all the genes on one chromosome. On page we stated that certain factors always come out of a cross together and we showed that if they were on the same chromosome, they must come out together *if the chromosome remained intact.* After placing all genetical characters of the *Drosophila* into one of four groups, Morgan found that members of each group did not always show this theoretically expected linkage. Some factors did always show it; others showed an absence of linkage almost as great as though their genes were situated on different chromosomes; yet again others showed linkage of intermediate values. But one thing in this variety of results was constant, and that was the amount of linkage shown by any two factors was always the same. This state of affairs can only be explained under the chromosomal theory by assuming the breaking of the chromosome. There is a certain amount of cytological evidence to support the view that such breaking does occur, and there is very definite evidence that during certain periods of cell development there are very favourable opportunities for it to occur. During the ripening of the germ cells, each chromosome is seen to approach its paired homologue, and lying side by side, they become united along their whole length until the individual chromosomes of each pair can no longer be recognised. Often they are entwined around each other, and then when the longitudinal split appears causing the separation and the reappearance of two chromosomes again, it may happen that the splitting may have resulted in the transference of a certain piece of one chromosome to its partner, its place being exactly filled by a similar piece from the other

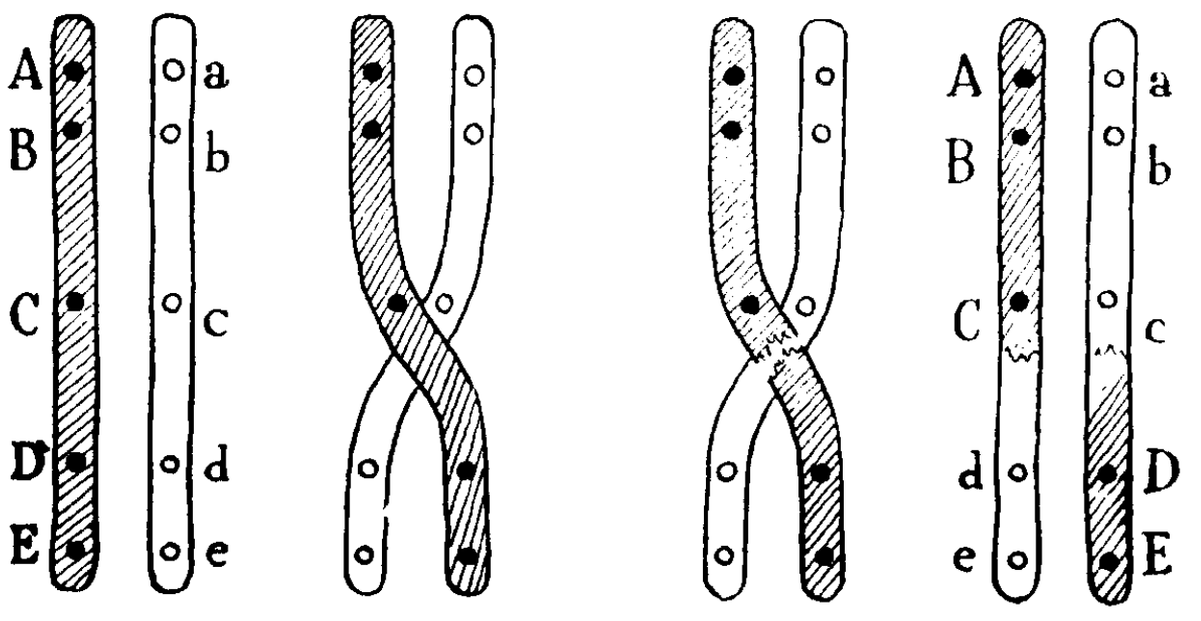


Figure 16. Showing the effect on gene positions in gametes of the phenomenon of crossing over.

chromosome. This mechanism of crossing over may be represented diagramatically as in Figure 16.

If the experimentally obtained constant amount of crossing over between two genes depends on this process, it involves the constancy of position of each gene on its chromosome or as Morgan has stated in his second law, the linear order of genes. By putting various genes on the chromosomes as in Figure 16, we can demonstrate how, if the same gene always occupies the same position in the same linear order on the same chromosome, the crossing over observed can be explained. We must notice that crossing over does not affect just one or two genes but a whole series in a group, leading one to suspect that large pieces of chromosome are involved in the crossing and not just small fragments. There is evidently a clear break in the chromosome, and if this break is just as likely to occur at one place as at another, and if the genes are always in a constant linear order, the further apart two genes lie the more is crossing over likely to occur between them. Similarly the closer two genes lie on the chromosome, the less will crossing over be expected to occur between them.

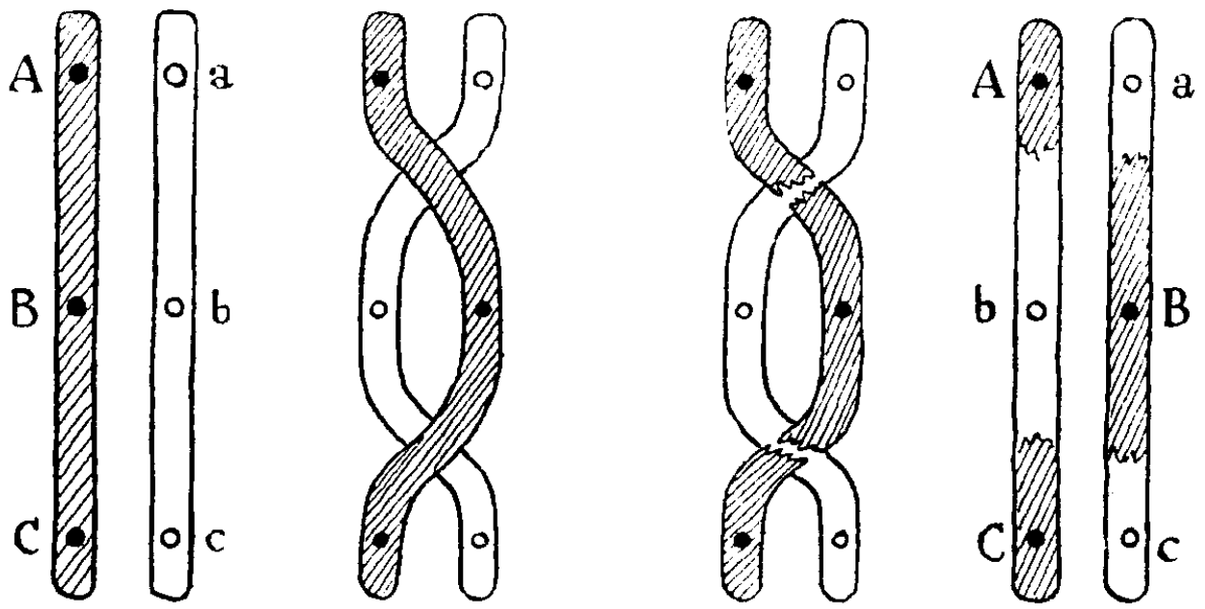


Figure 17.—Diagram showing how double crossing over between two genes 'a' and 'c' is not recognisable unless an intermediate gene 'b' is also taken into account.

This means that the distance apart of two genes on a chromosome is a function of the crossing over that occurs between them. If therefore we can measure this crossing over, we can establish the position of a gene on its chromosome *in relation to other genes and to the chromosome length*. This has been done by Morgan and his co-workers in America for the *Drosophila*, so that now all the known genes—some hundreds in all—can be placed on lines so as to represent accurately their true linear positions on their chromosomes. Such a chart of genes or chromosome map can be found in almost any genetical text book, and one of the outstanding tests and proofs of the theories of linkage, crossing

over and linear order of the genes is that, using *Drosophila*, modern geneticists can predict the result of any mating with an accuracy every bit as great as Mendel's when he used one pair of factors, or two pairs situated each on a different chromosome. It must be definitely under-

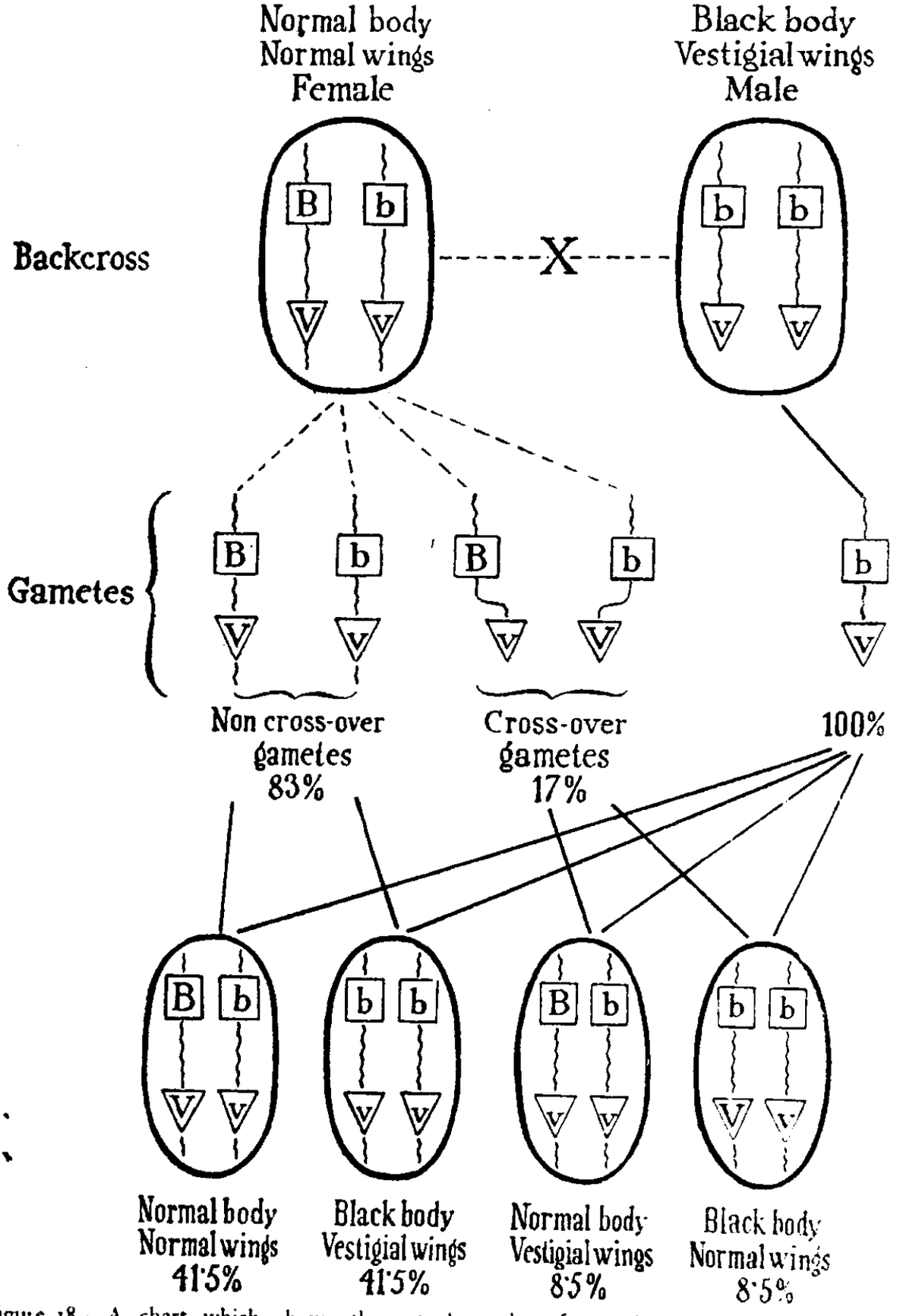
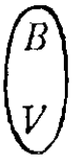


Figure 18.—A chart which shows the actual results of experiments whose theoretical results were diagramatically shown in Figures 8 & 9.

stood that by prediction one does not mean prediction in every single case; it means prediction of the *percentages* of different phenotypes that will occur in a large number of a generation resulting from the cross under consideration. This point is important and we shall have occasion to refer to it later in connection with human work.

We might here briefly discuss the method of measuring this much talked-of crossing over. If one refers to Figure 9, one sees that the back-cross results in only two phenotypes if the factors are completely linked. If the factors are completely independent we get two extra phenotypes as shown in Figure 8. They are black body with normal wings, and normal body with vestigial wings; and these extra two phenotypes will form 50% of all this generation, in other words they will be just as numerous as the phenotypes that occur when linkage is complete. If this experiment is actually performed we find that there occur *four* phenotypes as the result of back-crossing the F_1 female with the P_1 male. The result is *not*, as in Figure 8, 25% (black body with vestigial wings), 25% (normal body with normal wings) 25% (black body with normal wings) and 25% (normal body with vestigial wings), as it would be were the factors completely independent, nor is it 50% (black body with vestigial wings) and 50% (normal body with normal wings) without any black body with normal wings and normal body with vestigial wings at all, which we would expect were the foctors completely linked as shown in Figure 9. No, the result is in each case intermediate between these ratios namely, 41.5% (black body with vestigial wings) and 41.5% (normal body with normal wings), 8.5% (black body with normal wings) and 8.5% (normal body with vestigial wings). This is shown in Figure 18, which also shows how we can readily calculate the percentage frequency of crossing over in gamete formation by observing the percentage occurrence of the different phenotypes in the resulting generation.

Further experiments show that it is immaterial how the genes enter the crossing, for the frequency of crossing over is always the same; for example, in the case above a gamete with a $\binom{b}{v}$ chromosome united with a gamete containing a $\binom{B}{V}$ chromosome, gave the two cross-over chromosomes $\binom{b}{V}$ & $\binom{B}{v}$ in 17% of the zygotes formed. We would get exactly the same percentage of crossing over if the original

chromosomes were  &  giving, after crossing over,  &  chromosomes in 17% of cases.

This phenomenon is then a function of the locus and is independent of the genes situated on either side of the point of breaking. The only effect the presence of genes has is to make the crossing over visible, but it is generally believed that crossing takes place whether it can be thus observed or not. The number of cross-over individuals expressed as a percentage of the total number in the generation is known as the *cross over value*—in the above example it is 17%, and as the diagram shows, it simply represents the number of times, expressed as a percentage of the total number of individuals, in which the linkage is broken. If we have three genes, *p*, *q* and *r*, on the same chromosome and situated *close together*, and if we find the cross over value between *p* and *r* is say 6, and that between *q* and *r* is say 2, then we shall find the cross over value between *p* and *r*, to be 6 ± 2, i.e., 8 or 4. If it be 8 the linear order of the genes will be *pqr*, and if 4 it will be *prq*, and in each case they will be so spaced that the distance *pq* : the distance *qr* : : 6 : 2. If these genes are not close together, we should find the cross over value between *p* and *r* not equal to 6 ± 2 but a function of it. This is because when the genes are far apart, we get an increased possibility and happening of double crossing, and when this occurs it reduces the cross over value, for the double cases are counted among the non-cross overs.

From Figure 17, we see that double crossing between two genes far apart such as *a* & *c*, has the same effect as no crossing at all as far as the inter-relation between these two is concerned; and double crossing between two such genes is only recognisable by taking an intermediate gene such as *b* into account. As soon as we do this we see that there has been a cross between *a* & *b* and another between *b* & *c*, thus accounting for *a* & *c* still being together after the separation of the chromosomes. This double phenomenon is not of much interest to us here except that by its application we can explain many apparent anomalies, and thus add further corroborative evidence to the existing proof of the genetical laws.

There are three further points about crossing over which demand mention. (a) Its value in *Drosophila* is lowered by age and raised by deviation from average room temperature (Plough 29). This we shall refer to later on in discussing the effects of environment. (b) In the *Drosophila* it takes place only in the female, and in the case of the silk-worm moth, only in the male. In this latter case the sex formulae

are reversed, the male being *XX* so it may be that crossing over is a phenomenon shown only by the sex which is homozygous for the sex chromosomes. We are by no means near investigating this in man yet, but when we do, this work on lower forms should be of definite interest and importance, although we must remember that in the human the chromosomes are very short, and therefore there may be relatively little crossing over. But on the other hand this phenomenon may be much more complicated in man because the chromosomal shape and size may lead us from the linear order or genes to a spatial one, a possibility which if it does exist may account for the very complicated ratios found. (c) It has given us a method of investigating the phenomenon of interference, which, although of no great importance at the present undeveloped stage of human genetics, is of very great importance in the understanding of the ways in which crossing over values may be effected. It may be briefly described thus: we have seen that genes cross over in blocks and not singly and therefore a gene does not act completely independently of its neighbour, and precisely how independent one gene is of another will depend on the size of the block which crosses over. The very fact that crossing over has occurred between two genes D & E in a series such as ABCDEFGHIJKL makes it very improbable that another cross will occur simultaneously between E & F, makes it less improbable that another will occur simultaneously between F & G, less still between H & I until it has no effect at all on the probability of a simultaneous cross between K & L. This effect of a crossing over at one locus on another of the same chromosome is known as *interference*, and by it we can ascertain the modal length of chromosome enclosed between two breaks in a double crossover, and it is found that this modal length is different for each chromosome and even different for different parts of the same chromosome. Thus we see that linkage, linear order of the genes, crossing over, double crossing over and interference, progressive stages in the elucidation of the genetics of lower forms of life, will certainly be destined to play a much more important part in the investigation of the complicated and valuable study of human genetics.

CHAPTER V.

GENETICAL RATIOS IN HUMAN DATA.

In the preceding chapters we first of all showed how Mendel's elementary ratios were established and then proceeded to explain how the occurrence of different ratios, rather than nullifying Mendel's work, helps to establish it as the foundation of genetics more firmly than ever. We must now consider two other factors which make it difficult to fit human work in with experimental work; they are the small size of the human family and the impossibility of experimenting with various crosses as one is able to do with laboratory animals. The human problem has to be attacked from a different angle; instead of purposely

making the crossing, one has to be on the watch for examples of the cross already made, and in order to get sufficient data in this manner, much labour is needed extending over a period of many years. If the characters being studied are rare, it means that one person in his lifetime can hardly collect enough data, and hence data from many sources have often to be pooled, thus risking the introduction of varying personal errors in diagnosis and observation. To be always on the watch for examples of certain crosses is one thing, but to be able to recognise the type of cross seen is entirely a different matter, and unfortunately, often very difficult. In the experiments with the four o'clocks quoted above, one saw how easy it was to recognise the heterozygous plants because they were pink; thus recognising a cross between a recessive and a heterozygote in this instance was a very easy matter. With the tall and the short peas it was a little more difficult; the heterozygous and homozygous talls *appeared* the same; it was only when the off-spring of a cross between a tall and a short contained one short that the heterozygous condition of the tall parent was revealed; but to discover the type of tall in experimental work is very easy, one simply back-crosses it with the recessive short and notes whether any shorts appear in the offspring. In human work such experimental matings are impossible, and if one is dealing with a character which is phenotypically similar in both homozygous and heterozygous states, the only possible way of ascertaining whether the two partners of a mating are genotypically similar or not, is by means of the resulting progeny. For example if a certain abnormality be a recessive condition and the normal the dominant, then all heterozygotes will appear normal. When an abnormal child is born of two normal parents we know at once that both parents must be heterozygotes. But if no abnormal children are born we are none the wiser; their absence may be simply due to an uneven chance distribution. This is where the small size of the human families introduces such a great difficulty. The normal/abnormal ratio should be 3 : 1. If the family be of the Victorian size of 8-12, one would most probably get one recessive if possible i.e., if the parents in question were heterozygous, and one recessive in the family is all one needs to prove such heterozygosity; but where the family is limited to two or three, the chances that the one recessive will appear in these two or three are very much reduced. If one tosses a coin 100 times and notes each consecutive result, one will find that the heads and tails will number *about* 50 each, assuming the chances of each happening to be equal. The larger the number of tosses made, the more will the head/tail ratio approximate to 1; but if one takes blocks of 2 or 3 consecutive tosses from any part of the sequence, one may frequently find such blocks to contain no head at all, and this when the chances of a head or a tail are even. Much less would one expect to find any tails in any consecutive two or three tosses when the chance of a head is three times that of a tail.

In what way then are one's results affected by this state of affairs? It makes the ratio of affected to unaffected too great, as shown by considering the above purely hypothetical example as follows. Let the two allelomorphic factors be represented by *A* & *a*, then the genotype of a person showing the abnormality would thus be '*aa*' and that of a normal either '*Aa*' or '*AA*'. In order to prove the hypothesis concerning the genetical behaviour of the abnormality to be correct, all we have to do is examine all the matings between heterozygotes and show the offspring to be divided into normals and abnormals in the ratio of 3 : 1. But owing to the smallness of the families there will be a large number of these without any abnormal child and hence we will not be able to recognise these matings as being between heterozygotes. Their children will therefore be left out of the calculations, and since they are all normal, the normal members are reduced giving a ratio less than 3 : 1 its deviation from this varying inversely with the frequency of the abnormality.

Where the families are larger, there is a greater probability of the appearance of at least one abnormal child as the result of heterozygous matings and thus the error due to the non-inclusion of normals in the data is reduced. Modern statistical methods have shown us how we can, by considering both size of family and frequency of the abnormality in the population at large, apply a correction to the observed ratio and thus this hypothetical example shows us not only another reason why we get such a variation in our ratios, but also the dual nature of the human genetical problem requiring the co-operation of both expert clinicians and expert mathematical geneticists for its elucidation.

CHAPTER VI.

THE CLINICAL VALUE OF APPLIED GENETICS.

By far and away the commonest retort to the arguments used in previous chapters—even from those convinced by them—will be "But what is the profession going to gain from increased genetical knowledge? Is it going to place in our hands a keener weapon of diagnosis, a new and more powerful therapeutic agent, or gird around us a tougher protective armour against invading disease?" This chapter is an attempt to answer these questions.

During the last generation or two we have formed the habit of looking in the diagnostic or therapeutic direction for most of our medical advances, and we certainly have not been disappointed. So consistent has been the flow of valuable discoveries from these quarters that we have unconsciously come to think that any valuable advance must of necessity come along these lines. But this is no longer necessarily so. While applied genetics may supply some valuable diagnostic weapons, to my mind the greatest benefit to be derived from it will be

our increased insight into the innate forces of the living body. We have learnt so much of late of the effect of external forces physical, chemical and living, but we know so little of the forces of the living soil on which these others act; we have slaved at one half of the canvass and left the other half practically untouched. Is it any wonder that the whole picture gives an imperfect and unbalanced impression? The forces of the body cells which are the same as those of the zygote from which the body sprang, are just as important to the individual in his struggle with environment as the external forces which he meets. Yet of these former we merely guess, that is granting we take the trouble to admit their existence.

In discussing this part of the question let us first deal with some of the more obvious ways in which applied genetics can be of use to the clinician.

Diagnosis and Therapeutics.

Ultimately genetics will show us the way to assess the true value of a family history. It will be able to tell us the exact mathematical chances of morbidity in many individual cases, but it will not provide a diagnosis automatically. Genetics will merely fall into line with all other aids to diagnosis and give information, the ultimate value of which can only be assessed by one man, the personal physician. But before this time arrives we shall have to push the genetical study of man much further than it has gone at present. The methods which seem likely to yield the best results in man are comparative racial studies, linkage studies and the study of multiple births, especially when investigated under these four headings:—(*a*) morphology, (*b*) physiology, (*c*) pathology, and (*d*) psychology. Of the morphological characters a large amount has already been learnt concerning eye colour, cephalic index, stature etc., but as these are all characters which show continuous variation and each probably depending on a number of genetical factors, their actual method of inheritance is by no means easy to elucidate. Some physiological characters are much more simple, especially serological characters such as blood groups, Landsteiner's M & N substances, natural immunity to invading organisms causing certain infectious diseases, and these along with those of blood pressure, secretion of certain substances in body fluids, taste blindness, vital capacity and blood chemistry are now receiving attention the world over. Reports of genetical investigations concerning pathological characters are already beginning to find a large place in medical literature, as are also the results of comparative racial studies in physiology and in susceptibility or immunity to certain diseases. These are dealt with more fully in a later chapter.

One of the most surprising things however about human genetical studies is the great amount of fruitful work that has been done on the

inheritance of psychological characters. Since numerical values of psychological conditions are very difficult to assess, one would expect that this would perhaps be the very last clinical sphere to admit of the application of genetics. The fact is that it is perhaps more advanced here than in any other branch of medicine. Perhaps this is because therapeutics has not been the great boon to psychologists that it has been to specialists in other branches of medicine, and clinicians have been forced to look for help in other directions, or perhaps it is because they realise that it really does not matter much if a man inherits six fingers, or brown eyes, or even the ulcer diathesis; he can get rid of the first abnormality, the second may be a social asset, and the results of the third may even be amenable to treatment, whereas the only real method of dealing with many psychological conditions is prevention, and to prevent them we must know what matings are liable to produce them.

The advantage to be gained from linkage studies is obvious; if we can establish the fact that the factor causing susceptibility to a certain disease is closely linked with a factor which causes the appearance of a very easily observed morphological or physiological character, we have provided the clinician with a very useful aid in the diagnosis and prevention of that disease. This idea lies at the bottom of all the recent work on constitution being done by Draper and others. The genetical study of twins, especially uniovular twins, is another method of investigation which is not only going to supply us with much genetical information, but it is going to throw much light on the relative values of genetical and environmental forces. Yet another avenue of investigation which is likely to lead to a great increase in our genetical knowledge especially where recessive characters are involved is the exhaustive study of consanguineous marriages. In fact what was most probably the first modern clinical human genetical work done in England was that of Garrod when he established the connection of certain 'inborn errors of metabolism' with consanguinity, and practitioners will be helping greatly if they can provide facilities for the thorough investigation of any examples of consanguineous matings and plural births they may have in their practices.

One cannot leave this section of the chapter without mentioning cancer; in the writer's opinion cancer is the rock on which the edifice of the diagnostic value of applied genetics will either be firmly founded or else dismally but temporarily destroyed; it is also his belief that it will be firmly founded. As yet we are not able to say to what extent the cancer condition is hereditary, whether it is only the predisposition that is inherited or whether there are one, two or more factors involved, but carefully compiled family and twin data will certainly help to solve this problem in the next generation or so. It is a pity that members of the profession as a whole do not realise how valuable family histories of

cancer, especially if backed up by sections of the tumours, can be. Recently one of our leading medical men was reported as having said in public "Cancer is neither infectious nor contagious and there is no truth in the belief that it is hereditary or caused through food." It is perhaps wise at this stage that the public should not be worried about statements concerning the hereditary nature of cancer, but to allow such views to go unchallenged amongst the medical profession is to wantonly permit clogging the wheels of progress. The work of Little, Strong, Slye and others in America has furnished abundant evidence that whatever be the ultimate answer to the cancer problem, we can, by selective breeding, produce a race of mice which is highly susceptible to spontaneous cancer, just as we can produce a race which is highly cancer resistent. Even if the work went no further than that, it would be of great importance to us. What is a proven fact in animal genetics must be taken into serious consideration in human work and should be actually disproved before being cast aside, and where cancer is concerned we can take no chances. On top of this we have the evidence of Macklin (29), which undoubtedly indicates that there may be, in certain cases at any rate, hereditary factors involved in the occurrence of human neoplasms. Cancer looms so large in the public mind and besets the physician's path so commonly at every step and turn that the profession would be failing in its duty to humanity if such evidence as that were neglected. No clue, however slender, can we afford to treat lightly in the fight against cancer, and those responsible for putting current views before the profession should realise this, whatever their private convictions may be. This reason alone should be sufficient to cause a string of protests to be lodged against statements such as the following which appears on page 377 of 'The Chances of Morbid Inheritance' (4) "Whatever be the explanation, it is clear that inheritable factors can play but little part in the human as compared with selected mice". No scientific grounds can be brought forward at all to warrant such a statement. Some people are apparently impressed by the fact that to get the highly susceptible stock of mice, many generations of selected matings were necessary, and because there is little chance of this selection taking place at random in the human, they jump to the astounding conclusion quoted above. It is because of this absence of selection in the human that there does not appear a highly susceptible human race comparable to the laboratory mice strains, but the individual cases in man are just as likely to be subject to laws of heredity as the frequent cases in susceptible mice strains are. The above quotation also seems to be founded on the erroneous impression that a large incidence of neoplasms may be due to inheritable factors playing a large part, whereas a small incidence indicates that these factors are playing a minor part. Such a view is absolutely foreign to any modern ideas of heredity as a perusal of the foregoing chapters should prove. The above quoted author in his final paragraph states " . . . . . there does not appear to

be any need for a heritable factor as an explanation of the genesis of human neoplasms, except in the uncommon instances already cited." Why? Is he so complacently satisfied with our present questionable knowledge of the genesis of neoplasms as to be able to ignore any further suggestions however strongly they may be backed by evidence? Genetics provides a case which, if it can be proved that heredity is a factor in neoplastic origins, can also assist in the early diagnosis and cure, and if this be so, its help cannot or should not be despised. Genetics will yet give surgery such a new lease of life that though surgery may have cured its thousands, surgery plus genetics will cure its tens of thousands.

On page 376 of the book referred to above the writer states: "It must be realised that cancer is a common malady and, therefore, it is very improbable that any family has been quite free from it during the past two or three generations. Furthermore, with so widespread a disease it is not surprising to find several cases in closely related persons; but this alone is but a poor reason to accept the view that inheritance is of great importance." This passage reveals the fallacious ideas that can implant themselves into scientific work when proper statistical review of the data is not made. It is true that if one takes into account the incidence of neoplasms in general in the population only, it may not be outside the laws of chance that two cases should occur in closely related people, but if one takes into consideration the *type* of neoplasm and its frequency, and the frequency of its onset at the age of the family members under investigation, the whole complexion of the value of the facts may be altered.

Leschoziner (26) puts on record a family in which the mother and three daughters died of cancer of the breast. Although the incidence of four cases of breast cancer in one family may not be altogether outside the realms of chance for the region from which the cases came, yet when we estimate the chance of a person dying of cancer of the breast *at 21 years of age, and of her three daughters dying of the same trouble at the ages of 14, 19 and 22* respectively, then the case looks very bad against a mere chance explanation of such an occurrence in *one family*. Of course there may be other factors involved, but that is no valid reason for so summarily dismissing the case of heredity as a causative factor.

Lockhart-Mummery (28), whose book "The Origin of Cancer" gives a very up-to-date revision of this whole subject and one which no one interested in this subject should miss, states on page 26, "There is an hereditary factor in tumour formation which is of great importance in tumour incidence. . . . . The exact nature of this factor we do not know, but it is certainly not one for cancer or for simple tumour, but a susceptibility of certain tissues to tumour formation." And again on page vi—"In fact, cancer is the result of a genetic change in a normal growing somatic cell." This is not a treatise on cancer and therefore a detailed account of one's views is not called for here, but one must

emphasise the fact that we have an increasing amount of definite evidence that heredity may play *a part* in cancer incidence, and it is evidence of a type that demands elucidation and challenges disproof.

There is yet another reason why the genetical study of cancer is of prime importance. In a later chapter we shall discuss the effect of both genetical and environmental forces on the living body. There is no doubt that environmental forces such as irritation play a part in the cancer incidence, a part which may vary for different cancers and in different people; but this very fact shows that the study of this subject should reveal some important information concerning the relative effects of internal and external forces on the life of the cell. Such family investigations would of necessity have to be on a very large scale and would best be done by the establishment of a central clearing house to deal with the records of all cancer cases in the country. It might first of all be attempted for a city like London. At present there must be many valuable family records lost to science annually for the simple reason that members of the same family often attend different hospitals; but under this scheme not only would all such data be saved, but greater accuracy and uniformity of diagnosis would be ensured. If at the same time it could be possible to keep with the records sections of all tumours removed, invalidation of the data by advances in histological diagnosis would be avoided and the records made of more or less permanent value. The two most important parts of such a scheme are (*a*) the supplying of accurate family histories, and (*b*) the filing of a section of all tumours. The necessity of this latter has been exemplified in America where an attempt was made to analyse genetically data derived from death certificates alone, but the variations and inaccuracies of diagnoses soon showed this method to be valueless.

Preventive Medicine.

The other main way in which genetics will be of use to the clinician is in the realm of preventive medicine. Where the development of a pathological condition can be proved to depend on both genetical and external factors, then those individuals with the necessary genetical background for the development of such a condition are the only ones which will have to be shielded against the forces of environment. Herein lies the value of a great part of all the work being done on diathesis and constitution, and there is no doubt that from this direction preventive medicine will witness very definite advances. The other preventive branch of this subject which is attracting a lot of attention at present is *Eugenics* and it is essential that we should understand the exact relation of this part to the whole subject of human genetics.

The word 'Eugenics' was first used by Galton (15) and, in his book 'Human Faculty' (1883), was defined by him as follows: "National eugenics is the study of agencies under social control that may improve

or impair racial qualities of the future generations either physically or mentally." As we shall endeavour to show in the next chapter, Galton's idea of eugenics not only includes our idea of human eugenics, but implies the idea of 'human genetics pure and applied.' This definition shows that he was aware of the importance of both heredity and environment, of both nature and nurture; but unfortunately during the intervening years the word eugenics has come to be applied by many people only to that part of the subject dealing with the *genetical* agencies that may improve or impair the racial qualities of future generations either physically or mentally, and more unfortunately still it has become allied more especially with two agencies, contraception and sterilization, both of which are very dangerous agencies and of very questionable value unless rigorously and scientifically controlled. Whether this conception of modern eugenics is due to the direction in which eugenists have been expending their energies or due to the general misconception of the word, matters not at the moment; what is important is that we should have a clear conception of the ideas involved in the terms used whenever we come across them; in this thesis we have purposely tried to avoid any chance of ambiguity by using the terms 'Human Genetics' and 'Applied Genetics' in preference to 'Eugenics' which word is used in its narrower meaning. By its effort to prevent people with undesirable characteristics from reproducing their kind, some people are greatly impressed by the possible benefits eugenics may bestow upon human society. With regard to certain rare diseases the genetics of which have been thoroughly elucidated, the methods of contraception and sterilization may to a certain extent yield the results expected of them. Especially may this be so when the undesirable character is due to a dominant factor, for then all carriers of the character can be recognised and dealt with; such conditions as brachydactyly, lobster claw, diabetes insipidus, Huntington's chorea are examples of this type and there is no doubt that these could be eliminated in one generation if people exhibiting such abnormalities were not allowed to reproduce their kind. They would perhaps not be eliminated completely because, as they most probably arose in the first instance by a gene-mutation, and as we know these mutations recur with a definite frequency, they are sure to crop up again, and thus this type of treatment is not permanent but will have to be reapplied at intervals. But where the character is due to a recessive condition such as in amaurotic familial idiocy, one type of retinitis pigmentosa, albinism, etc., this method is practically useless, for the carriers cannot be recognised until after an affected child has been born. Hogben (19) stated that "if all albinos were sterilised in every generation it would take many centuries to reduce the incidence of albinism to half its present dimensions". Eugenics will fail miserably here, and such methods will always be open to the objection that although certain individuals may be carriers of factors for undesirable characters, they may also at the same time be carriers of factors for some very desirable

qualities; and who is to draw the line between a *group* of characters which will improve racial qualities and a *group* which will impair them? Selection for one character is one problem, but selection for a large group of characters especially in man is as yet a fantastic dream. In spite of continental experiments we are not yet ready for the wholesale compulsory application of the extreme eugenists' ideas. Such a compulsory application, in addition to the fact that it is as yet not scientifically warranted, would certainly adversely effect the marked progress that is now evident in the study and application of human genetics.

The great eugenic need of the moment is legislation to make permissable voluntary sterilization in certain cases, and such cases should be very rigidly and rigorously limited to those falling well within the bounds of our exact genetical knowledge. This can only be achieved by awakening amongst the members of the medical profession the realisation that we do understand the method of inheritance of certain abnormal conditions and that it would be in the interest of the community as a whole as well as the family concerned, if individuals showing such abnormalities were prevented from propagating. As soon as this is realised and the use of this method firmly and strictly safeguarded, eugenics will definitely provide one of the valuable advances achieved by applied genetics.

There is one aspect however of medical practice, indeed its most important aspect, which must ever lie beyond the help of eugenics and that is the personal aspect. When two people consult their family doctor concerning the chances of their offspring developing some undesirable character, they will be told such chances are "one in *x*". But the future parents care nothing for the number of children in 100 that are likely to be affected. Naturally their whole concern is "what will happen to *our child*" and when confronted by this personal, individual situation, eugenics is powerless. The only sure eugenical way of preventing the appearance of the abnormality is by preventing the birth of the offspring altogether. Eugenics as at present conceived, is a coarse, crude method of attaining a desired end (the eradication of an undesirable character) by preventing a new individual from coming into being. The ultimate aim of this part of applied genetics however should be to attain that same end, by so learning to *modify and control* the inner genetical forces of man that offspring of affected parents may be allowed to develop assured of freedom from the undesired character.

CHAPTER VII.

HEREDITY AND ENVIRONMENT IN MEDICINE.

No discussion of the situation of human genetics would be complete without some reference to the question of the effects of heredity

and environment on the development of human characters. If we refer back to the experiments quoted in the early chapters we see that they dealt with characters which were almost totally dependent on heredity, and only dependent on environment to the extent that they needed ordinary environmental conditions for their expression. Now there are other examples which show that environment plays in certain cases a much more important part than that. One can not do better than quote here the example given by Hogben (19) on page 11 of his book 'Nature and Nurture'.

> "If chickens are fed on yellow corn or given green food, we can distinguish between some varieties which breed true for yellow shanks and others which breed true for colourless shanks. *This is a genetic difference.* Crosses between such varieties, when all the progeny are fed on yellow corn or given green food, yield numerical ratios of the two types in conformity with Mendel's principle. If chicks of the variety with yellow shanks are fed exclusively on white corn they grow up with colourless shanks. The difference between a fowl of the yellow variety fed on white corn is a *difference due to environment.* If we crossed fowls of the yellow variety and fowls of other varieties giving some of the progeny yellow corn and others white corn, we could not expect to obtain constant numerical ratios such as Mendel's principle predicts."

It is more than probable that in the study of human genetics, we shall find examples of all the stages between those in which environment is of minimum importance and those in which it is of maximum importance, and one may predict that nowhere will this be better shown than in the causes of cancer. There is no doubt that here we have to deal with an environmental factor as well as a genetical one, the former varying in importance in different cases. Perhaps the explanation of the high incidence of rodent ulcer in the hot dry climate of Australia is not that there is a difference in genetical equipment between the Europeans in Australia and the people of England, but that the genetical forces of Australians are subjected to different environmental treatment with different results. The whole question of the geographical and racial distribution of disease needs careful and thorough genetical as well as environmental investigation and will be discussed in detail later. A comprehension of the manner in which human cells and individuals react therefore demands a clear understanding of the interaction of the two sets of forces which affect their existance, namely the intrinsic, innate, inborn or genetic forces and the extrinsic or environmental forces. Newton laid down laws governing the behaviour of bodies under the action of external impressed forces. These bodies were considered as being inert. A live body however is subjected not only to external forces, but also to those forces with which its inherited genes endow it. These inborn forces we shall describe as intrinsic, and by the application of laws

based on those of Newton, but designed to apply to bodies subjected to both extrinsic and intrinsic forces, we shall now procede to attempt to explain the general reactions of a living cell. We must first of all enunciate an axiom which will provide both a foundation for our laws and the differentiation between inert and living bodies, and it is as follows :—

> *"Every living body exists in a state known as the state of being, every inert body in a state of inertia".*

Here "body" may be interpreted in its biological sense as a cell, or according to its every-day use as an individual—an aggregate of cells all derived from one zygote. Inert and living bodies are thus conceived of as existing in totally different states, the relation between which will become apparent from the following laws.

Newton's 1st Law.	1st Law of Being.
Every body continues in its state of rest or uniform motion in a straight line except in so far as it is compelled by an external force to change that state.	Every living body continues in its state of being as the result of the action of both intrinsic and extrinsic forces.

Note the difference between the state of an inert body and the state of being of a live body; an inert body continues in its state unless compelled to change that state by external forces while a live body only remains in its state of being while it is in dynamic equilibrium under the action of both intrinsic and extrinsic forces. This law introduces us to the two types of forces, those of heredity (intrinsic) and those of environment (extrinsic), under whose balanced action only is continuance in the state of being or life possible. The condition of an inert body implies its inertia; the condition of a living body is a dynamic one and implies the tendency of such a body to revert to the inert state, either by the intrinsic forces overcoming the extrinsic or vice versa, in both cases the result is the transference of the living body out of the state of being. A living cell or body is thus continually in a state of dynamic equilibrium under the action of two groups of forces. Outside the confines of this state is the state of inertia which differs from the state of being only in the absence of intrinsic forces, and the passing through these confines from the state of being to the state of inertia is what we term death. This introduces us to the spatial relationship existing between the two states of which Fig. 19 is a two-dimensional representation. The state of inertia everywhere surrounds that of being, which

simply means that if we give forces arbitrary directional values, bodies can be represented as passing from being to inertia through any direction.

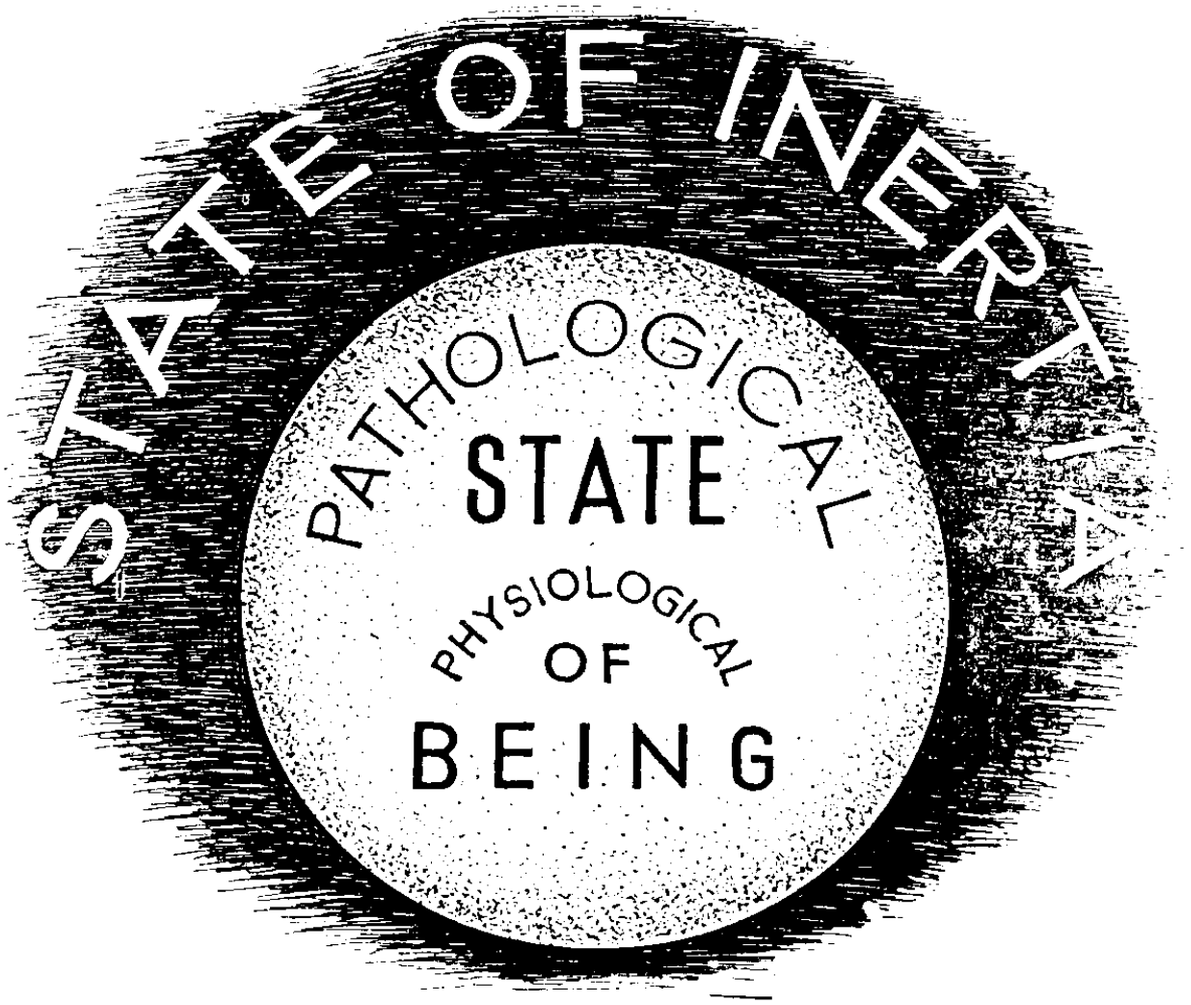


Fig. 19. A two dimensional representation of the idea put forth in the text that the state of being, in which every living cell may be conceived of as existing, is everywhere surrounded by the state of inertia into which state a cell may be considered to pass on ceasing to live. The state of being is imperceptibly divided into two, (*a*) physiological, or the state of well-being (clear area) and (*b*) pathological or the state of ill-being (shaded area).

That part of the state of being where the two sets of forces are so adjusted as to result in the best functioning of the living cell or body is the physiological state of health or *well-being*, which state merges imperceptibly into the pathological state of *ill-being*. From this law we see that a body can pass from the state of well-being to that of ill-being through the over-action of either the intrinsic or extrinsic forces and further than that, the particular state of being in which any living body finds itself at any moment depends on these two sets of forces. A change of environment may so alter the extrinsic forces (i.e., the administration of poisons, lack of oxygen, marked rise in temperature etc.,) that the intrinsic forces are powerless to prevent the change from the state of being to that of inertia. (Note that there is a difference between intrinsic forces of the human body such as are brought into play by inoculation or immunisation; these latter forces are still external to the cell and thus act by modifying the extrinsic forces to which the cells

are being subjected.) On the other hand the intrinsic forces may be such that no matter what we do to modify those of the environment we cannot maintain the body in the state of being; this is the explanation of the so-called unaccountable death of the newly born referred to in an earlier chapter.

Newton's 2nd Law.	2nd Law of Being.
Rate of change of momentum is proportional to the external impressed force and takes place along the line of action in which the force acts.	Rate of change in state of being is proportional to the resultant of the intrinsic and extrinsic forces and takes place along the line of action of that resultant.

A change for the moment from the biological to physiological ideas introduces us here to acute and chronic conditions with which every clinician is acquainted and which will be considered again with the next law.

Newton's 3rd Law.	3rd Law of Being.
To every action there is an equal and opposite reaction.	Every extrinsic force acting on a body in a state of being tends to evoke the action of an equal and opposite intrinsic force.

To the medical man this is the most important of all these laws for it differentiates the reaction of a living body from that of an inert body. A living body when subjected to a change in environmental forces tends to react, and the type of its reaction depends entirely on the inherited mechanism with which it is endowed. If it is endowed with the mechanism which can respond to these external forces, the tendency to react results in the realisation of the reaction, and the external forces are met by equal and opposite intrinsic forces resulting in the body remaining in its state of being, but if the living body has not the genetical factors to enable it to thus respond, the result is an unopposed action of extrinsic forces and the consequent transference of the body from the state of well-being, through that of ill-being to the inert state.

Referring back to the 2nd law we see that the state in which we find a body is dependent not only on the resultant of the two types

of forces acting on it, but also the rate at which the change in external forces takes place, and the rate at which the body is capable of internal response; such reaction may be so slow in developing that the body is removed from the state of being before the internal forces are strong enough to neutralise the external ones, or again their production may be so rapid that the effect of changed environment is so quickly neutralised that no recognisable change of state is produced. It must be understood that there is no suggestion of scientific proof of these Laws of Being. They are simply enunciated in the hope that by taking advantage of our knowledge of the Laws of Newton, they may increase our understanding of the reactions of the complex forces which govern living cells.

Let us now see how these ideas affect our understanding of the relative importance of nature and nurture on the human body.

The extrinsic forces acting on the body may be purely physical —temperature, irritation, etc.,—purely chemical—change in chemical constitution of the blood, drugs, toxins, food,—or they may be a combination or both—the invasion of a body by organisms, changed climatic conditions, etc. During the last 50 years medical science has witnessed an immense advance in our knowledge of the minute organisms whose presence in the body causes one of the most devastating, and therefore important, changes in extrinsic forces. But the recognition of the importance of these extrinsic forces has pushed into the background the study of the intrinsic forces and has led to the unbalanced development of medical science referred to previously. Ryle (39) says:

> " . . . the whole subject of constitution as a factor in morbidity had continued to suffer a curious neglect at the hands of the profession. This neglect was in part due to the birth and growth of bacteriology with its concentration on the extraneous causes of disease, and in part also to the perfection of biochemical and histological methods and a pre-occupation with the intimate processes and effects of disease which these in turn engendered. It is true that physicians have never omitted to place a certain reliance upon family histories, and that the genetics of a few rare maladies have been carefully and profitably studied."

Collins (6) in his Presidential Address to the Conference of the Sanitary Inspectors' Association at Buxton, 1922 stated:

> "But one has sometimes been inclined to enquire whether it may not be that the microbes have been conceded too exclusive consideration, whether too great regard has not been given to the seed—too little to the soil, and whether we have not sometimes lost sight of the man and his environment amid the luxurient flora and fauna so assiduously cultivated in the bacteriological laboratory."

This point should need no further labouring, that the resulting reaction of a living body to an extrinsic force can only be accurately understood when the intrinsic forces are also understood and when both are taken into consideration. The foregoing leads us to a new conception of idiosyncrasy, diathesis and constitution which we shall now consider.

Idiosyncrasy and Diathesis.

If the action of extrinsic forces on a living body results in the retention of that body within the confines of the state of well-being, the intrinsic response may be said to be physiological, and since this state is dimensional there is a certain latitude in these physiological responses; they vary between limits which we come to call normal merely because they are the average limits. *A living body is in a physiological state of well-being when average environmental forces call forth average intrinsic responses.* If the intrinsic forces of a body are such that their response to average environmental conditions is exgagerated in one direction, either positively or negatively, then that body is

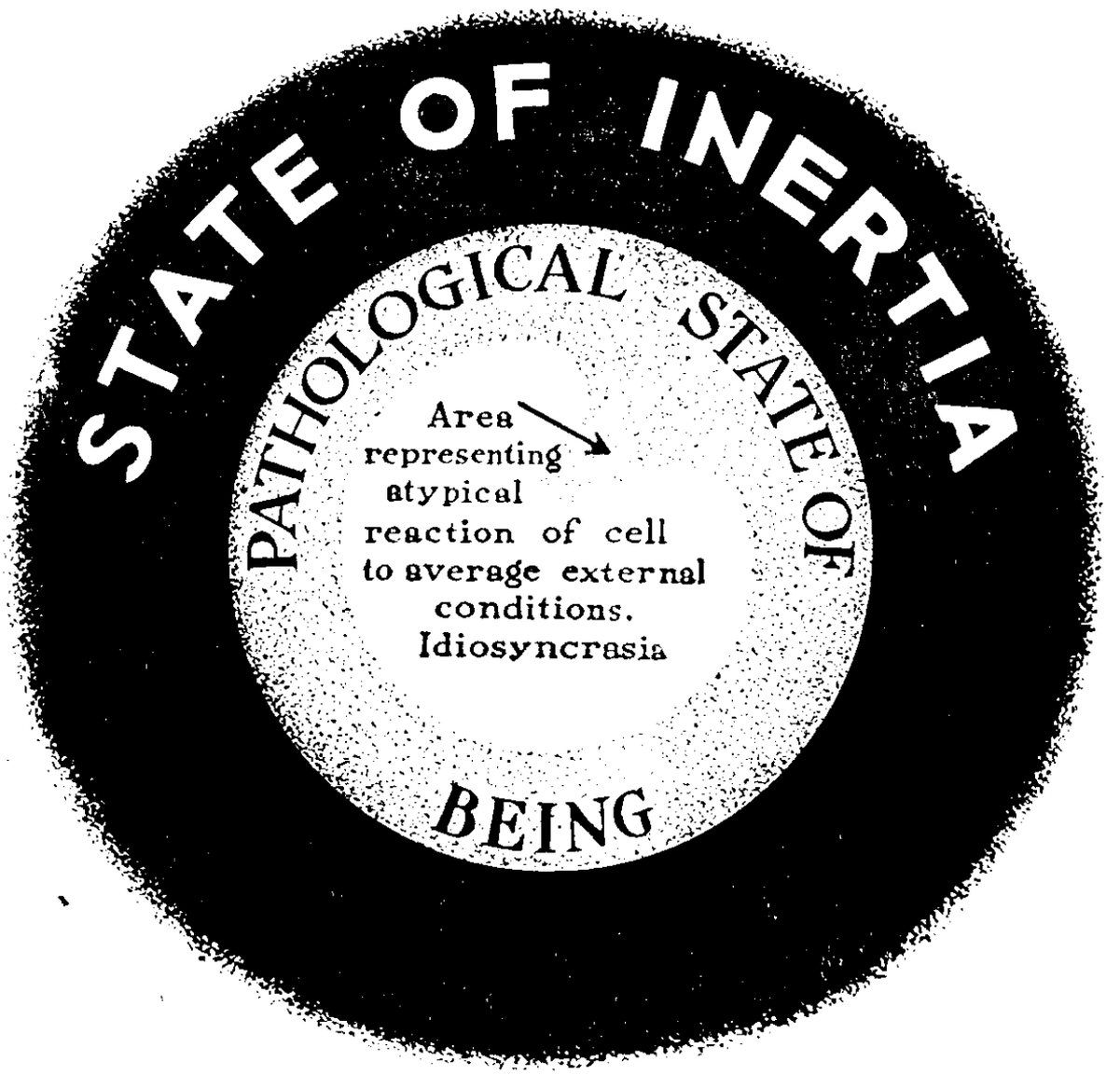


Figure 20.—A two dimensional representation of the relation existing between idiosyncrasy and the different states of being after the manner of Figure 19.

displaying an *idiosyncrasy*. Note the importance of both internal and external forces in the expression of an idiosyncrasy. It is the physiological response, either positively or negatively exaggerated in one direction, evoked in an otherwise average body by average extrinsic forces or as Rolleston (38) so aptly describes it, "an unusual physiological personal equation." In Figure 20 the irregularity in the inner area of the overlap between the states of well-being and ill-being would represent this state idiosyncrasy.

This 'fundamental aberration' has its anatomical counterpart in isolated morphological departures from the average, generally known as anatomical abnormalities, e.g., hereditary deafness, polydactyly, etc. The only difference between an idiosyncrasy and an abnormality is that we generally have some means of detecting the presence of the latter whereas the former is purely functional and only disclosed when certain responses are evoked. According to this view the boundary line between the two is purely artificial and as our knowledge increases, more and more idiosyncrasies will have to be renamed abnormalities, because ultimately a change in physiological response must be dependent on a structural change, and it is only the minute size of such change which prevents us from detecting them at present. Not the least interesting and instructive of these conditions are the 'chemical malformations' of Garrod which in the end must depend on some minute structural (even molecular) malformation. Thus while agreeing with Rolleston in his differentiation between idiosyncrasy and abnormality, I would urge that it is purely arbitrary, and that they are both conditions exhibited by a living body which, when acted on by average extrinsic forces, passes into the ground sometimes found between well-being and ill-being which we might call *idiosyncrasia*. It is *because* of its idiosyncrasy or abnormality that a living body will react to extrinsic forces by passing into this state, and therein lies the difference between idiosyncrasies and abnormalities on the one hand and diathesis on the other.

As long ago as 1884 Jonathan Hutchinson (22) in 'The Pedigree of Disease' (London 1884) set forth his ideas on temperament, idiosyncrasies and diathesis, and these ideas have in the main been elaborated by recent workers such as Garrod (17), Hurst (21), Rolleston (38), and Ryle (40). It must not be thought that Hutchinson was alone in the early days in his beliefs in diathesis, for this conception had long been universally held at any rate with regard to arthritic, scrofulous and such diatheses, and it only fell into abeyance with the rise of bacteriology and the consequent focussing of all attention on the external factors causing disease. Hutchinson defines diathesis as 'any bodily condition of prolonged peculiarity of health giving proclivity to definite forms of diseases.' It is a condition involving a large part of the body, while idiosyncrasies or abnormalities involve small parts, the former involving parts even too small to detect. Hutchinson wrote

well therefore when he described idiosyncrasy as 'indeed to a large extent nothing but diathesis brought to a point.'

There are certain points of similarity and dissimilarity between idiosyncrasy and diathesis which we should notice. The first point of similarity is that both result in the passing of a body from the physiological state of well-being when acted on by *average* external forces, forces which would be completely neutralised by the average body and leave it in the state of well-being. Under ordinary average conditions the average person does not develop a peptic ulcer, but under precisely the same conditions the person with the ulcer diathesis develops one. The second point of similarity is that just as abnormality is the anatomical counterpart of idiosyncrasy, so diathesis has both a functional and morphological side. It is hard to tell whether a person has the gouty diathesis until his repeated state of ill-being discloses the fact; we cannot tell whether a person has an idiosyncrasy for a special protein until he has shown it by his exaggerated response when exposed to the action of that specific protein. We can however tell by observation whether a person is likely to have the ulcer diathesis or not, just as we can tell by observation whether he has a morphological abnormality. The gouty diathesis belongs to the group of functional diatheses whereas the ulcer diathesis belongs to the morphological group; but again the dividing line is merely arbitrary, and further work may reasonably be expected to discover the morphological changes underlying all diatheses. In view of the fact that all diatheses are not obviously morphological, it is wise to follow the suggestion of Ryle (40) that 'In naming a particular diathesis we should couple the term with the disease to which the predisposition exists, ... and not with the constitutional peculiarities which are found in association with it.'

Now for the points of dissimilarity. We have seen that a body with an idiosyncrasy shows its exaggerated response *because* of its morphological change; a body with a diathesis does not necessarily pass into a state of ill-being *because* of the morphological change indicating the diathesis, but rather because of some unknown factor genetically linked with those causing the appearance of the morphological change. Pernicious anaemia does not develop in a man because of his 'somewhat large and bulky frame' and his 'strongly marked tendency to the formation of fat' but rather because of some genetical factor linked with those which cause these characters to appear. The other important dissimilarity is that whereas an idiosyncrasy leads to an exaggerated physiological response, the diatheses leads further, to a state of ill-being. These ideas just enunciated fit in very well with the definition of diathesis given by Ryle (39)—'a transmissable variation in the structure or function of tissues rendering them peculiarly liable to react in a certain way to certain extrinsic stimuli,' the only

points of difference being that the above ideas definitely imply that the certain way of reacting is the setting up of a diseased condition, and that the extrinsic stimuli should be average ones. The following definition, although not so neat and compact as Ryle's does affect the inclusion of those ideas—*A living body exhibits a diathesis for a certain pathological condition when the reaction of the intrinsic forces of that body to average extrinsic ones, tends to cause it to exhibit the symptoms usually associated with that pathological condition.*

Constitution.

Now what of constitution? Thanks to the energies of such men as Julius Bauer, Draper and Faber, interest in this field is undergoing a long overdue awakening. Draper (8) defines constitution as the 'aggregate of hereditary characters influenced more or less by environment which determines the individual's reaction, successful or unsuccessful to the stress of environment.' One must draw attention to the fact that Draper recognised the importance of three things (*a*) aggregate hereditary characters, (*b*) the influence of environment and (*c*) the individual's reaction. From the rest of his work one rather gathers that through not saying 'the aggregate of *all* the hereditary characters' he has allowed himself to be free to pick out certain characters in contradistinction to considering *all* of them, and thus his ideas of constitution correspond very nearly with the above idea of diathesis. One must also draw attention to the phrase 'influenced more or less by environment;' as we have seen in the above pages the state of being is not influenced by environment (as if there were just one set of forces to be taken into account—the extrinsic ones) but is rather the result of the action of the body to *the resultant of two forces*, intrinsic and extrinsic. The former phrasing gives the idea of *one* set of influencing forces, an idea which it is the aim of this argument to destroy.

Faber's definition (12) is 'the nature of the body, including under this all the inherent properties, such as the anatomical structure of the body, its morphological composition as well as the functional properties of the separate organs and cells.' This is an excellent definition as far as it goes, but it again deals with only one side of the question, this time the intrinsic forces, and deals with them very fully, but it fails to show the application or value of the idea of constitution as our other definitions have done for diathesis, idiosyncrasy, etc. I should like to suggest the following modification of Draper's definition as follows:—*Constitution of a living body is the aggregate of all the hereditary characters which, by their reaction to the extrinsic forces of environment, determine the state of being of that body.* Thus constitution in its reaction to environment may lead to the state of well-being, of idiosyncrasy, of ill-being or of inertia. It includes both

idiosyncrasy and diathesis, and temperament is merely a psychological constitution, in its turn embracing both psychological idiosyncrasies and diatheses.

In conclusion we might make brief mention of *'allergy'* which Von Pirquet originally described in 1911 as 'altered reaction' and which therefore includes, as Rolleston shows, hypersensitivity, anaphylaxis and immunity. Allergy has now come to be used almost entirely for describing states of hypersensitivity and anaphylaxis, but even in its original meaning it was not—as Rolleston says—the equivalent of idiosyncrasy. Allergy is the condition in which an individual gives an altered response to a special type of external force —a chemical one; allergy is thus really a special type of idiosyncrasy, and so also are hypersensitivity and anaphylaxis, the latter being a special state of hypersensitivity caused by the reaction to a previously applied chemical extrinsic force.

The importance of all this dicussion is that these terms diathesis and idiosyncrasy, constitution and allergy, etc., can not be rightly appreciated unless one realises that the state of being of any living body depends on the *resultant of two types of forces, one environmental and the other genetical.* In some cases the one may be overwhelmingly responsible for the state of being, in other cases the other, but in all cases it is the *resultant* of the two on which any change of state depends. One must here refer to a passage in *"Idiosyncrasies"* page 42, in which Rolleston says of the three types of abnormal hypersensitiveness or idiopathies atopic, anaphylactic and infective, 'that the first is inborn and determined by hereditary influence, whereas the other two are acquired.' But this cannot mean that hereditary forces have no influence on these latter two, for recent work both in animals and in man is leading us to believe that the *ability to acquire immunity or hypersensitivity is itself an inherited character,* and that therefore we cannot leave out of account the genetical forces in consideration of any of the states of the living body. Constitution, diathesis, idiosyncrasy, hypersensitivity, etc., all these are dependent on intrinsic forces and are to that extent subject to the same laws of heredity as any other character is, and thus in the elucidation of the clinical problems set by these states, the study of genetics must play a leading part.

It is the writer's hope and belief that ultimately the greatest contribution of the study of human genetics to clinical medicine will be the elucidation of the action of those intrinsic genetical forces of the body which together with the forces of its environment are responsible for the state of being of an individual.

CHAPTER VIII.

ANTHROPOLOGICAL PHYSIOLOGY.

Modern physiology has attained its present position and status amongst the sciences by means of help through many different avenues. Advances in the sister subjects of physics and chemistry have made possible the great advances in our knowledge of the minute structure of the body and have revealed the nature of the molecular and ionic reactions in its various fluids. A formidable list would result if an attempt were made to detail all the ways in which nervous and cardiac action, respiration, digestion, metabolism and secretion, to mention only a few, have been satisfactorily studied by the application of physical and chemical knowledge.

The daughter subjects of modern clinical medicine and surgery have also, as though in return for the natal help they have derived from physiology, provided that subject with some of its more important advances. But perhaps the most valuable advances have come from the comparative side of biology. Our physiology text books are full of descriptions of functions in the lower animals, and the result of most of our experimental work is naught unless we can assume or prove that what happens in the laboratory animal may also happen in the human. (Even in the subject of animal physiology, genetics should play a more important part than it now does. How often does one see a lengthy paper representing months of patient work and describing some part of the physiology of *the dog*, followed by another just as lengthy and as accurate proving the opposite to be true in *the dog*. If such investigations were made on animals so bred as to be as homozygous as possible for the characters being investigated, a great deal of the apparent contradictions of function in *the dog* would disappear, and a great deal of more accurate information would be acquired).

There is however one great source of physiological knowledge as yet practically untapped and that is the comparative study of the races of mankind themselves. All of us who have had the opportunity of working amongst non-European peoples must have been struck sooner or later by the realisation that our so called physiological "normals" are merely the averages found to exist amongst a very small proportion of the world's human inhabitants, and by no means must they be accepted as the "normals" or averages for mankind as a whole. No one would seriously take a group of individuals from the north of Europe and estimating their average height, proclaim it as the average height of human beings, nor have we any right to assume European physiological averages to be representative of mankind as a whole.

The interesting thing is that when we come to investigate functions in different races we find that though qualitatively similar, they are

often quantitatively different and that the quantitative difference is roughly a character of the race in question and hence we can confidently look forward to physiological differences being used as a means of anthropological classification, with just as much promise of usefulness as is at present derived from the study of morphological and psychological differences between races.

The study of racial classification from that angle might be aptly called physiological anthropology, and *the comparative study of these physiological characters in known races, comparative human or anthropological physiology.*

Any character whether it be physiological, morphological or psychological which is constantly found in a group of people large or small, must be hereditary; the study of anthropological physiology should therefore reveal to us a number of hereditary physiological characters. The genetical principles underlying the inheritance of such characters can be studied to no better advantage and with no more fruitful results than in families resulting from the mating of two individuals each being drawn from one of two races showing contrasting physiological characters.

Genetical studies of race mixture in America and Honolulu have already proved their value, and such studies will be much more valuable when it is realised that such a thing as a pure race (whatever that term might mean) does not exist, and therefore the physiological characters of any existing people or race are themselves the result of mixture of two or more earlier peoples, and to understand the physiology of race mixture is thus to understand better the physiology of a present day race itself; and who can gauge the value that clinical medicine will derive from such new physiological knowledge?

That some members of the scientific and medical world are fully aware of the importance of this work is shown by the fact that at its last meeting held in Zurich in 1934, the International Federation of Eugenic Organisations formed a special committee of Anthropological Physiology. The functions of this committee are roughly threefold (*a*) to stimulate the investigation of these problems in those parts of the world most suitable for such work, (*b*) to provide a mechanism whereby individual workers may be put in touch with one another, thereby promoting the correlation of such work as well as tending to ensure the use of similar methods amongst various peoples and (*c*) to promote at the meetings of the Federation, an opportunity for the discussion of the results of the comparative data obtained.

At this early stage one of the most promising results of the activities of this committee is the discovery of the immense amount of valuable work that is already being done in this branch of physiology. Radsma, Streef and Klerks (37) have shown that definite differences exist in the

urine reactions of the Chinese, Europeans and Natives in the Dutch East Indies, and that there is also a real difference in blood reaction between the Europeans and the natives whom they investigated. The importance to physiology and medicine of the elucidation of the causes of differences in acid-base balance, whether they be dietary, climatic or racial in origin, is of course too obvious to need further elaboration.

Earle (10) after investigating the basal metabolic rate of 253 individuals wrote:

> "We are thus forced to the conclusion that the Chinese *do* exhibit a lower metabolism than Westerners and that this difference exists irrespective of any disproportion that may exist between surface area and height-weight factors; also that this low metabolism has a true physiological basis not to be explained in terms of size, age and sex on which our present standards are based."

The extensive work of the Japanese investigators, as examplified by Sen Nagai (33) has laid invaluable foundations for the physiological investigation of racial differences in Japan. Here in our own School of Physiology we have already collected data on fertility (as evidenced by twin birth frequencies), systolic arterial blood pressures, gastric secretion, all such data showing definite differences between the various races examined. In India, Malaya, Manila and in Hongkong vital capacity investigations are again exemplifing racial differences, while the data presented by Cleland (5) resulting from his extensive investigations in Central Australia will provide invaluable opportunities for comparative studies in serology and metabolism.

These are but a few of the existing investigations which come to mind, but they should be sufficient to make one realise that we cannot claim to understand fully any physiological action until we can explain its racial variations, and this surely will result in a more complete understanding of that other type of physiological variation which concerns the clinician so vitally, the functional variation in disease.

The next logical step in these studies is the investigation of the behaviour of these physiological characters in racial crossing. Its great importance, apart from the sociological aspect, will be in the application of our knowledge of the result of crossing of masses to the crossing of individuals showing individual physiological differences, and, as stated previously, since every existing people is the result of racial crossing, the study of the physiology of any race or people existing today is fundamentally a study of the results of racial crossing.

This argument may give the impression that racial differences alone are responsible for physiological differences, but following on from our ideas of the relative values of heredity and environment we see that such an impression is far from the truth. The two great environmental forces we must take into consideration when discussing physiological

changes are diet and climate. Radsma (36) in a later paper than the ones referred to above has shown that some of the differences he has demonstrated are definitely due to differences in diet. Apperly (1) has demonstrated differences in the secretion of hydrochloric acid amongst Australians of European descent living in different parts of Australia and subject to different climatic conditions, and he has already drawn attention to a corresponding difference in incidence of peptic ulcer. Observations by clinicians on the seasonal incidence of diseases are too numerous to mention separately, but taken in conjunction with the work of Mills (30)—who has shown how variations in climatic conditions may greatly alter physiological functions—they show how important is the study of physiology in relation to climate.

There are two methods of carrying out these investigations.

(*a*) Simultaneous physiological and climatic observations on various groups of people in their normal environment.

and (*b*) repeated physiological examinations of the same group of people subjected to known climatic variations over lengthy periods.

The former method is being followed now in many countries by interested workers and Foundations, and it is hoped that the activity of the above mentioned committee will result in many more expeditions of this nature being made, and in most of the investigators concerned collecting data on similar functions using similar or comparable techniques.

The latter method should be used much more than it is, and more especially since nations with colonies and dependencies abroad have the opportunity of carrying out such work, I put forward the following scheme in the hope that it may prompt interested governments and trading companies to consider it. Annually there must leave England some thousands of adults all rigorously medically examined and graded A1, and yet a percentage of these is invalided home after varying periods of service, often before the value of their work can have repaid the cost of their venture. The rest return after periods varying from 2-5 years and are available for re-examination. The reason why some people can stand the tropics while others cannot, must be that even in any one people we have various physiological types which react differently to changes in environment, and a thorough bio-chemical and physiological examination of even a small percentage of these people would soon result in our ability to classify our A1 adults into physiological classes, and we could then after a period of years show how each class tends to react to climatic variations. We should then be able to go further than informing employers who amongst their servants are fit for service abroad and who are not, but which of their fit employees would react best in the various climates to which they may be exposed.

It would surely repay any large employing firm or the government of any colonizing country to endow researches along these lines and thus save the money annually spent in repatriating those who so quickly return to their native land victims of tuberculosis or sprue to mention only two of the common causes.

There is yet one other way in which anthropological studies may be of immediate and great utilitarian value in the legal branch of medicine. In a later chapter we deal at some length with the manner in which blood grouping evidence can help to settle paternity and identification problems and it will be seen that the whole value of this evidence is based on the fact that an agglutinogen cannot appear in the blood of an individual unless it was also present in the blood of at least one of the parents. This so called fact can only be considered as an absolute fact when it is proved that these agglutinogens cannot and do not arise as the result of mutations in the germplasm. From the family data already collected we can be reasonably sure that the rate of this mutation, if it exists, is relatively small, so that it will not greatly affect the value of blood grouping evidence in these cases, but as long as this question of mutation remains unsettled, there is always the remote possibility of a mistake being made.

How then are we to come to a decision about this possibility of mutation? The experimental breeding method so easy in animals is of course out of the question in human work. In a later chapter we also make brief mention of the principles underlying the application of blood grouping studies to anthropological problems. Briefly stated they are very parallel to those underlying the application to medico-legal work. Just as, in the one case we get some information about the parents from the characters of the children, so in the other case we can conclude the characters of parent races by the examination of the characters of the existing race resulting from the mixture of those parent races. In other words we can use blood grouping data to investigate the origin of races or the affinities between different peoples.

But the use of such data depends among other things on the truth of the statement that these serological characters are inherited from the previous generations and are not the result of gene mutations. Intense and thorough studies on a number of races will greatly help us to decide this question of gene mutation in man, and nowhere could they be carried out to better advantage amongst the people of Eastern Asia whence almost certainly arose the migrations which resulted in the peopling of the American and Australian continents, among which peoples we find the results which diverge most remarkably from those found anywhere else in the world. This point is stressed by Ruggles Gates and Darby (18) in their article on British Columbia Coastal Indians, and they bring forth further evidence to show that even in one generation this gross difference is being lost due to mixture with

Europeans. The lesson is this, that owing to the civilisation of these peoples and the introduction of modern trade and transport, changes are apparent in one generation which previously must have taken centuries to produce, and if we are to reap any benefit from the existance of this latent data, we must examine and record it in the very near future or it will be too late.

Anthropological studies are thus not only desirable but they are urgent; and their urgency may be deduced from the following two statements. (*a*) In an earlier chapter we showed how the small size of human family presented a great difficulty in genetic studies, but amongst certain peoples especially in Asia and in the Pacific Islands, large families are still economically possible and still to be found. Hence it is amongst such peoples that the more valuable and accurate family studies can be made. But just as our peculiar type of civilization is spread amongst these people, so will they find the large family to be no longer possible and in a generation or two the advantage of big families to the study of human genetics will be lost to science. (*b*) Amongst certain communities there exists a definite amount of inbreeding and in such communities we have the natural occurence of an experiment which, were we able to perform human experiments, would certainly be one of those purposely designed and investigated. These human inbreeding experiments are invaluable in our inheritance studies of recessive conditions, but the longer these studies are postponed, the more these natural experiments will be terminated by the spread of modern travel conveniences and civilization. Immediate investigation of inbred communities will thus save for science a large amount of data the value of which it is yet not possible to gauge.

But at the same time we must look to the future. Racial mixture certainly did occur in the past, but it is just as certainly taking place now on a greater scale than ever. If we cannot carry out human breeding experiments, Nature can and does, and it is our duty to investigate as thoroughly as possible, now, existing groups of people so that our successors shall have the valuable ground work from which to draw their conclusions when they have had the opportunity to examine the individuals resulting from racial mixtures at present being made.

(*To be concluded*)

STATISTICAL STUDIES OF PALMAR FORMULAE

by

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In previous articles (1) (2). a new method of expressing palmar formulae was described and it was claimed that one of the advantages over Wilder's method was that it admitted of much more statistical treatment than the older method did. In this paper it is intended to attempt to substantiate this statement by analysing the results given in one of the above mentioned articles (2) together with some more hitherto unpublished data, and it is claimed that the new method of treating the data makes palmar formulae much more exact and useful characters for anthropological genetical studies.

MEAN PALMAR FORMULA.

The first obvious application of this formula is the calculation of the mean palmar formulae for a group of individuals as shown in Table 1.

TABLE I.

Group		D_L	C_L	B_L	A_L	K_L	D_R	C_R	B_R	A_R	K_R
143 Natives of British North Borneo	Mean Value	3.15	2.30	1.88	1.11	4.89	3.44	2.54	1.98	1.41	5.16
	S.E. of Mean	.05	.04	.02	.02	.02	.06	.06	.03	.02	.01
53 North American Indians from British Columbia	Mean Value	3.43	2.79	1.91	1.26	5.02	3.78	2.93	2.20	1.56	5.23
	S.E. of Mean	.08	.07	.03	.03	.03	.09	.08	.06	.02	.01

Table I, in which is set out the mean value and its standard error for each palmar main line of both hands found amongst 143 natives of British North Borneo and 53 North Ameriian Indians from British Columbia. The main lines originating from the a, b, c, d and carpal tri-radii are indicated by the letters A, B, C, D and K respectively, the index L indicating left hand values and R those of the right.

The most obvious feature of the above data is the constant difference between the values of corresponding lines on the left and right hands, a difference shown in both the racial groups and graphically represented in Figure 1.

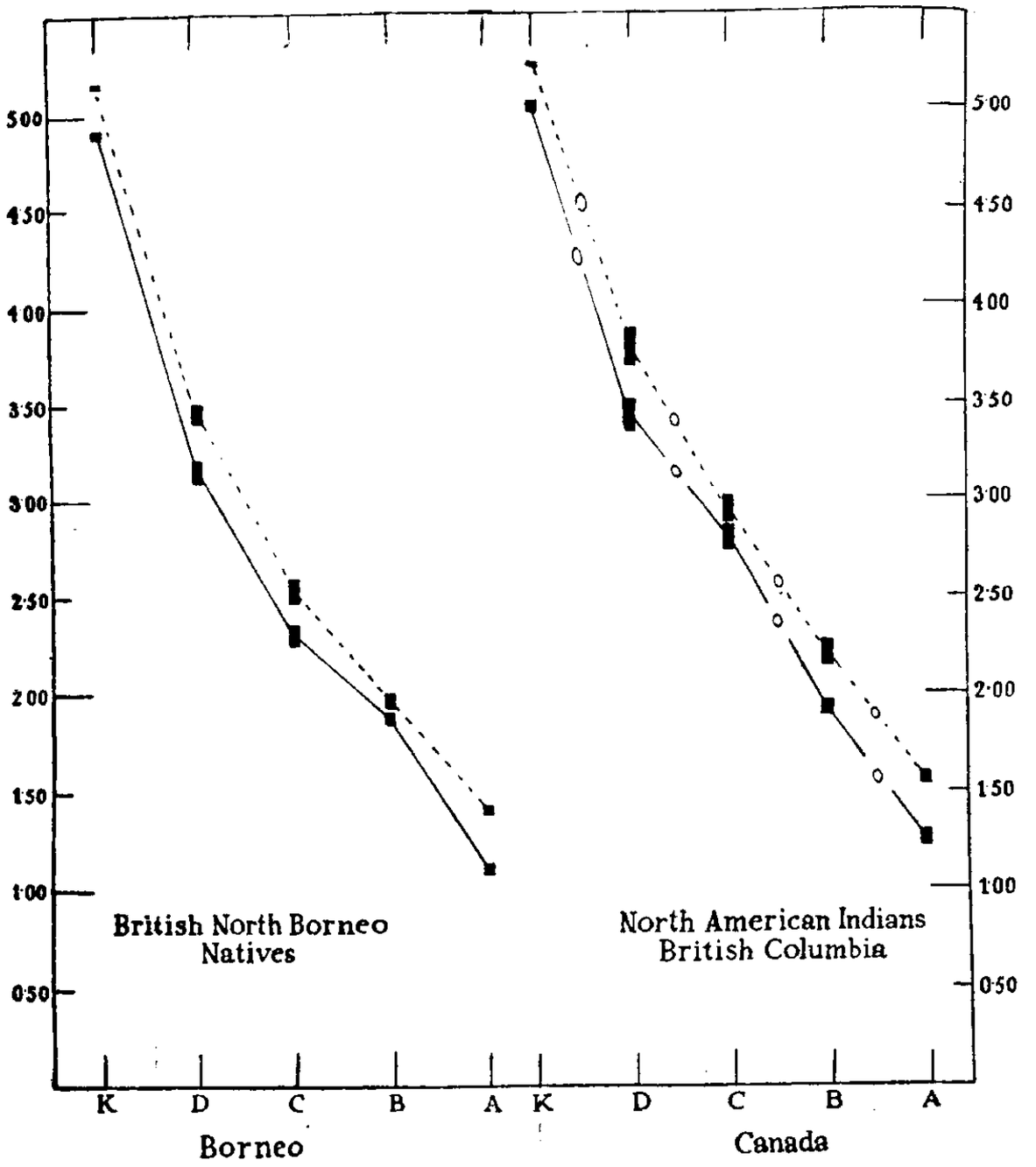

Figure 1. The vertical axis in this figure is divided off so as to be able to plot points whose distance from the horizontal axis is proportional to any value ranging from 0.00 to 5.+. Along the horizontal axis are marked points to represent the palmar main lines K, D, C, B & A. Opposite these points the centre of black rectangles marks the position of the mean value of the respective main lines, the height of the rectangle being roughly proportional to the standard error of the mean value. Graphs are formed by joining the centres of these rectangles by straight lines, the graph for the Borneo left hands being shown thus————————, Borneo right hands thus — — — — — — — —, North American Indian left hands thus ——— O ———, North American Indian right hands thus — — — O — — —.

The first question that arises from these data is whether this palmar asymmetry is real or whether it is merely due to the samples chosen. In Table II are set out the figures dealing with this question.

TABLE II.

Line	Frequency	Mean Value	Standard Error of Mean	Difference of Mean	Standard Error of Difference
D_L	137	3.145	.052	.290	.076
D_R	122	3.435	.056		
C_L	129	2.301	.044	.237	.070
C_R	117	2.538	.055		
B_L	130	1.882	.024	.099	.040
B_R	121	1.981	.033		
A_L	137	1.111	.020	.296	.027
A_L	129	1.407	.018		
K_L	139	4.888	.024	.275	.025
K_R	134	5.163	.009		

Table II, in which are compared the mean values of each left palmar main line with the mean values of the corresponding line on the right hand.

TABLE III.

Line	Frequency	Mean Value	Standard Error of Mean	Difference of Means	Standard Error of Difference
D_L	53	3.430	.076	.348	.116
D_R	53	3.778	.087		
C_L	53	2.785	.069	.144	.106
C_R	53	2.929	.081		
B_L	53	1.910	.033	.286	.066
B_R	53	2.196	.056		
A_L	53	1.258	.033	.297	.039
A_R	53	1.555	.020		
K_L	53	5.022	.031	.211	.032
K_R	53	5.233	.008		

Table III, in which the North American data are set out in the same way as the Borneo data in the last table. In this case however the difference between the C line values is not significant.

In the case of each main line, the right hand mean value is greater than that of the left hand, and in every case, with the exception of the C line in the Canadian series, this difference is more than twice its standard error. It is highly probable too that the difference in the C line would turn out to be significant if more cases had been available for examination. It is therefore claimed that this method has not only established the fact that there is a definite and significant asymmetry between the papillary ridge distributions on the two hands, but that this asymmetry can be accurately assessed quantitatively.

The frequency polygons given in the previous articles showed that the values of the D lines varied from 2.2 to 4.5, an expression of the fact that that line was found to end in the various individuals in the following three interdigital spaces, between *d* and *c*, *c* and *b*, and between *b* and *a*. It will be noticed that in arriving at the mean values, the integer values 2, 3 and 4, which are purely arbitrary, are calculated at their real numerical worth. The question arises therefore whether this is justified, and to answer it we shall have to see exactly what these integer values represent. In Wilder's method they are given to both *points* (*a*, b, *c* and *d* have values 11, 9, 7 and 5 respectively) and to *areas* (that between *d* and *c* having the value 6, that between *c* and *b* 8 and so on). They do not represent any units and are therefore not mathematically comparable. In the new method however, each integer is used to denote a morphological unit of the palmar skin (an area between two neighbouring tri-radii), and as long as this conception of the integers is remembered, their use as numerical values is justified. They are more than a mere re-numbering of Wilder's figures; they indicate the division of the palm into morphological units by means of the papillary ridge system, and that each ridge can be given a numerical value indicating its distance from an arbitrarily chosen zero point, measured in a definite direction and expressed in the above described units and fractions of a unit.

Whether the statistical methods used in this paper are applicable to data showing poly-modal frequency curves such as these do, is a question which will have to be left to more expert statisticians to decide, but in order to see whether this asymmetry was in any way due to this type of grouping, the Borneo data were rearranged into groups so that each group contained similar lines having similar integer values. Thus the first group contained all the D_L lines having values of 2, the second, D_L lines of values 3, and so on. The mean of each of these groups was ascertained and each left hand mean again compared with its corresponding right hand mean as before with the results as shown in Table IV.

TABLE IV.

Line	Integer Value	Frequency	Mean	S.E. of Mean	Difference of Mean	S.E. of Difference	Remarks
D_L	2	69	2.655	.019	.102	.031	S
D_R	2	43	2.757	.024			
D_L	3	40	3.379	.039	.068	.054	N.S.
D_R	3	45	3.447	.037			
D_L	4	28	4.146	.017	.088	.024	S
D_R	4	35	4.234	.017			
C_L	1	65	1.890	.010	.046	.013	S
C_R	1	40	1.936	.008			
C_L	2	50	2.565	.035	.051	.047	N.S.
C_R	2	49	2.514	.032			
C_L	3	14	3.262	.059	.178	.072	S
C_R	3	28	3.440	.041			
B_L	2	22	2.406	.043	.162	.062	S
B_R	2	32	2.568	.042			
B_L	1	108	1.775	.010	.046	.014	S
B_R	1	89	1.821	.010			
A_L	0	61	.912	.006	.020	.012	N.S.
A_R	0	5	.932	.010			
A_L	1	76	1.271	.021	.155	.027	S
A_R	1	124	1.426	.017			
K_L	4	59	4.607	.020	.181	.030	S
K_R	4	5	4.788	.023			
K_L	5	80	5.107	.007	.070	.009	S
K_R	5	129	5.177	.006			

Table IV. Here the main lines are grouped so that the values in each group have the same interger value. Thus the mean value of all the D lines ending between tri-radii 'd' & 'c' is shown separately from those ending between tri-radii 'c' and 'b' and these each separated from those between tri-radii 'b' and 'a'. These mean values for all lines on both left and right hands are given along with their standard errors, the differences between the two hands estimated, and their significance deduced.

The data detailed in Table IV show that the above mentioned palmar asymmetry is still in evidence even when the interger values are located separately and hence even if the objection to the method of ascertaining one mean value for each be sustained, the reality of this asymmetry remains unaffected.

In this Table special attention should be drawn to lines D, (value 3.+), C (value 2.+) and A (value 0.+). In one case, that of the C line

the mean right hand value is *less* than its corresponding left hand value. It will be seen however that the difference is not significant, the standard error of the difference being almost as great as the difference between the means. In the other two cases the difference shows the right hand values to be greater, but not significant. These results may therefore be best summarised by saying that in nearly every case the right hand value is greater than the left and in no case is the left significantly greater than the right. When greater numbers are published later perhaps a more precise general statement may be possible.

Naturally right handedness comes to mind when considering the significance of this finding and although this question is the subject of investigation at the moment, enough information has not yet been collected to warrant a statement on the correlation between these definite morphological and functional asymmetries. It should be noted that not only is this assymmetry shown in the mean values but, as previously stated, when similar lines are considered in separate individuals, the right hand value is generally higher than the left. If the individual be left handed it does not follow that the left hand has higher values than the right, but I have frequently found that if two or more of the lines on the left have higher values than the corresponding right hand lines, such an individual is often found to have some left hand tendencies.

SEX DIFFERENCES.

The next point brought out by this formula is the difference between the mean values for the two sex groups.

In Table V the mean value of each line in the male is different from the mean value of the corresponding line in the female but in no case is this difference between the sexes of any significance whatsoever; in many cases the standard error of the difference is many times the sex difference itself. To see whether any significant sex difference could be demonstrated by grouping in larger numbers, the data were rearranged as in Table VI.

It seems evident therefore that if there be a sex difference it is of such a small order that the numbers dealt with in this paper fail to reveal it. An attempt is being made at the present moment to settle this question one way or the other by collecting a large number of palm prints from families and comparing the mean results of the sisters with those of their brothers.

TABLE V.

LINES	MALES							FEMALES						COMPARISON OF SEXES		
	INTEGER VALUE	FREQUENCY	MEAN	STAND. ERROR OF MEAN	DIFF. OF MEAN	S. E. OF DIFF.	REMARKS	FREQUENCY	MEAN	S. E. OF MEAN	DIFF. OF MEAN	S. E. OF DIFF.	REMARKS	SEX DIFF.	S. E. OF SEX DIFF.	REMARKS
D_L	2	36	2.662	.029	.108	.042	S	33	2.649	.027	.094	.046	S	.013	.039	N. S.
D_R	2	21	2.770	.031				21	2.743	.037				.027	.048	N. S.
D_L	3	24	3.334	.041	.136	.066	S	16	3.446	.074	.046	.093	N. S.	.112	.085	N. S.
D_R	3	27	3.470	.051				18	3.400	.055				.070	.076	N. S.
D_L	4	20	4.140	.019	.081	.035	S	8	4.154	.040	.083	.053	N. S.	.014	.045	N. S.
D_R	4	21	4.231	.029				14	4.237	.035				.006	.045	N. S.
C_L	1	33	1.885	.016	.041	.021	N. S.	32	1.897	.013	.049	.015	S	.012	.020	N. S.
C_R	1	21	1.926	.013				19	1.946	.008				.020	.012	N. S.
C_L	2	28	2.558	.043	.085	.061	N. S.	22	2.569	.061	.008	.077	N. S.	.011	.075	N. S.
C_R	2	26	2.473	.042				23	2.561	.046				.088	.063	N. S.
C_L	3	11	3.257	.068	.151	.081	N. S.	3	3.280	.146	.217	.170	N. S.	.023	.161	N. S.
C_R	3	18	3.408	.043				10	3.497	.086				.089	.097	N. S.
B_L	1	59	1.769	.015	.051	.021	S	49	1.781	.011	.042	.014	S	.012	.019	N. S.
B_R	1	50	1.820	.014				39	1.823	.009				.013	.017	N. S.
B_L	2	14	2.415	.059	.142	.081	N. S.	8	2.390	.081	.192	.103	N. S.	.025	.100	N. S.
B_R	2	18	2.557	.056				14	2.582	.064				.025	.085	N. S.
A_L	0	35	0.910	.008	.040	.013	S	26	0.914	.008	.006	.014	N. S.	.004	.012	N. S.
A_R	0	2	0.950	.010				3	0.920	.012				.030	.015	N. S.
A_L	1	44	1.295	.027	.141	.036	S	32	1.236	.033	.177	.041	S	.060	.043	N. S.
A_R	1	71	1.436	.023				53	1.412	.025				.024	.034	N. S.
K_L	4	33	4.605	.028	—	—	N. S.	26	4.606	.029	—	—	N. S.	.001	.040	N. S.
K_R	4	2	4.825	—				3	4.763	—					—	N. S.
K_L	5	46	5.111	.009	.073	.012	S	34	5.101	.011	.069	.014	S	.010	.014	N. S.
K_R	5	72	5.184	.009				57	5.170	.008				.014	.012	N. S.

Table V. In this Table the data from the males are separated from those of the females and they are compared in the last three columns. It should be noticed that each interger value of each main line is treated separately and even in these circumstances, notwithstanding the small size of the resulting groups, the difference between the two sides is in many cases still significant. S = significant, N.S. = not significant. In no case is the sex difference found to be significant.

COMPARATIVE RACIAL STUDIES.

The next thing to consider concerning these formulae is the comparative racial results which they yield. From Table VII it in seen that

although the mean values differ in every case in the two Borneo tribes examined, in no case is this difference significant. Again smallness of numbers may be the reason, but it is hoped that work on some hundreds of these palms now nearing completion should decide the question. It seems likely that these two tribes may be so closely allied as to fail to reveal a difference of this type. That the method, however, is an important one and should provide a means of estimating quantitatively such racial differences where they exist, is shown in Table VIII.

TABLE VI.

Line	Freq.	Mean Value	Standard Error of Mean	Diff. of Means	S.E. of Diff.	Remarks
Male D_L	60	3.143	.080	.033	.114	N.S.
Female ,,	54	3.110	.081			
Male C_L	56	2.308	.072	.059	.095	N.S.
Female ,,	54	2.249	.062			
Male B_L	57	1.882	.039	.011	.051	N.S.
Female ,,	54	1.871	.033			
Male A_L	63	1.098	.027	.002	.040	N.S.
Female ,,	55	1.100	.030			
Male K_L	62	4.882	.034	.013	.050	N.S.
Female ,,	57	4.895	.037			
Male D_R	54	3.471	.082	.106	.121	N.S.
Female ,,	50	3.365	.088			
Male C_R	50	2.527	.084	.009	.117	N.S.
Female ,,	49	2.518	.082			
Male B_R	54	1.994	.048	.015	.069	N.S.
Female ,,	50	2.009	.050			
Male A_R	61	1.421	.025	.039	.038	N.S.
Female ,,	53	1.382	.028			
Male K_R	65	5.168	.011	.023	.018	N.S.
Female ,,	57	5.145	.014			

Table VI. Mean values for each main line have been calculated and grouped according to sex. These values are shown compared. in this table, but in no case is the sex difference found to be significant.

This table shows that in the case of every main line the mean value is greater in the group of Canadian Indians studied than in the Borneo group, and that with the exception of the B-line on the left hand, the difference is definitely significant. What this difference may mean we cannot begin to discuss here; we merely wish to make the point that by this method we have not only given expression to a racial difference but have measured it quantitatively with a reasonable amount of accuracy.

CORRELATION STUDIES.

The increased exactitude of this method makes the study of palmar patterns of definite value in a number of scientific directions. First of all in the study of genetics. Exact values for the main lines can be given to the parents and children and in this way the problem of the inheritance of these characters may be investigated. Especially valuable should this method prove to be in the studies of plural births and a study of the formulae obtained from some 50 pairs of twins is now being completed in this department. In this connection the question of body asymmetry is also being kept in mind and the quantitative nature of this formula should make its use in investigating asymmetry valuable.

TABLE VII.

Line	Freq.	Mean Value	S.E. of Mean	Diff. of Mean	S.E. of Diff.	Remarks
Dusun D_L	55	3.20	.075	.1453	.105	N.S.
Murut D_L	59	3.05	.073			
Dusun C_L	52	2.30	.067	.0395	.094	N.S.
Murut C_L	58	2.34	.066			
Dusun B_L	52	1.91	.041	.0704	.052	N.S.
Murut B_L	59	1.84	.032			
Dusun A_L	58	1.10	.026	.0097	.039	N.S.
Murut A_L	60	1.09	.029			
Dusun K_L	58	4.91	.035	.0519	.049	N.S.
Murut K_L	61	4.86	.034			
Dusun D_R	49	3.48	.089	.1079	.122	N.S.
Murut D_R	54	3.37	.084			
Dusun C_R	47	2.57	.088	.0987	.119	N.S.
Murut C_R	52	2.48	.080			
Dusun B_R	50	2.03	.048	.0464	.070	N.S.
Murut B_R	54	1.98	.050			
Dusun A_R	55	1.41	.028	.0032	.038	N.S.
Murut A_R	59	1.41	.026			
Dusun K_R	60	5.16	.014	.0034	.018	N.S.
Murut K_R	62	5.16	011			

Table VII. In this Table are given the mean values for all the main lines, the values given by Murut hands being given separately from those of the Dusuns. The Standard Errors (S.E.) of the mean and the Standard Error of the difference between the tribal means are given together with the significance (N.S.=not significant) of these differences.

TABLE VIII.

Line	Freq.	Mean Value	S.E. of Mean	Diff. of Means	S.E. of Diff.	
Borneo D_L	137	3.145	.052	.285	.091	S.
Canada ,,	53	3.430	.076			
Borneo C_L	129	2.301	.044	.484	.081	S.
Canada ,,	53	2.785	.069			
Borneo B_L	130	1.882	.024	.028	.041	N.S.
Canada ,,	53	1.910	.033			
Borneo A_L	137	1.111	.020	.147	.039	S.
Canada ,.	53	1.258	.033			
Borneo K_L	139	4.888	.024	.134	.039	S.
Canada ,,	53	5.022	.031			
Borneo D_R	122	3.435	.056	.343	.104	S.
Canada ,,	53	3.778	.087			
Borneo C_R	117	2.538	.055	.391	.098	S.
Canada ,,	53	2.929	.081			
Borneo B_R	121	1.981	.033	.215	.065	S.
Canada ,,	53	2.196	.056			
Borneo A_R	129	1.407	.018	.148	.027	S.
Canada ,,	53	1.555	.020			
Borneo K_R	134	5.163	.009	.070	.012	S.
Canada ,,	53	5.233	.008			

Table VIII, in which are compared the main line values of the Canadian Indians and the Borneo Natives. S = significant, N.S. = not significant.

As a first step towards the solution of the inheritance of palmar patterns, the data in this study were subjected to correlation studies as follows. The correlation coefficients between each line and every other line were ascertained and are set out in Table IX together with their standard errors. Unfortunately tables are not accessible here to estimate the values of P in each case, but considering the number of pairs is about 130 in each case, it is certain that P is definitely less than .01 in all cases where the coefficient is greater than .25.

Table IX shows how the palmar main-lines may be divided up into two big groups, the first group being comprised of lines A_L, A_R, K_L, K_R, and the second group D_L, D_R, C_L, C_R, B_L, B_R, and the line values are such that the coefficient of correlation between any two belonging to the same group is greater than +0.5 while that of two lines each belonging to different groups is less than +0.5. The greatest correlation is found between lines of the same group on the same hand, the next between lines of the same group on opposite

hands and the least between lines of opposing groups on the same hand and opposing groups on opposite hanls. This seems to indicate that the ridge distribution found on the palm is derived from two systems, an ulnar system covering the area of distribution of main lines D, C, & B, and a radial one covering the area limited by the distribution of main lines A & K. The genetical application of this is obvious for if these ridge distributions are in any way inherited. we might expect the inheritance of the palmar ridge system as a whole to depend on two sets of factors at least, one for the radial and one for the ulnar ridges.

	D_L	C_L	B_L	A_L	K_L	D_R	C_R	B_R	A_R	K_R
D_L		+.83±.03	+.83±.03	+.39±.07	+.23±.08	+.68±.03	+.55±.03	+.67±.05	+.27±.08	+.27±.08
C_L			+.65±.05	+.30±.08	+.14±.09	+.50±.02	+.48±.06	+.60±.06	+.24±.08	+.26±.08
B_L				+.21±.05	+.16±.08	+.61±.06	+.53±.07	+.66±.03	+.35±.08	+.34±.08
A_L					+.78±.03	+.33±.08	+.26±.09	+.38±.08	+.59±.06	+.57±.06
K_L						+.20±.09	+.17±.09	+.26±.09	+.53±.06	+.65±.03
D_R							+.79±.03	+.79±.03	+.27±.08	+.28±.08
C_R								+.74±.04	+.26±.09	+.27±.09
B_R									+.35±.08	+.30±.08
A_R										+.70±.04
K_R										

Table IX showing the correlation coefficient between the value of each main line and every other main line together with the standard error of the coefficient. The shaded areas in the lower left of the table show those pairs of lines between which the correlation coefficient is greater than .5

That hereditary factors are not the only ones to play a part in the development of these systems however is shown by the asymmetry found to exist between left and right hands. Environment is also playing a definite part, and hence we do not expect to find one hand the mirror image of the other, much less would we expect such imagery to be evidenced by the ridge systems of uniovular twins. This environmental effect is very important because were it not for its existance identical patterns would be a possibility with the consequent undermining of the whole foundation of the use of finger and palm prints in personal identification.

CONCLUSIONS.

The new method of expressing the distribution of the papillary ridges on the hand provides a formula for each individual palm which is exact enough to be used as a basis for personal identification and the formula is of a type which allows of such statistical treatment as to permit mean formulae for groups of individuals to be calculated. Such statistical treatment reveals a constant asymmetry between the left and right hands, by virtue of which the ridges on the right hand tend to be arranged in a more transverse direction than those of the left. Whether this asymmetry is at all correlated to right-handedness remains to be proved.

When the mean formulae of groups drawn from natives of British North Borneo and North American Indians are compared, a significant difference is found to exist between the two and this method of expressing ridge distributions of the palm provides a quantitative character of use in anthropological studies. The use of this formula however fails to detect any significant difference between two of the main tribes of British North Borneo, the Dusuns and the Muruts.

More detailed treatment of the data fails to uphold the suggestions made in an earlier paper that these formulae may reveal the presence of a sex difference in the hands.

Correlation studies show that the palmar main lines of the hands may be divided up into two groups, the A & K lines of both hands being in one group and the D, C & B lines in the other. Since the correlation values between similar lines on the two hands are all rather high, it seems likely that the ridge distributions are to some extent due to hereditary factors, one factor or group of factors controlling the ridges adjacent to the A & K lines and the other those near the D, C & B lines.

This more exact formula when applied to family and twin data should help to provide a means of investigating the exact part that hereditary plays in the formation of ridge patterns on the skin of the human hand.

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Review of Books.

Manipulative Methods in the Treatment of Functional Disease by Edwin L. Hopewell-Ash, John Bale Sons & Danielsson, Ltd., London, 1935. Price 3/6 net.

This is a useful little handbook and should prove of real value to those who have found that the treatment of Functional Disease by ordinary therapeutic means has been unsuccessful.

The brief outline of the methods used is not likely to be of much practical value to the average practitioner. Such methods can be successful only in the hands of one who, like the author, has devoted himself to the special study of the treatment of functional disease. Much depends on the personality of the practitioner and "suggestibility" of the patient. There is, no doubt, much scope for the further study and improvement in methods of neuromedical treatment. This small volume should prove of much interest to all psychotherapists.

W. I. G.

Melancholia in Everyday Practice by Edwin L. Hopewell-Ash, M.D. (Lond.). London, John Bale Sons & Danielsson, 1934. 136 p. price 7/6.

The author bases this "clinical review" on twenty-five years "medico-psychological" practice. He first deals with the clinical characteristics of melancholia, of which he differentiates seven types and in addition to these five further "forms of mild psychosis of definitely melancholic type." A number of clinical pictures are given as illustrations. In the third chapter the modern conception of melancholia and mania is discussed as expressions of the same basal mental disease, known by the term manic depressive psychosis. The next chapter is wholly dedicated to the discusssion of involutional melancholia, the melancholia par excellence of the older schools, which considered this disease as a separate psychopathological group. Then follow three chapters on diagnosis and differential diagnosis, a note on dilusions and hallucinations, and at last treatment and etiology are discussed.

Kraepelin, whose classification the author follows in his book in principle, emphasized the need of discarting the dissecting of too many separate groups by showing that types of an apparently different nature may pass into another in one and the same case. In reading the present book the reviewer, who himself is an old pupil of Kraepelin, feels that the author by working out a dozen types of very uncertain limitations does not help to make the subject simpler and clearer. By further using the term melancholia as a symptom and then again as a type

or undergroup of a psychotic entity he makes reading for the student rather confusing. For another edition the reviewer would recommend the elimination of unnecessary repetitions and rearrangement of chapters. For example, chapter 3 would serve as a better introduction into the subject than chapter one of the present arrangement.

M. O. P.

Medicine for Nurses by W. Gordon Sears. Messrs. Edward Arnold & Co., London 1935. 8/6 net.

The author of this book of 412 pages set himself the task of collecting "the essential facts of medicine for the nurse who is taking her course of medical lectures" and presenting these in book form. In the Introduction definitions, pathology, bacteriology, immunology, therapeutics and classification of diseases are all dealt with in 24 pages. Then follow chapters dealing with diseases of the various systems in the ordinary test book manner. A chapter on Materia Medica, four pages of tables, medical terms and abreviations in common use, caloric values of some of the more common foodstuffs, and an index, complete the book. Of the result, and of the way in which the subject matter is set out and treated, we have nothing but praise and practically the only criticisms we can make are that the mid-brain might be mentioned as a part of the brain stem and in the paragraph on "The Sensory Path" on p. 278 no mention is made of the lateral columns.

The most striking result of reading such a book as this however is the realisation of what a nurse is expected to know in these days. From statements such as "The nurse learns about reflex action in physiology" one gathers that the budding nurse has texts books in Anatomy and Physiology to deal with as well, and one rather wonders if she has any time for the real part of her profession, viz., nursing, and whether the product of this system will not be more a doctor than a nurse. Certainly the way in which this book is written bears out this contention, because the wording is typically that of a medical text book and could only be fully appreciated by one who had been steeped like a medical student in medical literature for years. This however is not a criticism of the book but of the system which prompted its author to write it. It could not only be used by nurses, but by junior medical students as a general introduction to their clinical medical studies.

L. T. R.

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