BRITISH MEDICAL JOURNAL

LONDON SATURDAY AUGUST 6 1955

SOME NEW DISEASES IN PAEDIATRICS*

BY

JAMES H. HUTCHISON, M.D., F.R.C.P., F.R.F.P.S.

Visiting Physician, Royal Hospital for Sick Children, Glasgow; Gow Lecturer on Medical Diseases of Infancy and Childhood, University of Glasgow

In the twenty-odd years since I qualified in medicine the practice of paediatrics has undergone profound change. Some of the diseases which were commonplace in my resident days have become rarities; others, while still of frequent occurrence, have all but lost their power to kill. Infantile rickets due to vitamin-D deficiency has disappeared from the city where Leonard Findlay and Noel Paton found so much clinical material. We no longer have the dreadful epidemics of gastro-enteritis which used to carry off hundreds of infants each autumn. Pneumonia is still common enough but is now rarely fatal, save in the neonatal period. Marasmus, of course, is not a disease but a clinical state of wasting or atrophy. We used to see many marasmic infants, and the most common causes of their feeble and miserable state were underfeeding and infection. To-day, infant feeding is not often a problem, and most infections can be cured before they have led to serious tissue-wasting.

The "new" diseases which I wish to discuss have been thrown into focus largely as a result of these changes in the paediatric picture. For example, marasmus is now more often due to diseases such as pancreatic fibrosis, hyperchloraemic acidosis, and idiopathic hypercalcaemia than to incorrect feeding or infection. When we see a case of rickets to-day it is more probably due to renal glomerular or tubular deficiency than to vitamin deficiency. The rapid response of pneumonia to antibiotics is now so much the rule that we have learned to suspect the existence of a fibrocystic pancreas when such response fails to take place.

Other influences at work in helping to define these new clinical entities, and running concurrently with the changing incidence of disease, have been the technical advances of the biochemist, the pathologist, and the radiologist.

Fibrocystic Disease of the Pancreas ("Mucosis")

This disease has an incidence of at least 1 in 1,500 new births (Bodian *et al.*, 1952). It is inherited as an autosomal recessive characteristic, and the gene is carried by about 1 in 50 of the population. An affected infant is the result of the mating of two carriers. The chances of any child of such parents being affected by the disease is 1 in 4. Although Dorothy Andersen has considered it to be a primary pancreatic disorder (Andersen, 1938; Andersen and Hodges, 1946), many

paediatricians now incline towards the view that there is a generalized disorder of the mucous glands throughout the body (Farber, 1944), hence the names "mucoviscidosis" and "mucosis." This might be due to the absence of an enzyme concerned in mucus production or to the absence of a mucinase so that the mucus is scanty and excessively viscid (Norman, 1954).

Pathology.—The pancreas is consistently abnormal. It may show cystic dilatations of acini and ducts which contain eosinophilic material having a homogeneous, granular, or laminated appearance, but cystic change is not a constant feature, and in many cases fibrosis and atrophy of the exocrine parenchyma are the essential changes. The islet cells are not involved. Another typical and often widespread change is distension with mucus of the salivary glands and the mucous glands of the bronchi, oesophagus, duodenum, and gall-bladder. An inborn dyscrasia of the sweat glands may explain the recent observation that in this disease there is an excessive loss of sodium, chloride, and potassium from the skin (Darling *et al.*, 1953). Respiratory infection by the *Staphylococcus aureus* is so frequent as to be part of the disease. It produces widespread bronchiolitis with obstructive emphysema and patchy atelectasis. The bronchioles are plugged with viscid mucus. It may go on to bronchiectasis or multiple abscesses—less commonly to alveolar consolidation, empyema, and spontaneous pneumothorax. A rather characteristic finding is squamous metaplasia of the bronchial epithelium, which is probably due to a combination of chronic sepsis and vitamin-A deficiency.

Clinical Picture.—As we might expect from these widespread tissue changes, the clinical patterns of the disease may vary widely. They can conveniently be described, as they tend to appear at four different age periods, although there is, of course, considerable overlapping.

Meconium Ileus.—The disease may appear within a few hours or days of birth as an acute intestinal obstruction with bilious vomiting, gross abdominal distension, and absolute constipation. Rectal examination reveals only a little inspissated mucus. X-ray examination of the abdomen shows gaseous distension and fluid levels, and a typical but not constant sign is the appearance of minute gas bubbles in the inspissated meconium which is causing the obstruction. Meconium ileus must be distinguished from other causes of neonatal obstruction, particularly Hirschsprung's disease; in the former, a small barium enema will show a congenital microcolon, whereas in the latter the large-bowel appearances at birth will not be greatly abnormal (Ehrenpreis, 1955). Occasionally meconium ileus is associated with antenatal perforation of the small bowel, which results in *meconium peritonitis*. The infant presents at birth with a grossly distended abdomen, a fluid thrill can be elicited, and x-ray examination shows a fine widespread peritoneal calcification. Although the perforation has usually sealed itself before birth, it may fail to do so, in which case

*Abridged from a postgraduate lecture delivered before the Royal Faculty of Physicians and Surgeons of Glasgow on March 18, 1955.

bacterial peritonitis develops within a few hours of birth. In these circumstances x-ray examination shows free fluid and air within the peritoneal cavity.

Intractable Respiratory Infection.—Very often the first signs of disease appear in the early weeks or months after birth in the form of an acute respiratory illness. The outstanding features are severe dyspnoea and expiratory wheezing. There may be little fever. The chest is often "blown up" with obstructive emphysema, and commonly there is marked subcostal and suprasternal retraction due to bronchiolar obstruction. The clinical signs over the lungs, especially sticky rales and rhonchi, are often much more striking than the x-ray appearances, which may show only hypertranslucency due to emphysema. In fact, one or other lung may herniate into the mediastinum. At a later stage the x-ray films show a rather typical streaky appearance radiating outwards from the lung roots and due to interstitial infection and fibrosis. This may be followed by multiple "soft" opacities representing small abscesses or bronchiectasis. In a few cases the onset takes the form of an acute pneumonic consolidation which may be complicated by empyema. As in other staphylococcal infections of the lung, a spontaneous pneumothorax may produce a sudden emergency. A pointer to the true diagnosis may be found in the infant's stools, which are often, but not always, greasy and possessed of a strikingly foul odour. In its absence the diagnosis may yet be suspected when it is found that antibiotics in adequate doses afford the infant but little relief from his acute distress.

Marasmus and Steatorrhoea.—Although steatorrhoea is present from birth, the excellent, and at times ravenous, appetite of these infants in the absence of severe respiratory infection may prevent serious wasting during the period of pure milk-feeding. After the age of 4 months or thereabouts, the introduction of cereals to the diet results in the stools becoming frothy, foul-smelling, and often loose. The typical combination of failure to thrive, excellent appetite, and excessively foul stools in the first year of life should always suggest the diagnosis of pancreatic fibrosis.

The Coeliac Syndrome.—With milder degrees of the disease the child may not reach the physician until the toddler age, when he appears wasted and underdeveloped, with a distended abdomen, and passes frothy or greasy semi-formed foul-smelling stools. The unwary may make a diagnosis of idiopathic coeliac disease, but the differential diagnosis can be made on clinical grounds alone. In pancreatic fibrosis a careful history will reveal that symptoms first appeared in the early weeks of life, whereas coeliac disease rarely presents before the age of 9 months. The excellent, often voracious, appetite in pancreatic fibrosis is in marked contrast to the unhappy anorexia of the coeliac child. Chronic respiratory infection with a spasmodic harsh unproductive cough is rarely absent in pancreatic fibrosis; it is not a feature of coeliac disease. Severe hypochromic anaemia is common in coeliac disease, rarely seen in pancreatic fibrosis. Finally, as pancreatic fibrosis is a familial disease there is often a history to suggest that previous infants have been similarly affected—for example, of death in the neonatal period or of death from pneumonia in the early months. It is rare to see more than one child with coeliac disease in a family. Faecal fat analysis will not serve to distinguish the two diseases, as in pancreatic fibrosis the excess fat in the stools may be normally split despite the lack of pancreatic secretion.

Diagnosis.—The final proof of the diagnosis rests upon the finding that trypsin is absent, or present only in very low titres (under 1 in 50), in the duodenal juice obtained by aspiration (Andersen and Early, 1942). The aspiration of scanty and viscid duodenal juice is sometimes difficult in this disease, but, in my experience, it is not necessary or particularly helpful to resort to fluoroscopy during this manoeuvre. The faeces may also be tested for proteolytic activity (Emery, 1952), although this may be due on occasion to bacterial enzymes and not to trypsin. However, in children under 2 years of age the finding of proteolytic

activity in high titres excludes fibrocystic disease of the pancreas, and this simple technique is a useful screening test which can be used to avoid some unnecessary and time-consuming duodenal intubations. The failure of the faeces to digest gelatin at a dilution above 1 in 50 in three consecutive specimens is strong presumptive evidence of pancreatic fibrosis, but I am always hesitant to accept as firm a diagnosis which is not based on the examination of the duodenal juice. Other diagnostic tests, such as vitamin-A absorption, amino-acid absorption curves, glucose tolerance, microscopy of the faeces, and the like, are probably not worth the trouble involved for routine work.

Prognosis.—So far as I am aware no child has ever been cured of this disorder, although, in many, life has been prolonged for years and been made immeasurably happier. Perhaps the majority of these unfortunate children die in infancy of progressive lung destruction. In older children, some of whom are reaching puberty, the chronic lung fibrosis results in death from cor pulmonale.

Treatment.—The neonatal emergencies come within the province of the paediatric surgeon. He has achieved some remarkable results in patients who have reached him soon enough after birth. After this stage there must be two aims in the treatment of these children—the prevention or control of respiratory infection and the maintenance of reasonable nutrition. Neither is fully within our present capabilities. None the less, the outlook has been vastly improved by the broad-spectrum antibiotics—chlortetracycline, oxytetracycline, and chloramphenicol. Penicillin, given intramuscularly or in aerosol form, has proved of very limited value, although in some patients it may usefully be combined with streptomycin. Periodic laboratory tests of the sensitivity of the staphylococcus, cultured from pharyngeal or laryngeal swabs, enable us to use the available antibiotics, singly or in combination, to the best advantage. Strain resistance is probably less of a problem if exacerbations of respiratory infection are treated as they occur than if, as is commonly practised, permanent antibiotic prophylaxis is attempted. A high-protein intake is rational, but there is probably no advantage in strict limitation of fat. Triple-strength pancreatin in the form of enteric-coated granules seems to be of value in some patients. Infants should be given 15–45 gr. (1–3 g.) in each feed; older children may be coaxed to ingest double this amount. A water-soluble preparation of vitamins A and D should also be prescribed.

There can be no doubt that the future of these children is influenced more by the degree of respiratory infection and the extent to which it can be kept under control than by any other therapeutic measures. Good hygienic surroundings naturally improve the prognosis by diminishing the chances of exposure to infection. For the same reason, it is wise to limit the stay of these patients in hospital to the minimum, and, when they must be admitted, to isolate them in cubicles whenever possible.

Infantile Renal Acidosis (Hyperchloraemic Acidosis)

I imagine that even the least chemically minded of physicians must be intrigued when an infant goes into a state of chronic acidosis and dehydration in the absence of any excessive loss of fluid or electrolytes from diarrhoea or vomiting, in the absence of an excessive intake of acid-producing substances, and despite an adequate intake of water and salt (Butler *et al.*, 1936; Hartmann, 1939; Latner and Burnard, 1950; Hutchison and MacDonald, 1951; Doxiadis, 1952; Lightwood *et al.*, 1953). He finds a clue when he discovers that this acidotic infant habitually passes an alkaline urine.

Clinical Picture.—The age of onset is between 4 months and 1 year. An infant who has been making satisfactory progress develops anorexia, occasional vomiting, and constipation without obvious cause. The constipation is severe and the abdomen is found to contain many small hard faecal masses. Weight loss is inevitable. Irritability is often in striking contrast to previous contentment. Observation

reveals a dehydrated infant with sunken eyes, dry inelastic skin, pale greyish complexion, and a diminutive appearance which itself often suggests the diagnosis to the thoughtful clinician. Inconstant features are the sighing respirations of acidosis, excessive thirst, and recurrent bouts of unexplained fever. The urine when passed will be found to be neutral or alkaline, and in some cases there is also a low-grade urinary infection with a resultant but often rather unimpressive pyuria.

Blood Chemistry.—The constant diagnostic finding is lowering of the plasma bicarbonate level, which is indicative of a state of metabolic acidosis. The plasma chloride level is usually, but not in every patient, considerably raised. The blood urea may be above normal. Other chemical levels are not affected.

Aetiology.—It would appear that in this disease the proximal renal tubules lose the ability to reabsorb bicarbonate from the glomerular filtrate, the acidosis being brought about by the constant drain of body base from the kidneys (Hartmann, 1939; Latner and Burnard, 1950). It is not known why this defect occurs; presumably it is acquired, not congenital. A fall in the incidence of this disease has occurred in the past year or so. It has been suggested that this may be related to the withdrawal of mercury from some popular "teething powders." A similar dysfunction with identical chemical changes in the blood has been described in older people (Baines *et al.*, 1945; Albright *et al.*, 1946). In them, however, the clinical picture has taken the form of osteomalacia or nephrolithiasis, and is quite dissimilar to that seen in young infants. It seems possible that these two very different clinical entities represent the same abnormality in body function, the effects being determined by the age at which it appears.

Pathology.—In the fatal cases necropsy always reveals a fine calcinosis confined to the renal medulla. It has only rarely been radiologically demonstrable during life. The calcium is deposited in and around dilated distal tubules, and is presumed to be an effect, not the cause, of the disease. Nephrocalcinosis is not, of course, confined to hyperchloraemic acidosis, but is found in several other unrelated diseases.

Treatment.—Prompt improvement may be expected to follow the administration of alkali, either as sodium bicarbonate 15–45 gr. (1–3 g.) four-hourly, or as Shohl's solution (10% sodium citrate and 6% citric acid), 60–120 ml. in divided doses. The dose should be sufficient to raise the plasma bicarbonate to 45 vols. per 100 ml. (20 mEq per litre), and it should be regulated by frequent blood estimations until ultimate recovery takes place. The alkali should only be gradually withdrawn, when weight gain is satisfactory and the plasma bicarbonate remains within normal limits.

Idiopathic Hypercalcaemia

Lightwood (1952) described a syndrome—"idiopathic hypercalcaemia with failure to thrive"—in infants who showed no obvious evidence of any of the known causes of hypercalcaemia such as hyperparathyroidism, hypervitaminosis D, excessive ingestion of alkali and milk, prolonged immobilization, sarcoidosis, and the like.

Clinical Picture.—The age of onset is often as early as 6 weeks. The disease has not been described in a wholly breast-fed infant. The clinical findings are almost identical with those in hyperchloraemic acidosis. They have been well described recently by Lowe *et al.* (1954) and Creery and Neill (1954). There are, however, some points of dissimilarity which, although not perhaps of diagnostic value, can often be noted. The hypercalcaemic infant is usually strikingly apathetic, which contrasts with the irritability of the acidotic infant. In hypercalcaemia, muscular hypotonia may be so severe as to lead to a suspicion of amyotonia congenita, whereas dehydration is often absent unless vomiting has been severe. The complexion of the baby with a high serum calcium is pink, whereas in acidosis pallor is more typical. The urine in hypercalcaemia is acid when passed; it may contain a little excess protein, and mild infection is not infrequent.

Blood Chemistry.—The differential diagnosis from hyperchloraemic acidosis rests upon the blood chemical findings. The plasma bicarbonate and chloride levels are usually normal, but the serum calcium level is raised above 12 mg. per 100 ml. and there is azotaemia. The plasma proteins are often raised, and it can be shown by paper electrophoresis that this is mainly due to a rise in the α_2 -globulin and sometimes also in the γ -globulin.

Aetiology.—It has been suggested that there may be an abnormal sensitivity to vitamin D. Certainly, many infants now receive more vitamin D than is strictly necessary for health, because most dried milks are fortified with calciferol and most bottle-fed infants receive further supplies in the form of official or proprietary preparations. There is evidence also that excessive calcium is absorbed from the gut by these infants, who have all been fed with cow's milk, which contains four times as much calcium as human milk. It is just possible that the very measures which we have used to abolish rickets from the land may have resulted in the appearance of hypercalcaemia in some susceptible infants.

Pathology.—The disease is rarely fatal, but nephrocalcinosis has been found in all such cases.

Treatment.—There is at present no treatment of proved value. The benign course towards eventual recovery over a period of some months makes assessment of therapeutic attempts difficult. A specially prepared low-calcium milk (Ferguson and McGowan, 1954) and cortisone (Anderson *et al.*, 1954) have been recommended; one is laborious to prepare, the other carries well-recognized risks.

Idiopathic Hypercalcaemia with Osteosclerosis

Fanconi *et al.* (1952) described the cases of two patients with hypercalcaemia who showed several abnormalities in addition to those which I have just described. Other workers have since reported similar cases (Creery, 1953; Dawson *et al.*, 1954; Lowe *et al.*, 1954). The main points in the clinical picture are physical and mental retardation, microcephaly, an abnormal facies and low-set ears, hypotonia, hypertension, and a loud precordial systolic murmur, and a most striking degree of osteosclerosis. The bones show sclerosis at the base of the skull, in the vertebrae, the shafts of the long bones, and the epiphyses, and the appearances somewhat resemble those seen in Albers-Schönberg disease. In addition to hypercalcaemia and a raised blood urea there is hypercholesterolaemia. It is not yet clear whether these cases, which run a progressive course to death, represent a difference in severity or in aetiology from the more common benign idiopathic hypercalcaemia.

Lignac-Fanconi Syndrome (Cystinosis)

This familial disease was described by Fanconi (1931) under the name "non-diabetic glycosuria in childhood." Since then it has come to be realized that most if not all of these cases are associated with the widespread deposition of cystine throughout the tissues. Lignac (1924) had, in fact, described cystinosis long before. Bickel *et al.* (1952), in their exhaustive account of the disease, regard the demonstration of cystine deposits as essential for diagnosis. They present evidence to indicate that this severe metabolic disorder is inherited as a simple Mendelian recessive character. They suggest an incidence of around 1 in 40,000 of the population and a gene-carrier rate of 1 in 100. The Lignac-Fanconi syndrome, which is a severe upset of metabolism, is quite a separate disease from the benign inborn error of metabolism called cystinuria in which excessive amounts of cystine are excreted in the urine, but in which cystine crystals are not deposited in tissue cells outside the kidneys.

Pathogenesis.—There is still much uncertainty about the nature of the metabolic disorder in this complicated disease. The hypothesis that there is a primary renal tubular deficiency in the reabsorption of glucose, phosphate, body bases, and amino-acids would account for the known biochemical abnormalities, but it fails to explain the cystinosis. An alternative and probably more tenable theory is that there is

a block in protein synthesis, so that the amino-acids collect in the body fluids; these are excreted in excess in the urine, and cystine, owing to its insolubility, is deposited intracellularly.

Clinical Picture.—It is only possible for me to outline briefly the wide variations in clinical signs which may be produced. They have received detailed attention from McCune *et al.* (1943) and Bickel *et al.* (1952). The first evidence of the disease may appear in infancy, usually after the first six months of life, as an acute disorder with acidosis, dehydration, thirst, and polyuria, anorexia, vomiting, constipation, pyrexial bouts, and failure to thrive. In fact, it may not be clinically distinguishable from hyperchloraemic acidosis or hypercalcaemia, although in these diseases there is no amino-aciduria or glycosuria. In older children there will be dwarfism, and often bone deformities, vitamin-D refractory rickets, or pathological fractures. A quite characteristic but not constant sign is photophobia, which is caused by deposits of cystine crystals in the cornea, iris, and conjunctiva. This form of the disease must be clearly separated from the so-called "renal rickets" of chronic glomerular insufficiency, in which amino-aciduria, glycosuria, and cystine storage do not occur.

Chemical Picture.—Bickel *et al.* (1952) point out that no single chemical change is constantly found in cases of this disease. The typical findings in the urine, which is alkaline when passed, are albuminuria, excess amino-aciduria, glycosuria, and hyperphosphaturia. Several specimens may have to be tested by sensitive methods such as paper chromatography (Dent, 1946) before these features are revealed. Up to twenty amino-acids may be excreted in excess, especially proline, leucine, valine, lysine, serine, cystine, threonine, glutamine, and alanine. The typical blood changes are lowered plasma bicarbonate due to metabolic acidosis, low plasma phosphorus, and low serum potassium levels. The blood urea may rise in the course of the disease. As renal failure supervenes there may develop hyperphosphataemia and hypocalcaemia, when the blood chemistry comes to resemble that seen in "renal rickets" due to glomerular inadequacy.

Diagnosis.—The demonstration of cystine storage should be regarded as the final proof of Lignac-Fanconi disease. This may be achieved in various ways: (1) Crystalline deposits may be seen in the eye with the slit-lamp. They may be identified as cystine by x-ray diffraction photography of a conjunctival biopsy specimen. (2) Thick bone-marrow smears may be examined for cystine crystals after fixation in absolute alcohol and staining with a solution of 0.5 g. basic fuchsin in 100 ml. of 50% alcohol. Cystine is dissolved out of tissues by routine fixatives and stains. (3) Microscopical examination of a lymph node.

Prognosis.—In the acute infantile form of the disease death occurs from acidosis and hypopotaemia, often aggravated by infection. The older children die ultimately of chronic progressive renal failure.

Treatment.—Healing of the rickets can be achieved by massive doses of calciferol (50,000 to 600,000 units daily). Acidosis should be corrected by Shohl's solution. If there is a lowered serum potassium, some of the sodium citrate may be replaced by the potassium salt. Strict blood chemical control is necessary. We cannot yet talk in terms of cure, but life can be prolonged along these lines.

Conclusion

It has been possible for me to outline only a few of the new diseases which have been defined within recent years. There are quite a few others, such as galactosuria (Holzel *et al.*, 1952), neonatal diabetes mellitus (Wylie 1953), sucrosuria (Moncrieff and Wilkinson, 1954), toxoplasmosis (Hutchison, 1949), and agammaglobulinaemia (Hayles *et al.*, 1954), most of which have been less fully studied up to the present. They may serve to refute the suggestion, made at times, that there is little left for the astute investigator in the field of curative paediatrics.

REFERENCES

- Albright, F., Burnett, C. H., Parson, W., Reifstein, E. C., and Roos, A. (1946). *Medicine*, 25, 399.
 Andersen, D. H. (1938). *Amer. J. Dis. Child.*, 56, 344.
 — and Early, M. V. (1942). *Ibid.*, 63, 891.
 — and Hodges, R. G. (1946). *Ibid.*, 72, 62.
 Anderson, J., Dent, C. E., Harper, C., and Philpott, G. R. (1954). *Lancet*, 2, 720.
 Baines, G. H., Barclay, J. A., and Cooke, W. T. (1945). *Quart. J. Med.*, 14, 113.
 Bickel, H., Baar, H. S., Astley, R., Douglas, A. A., Finch, E., Harris, H., Harvey, C. C., Hickmans, E. M., Philpott, M. G., Smallwood, W. C., Smellie, J. M., and Teall, C. G. (1952). *Acta paediat. (Uppsala)*, 42, Suppl. 90.
 Bodian, M., Carter, C. O., and Norman, A. P. (1952). *Fibrocystic Disease of the Pancreas*. Heinemann, London.
 Butler, A. M., Wilson, J. L., and Farber, S. (1936). *J. Pediat.*, 8, 489.
 Creery, R. D. G. (1953). *Lancet*, 2, 17.
 — and Neill, D. W. (1954). *Ibid.*, 2, 110.
 Darling, R. C., di Sant' Agnese, P. A., Perera, G. A., and Andersen, D. H. (1953). *Amer. J. med. Sci.*, 225, 67.
 Dawson, I. M. P., Craig, W. S., and Perera, F. J. C. (1954). *Arch. Dis. Child.*, 29, 475.
 Dent, C. E. (1946). *Lancet*, 2, 637.
 Doxiadis, S. A. (1952). *Arch. Dis. Child.*, 27, 409.
 Ehrenpreis, Th. (1955). *Ibid.*, 30, 8.
 Emery, J. L. (1952). *Ibid.*, 27, 67.
 Fanconi, G. (1931). *Jb. Kinderheilk.*, 133, 257.
 — Girardet, P., Schlesinger, B., Butler, N., and Black, J. (1952). *Helv. paediat. Acta*, 7, 314.
 Farber, S. (1944). *Arch. Path. (Chicago)*, 37, 238.
 Ferguson, A. W., and McGowan, G. K. (1954). *Lancet*, 1, 1272.
 Hartmann, A. F. (1939). *Ann. intern. Med.*, 13, 940.
 Hayles, A. B., Stickler, G. B., and McKenzie, B. F. (1954). *Pediatrics*, 14, 449.
 Holzel, A., Komrower, G. H., and Wilson, V. K. (1952). *British Medical Journal*, 1, 194.
 Hutchison, J. H. (1949). *Arch. Dis. Child.*, 24, 303.
 — and MacDonald, A. M. (1951). *Acta paediat. (Uppsala)*, 40, 371.
 Latner, A. L., and Burnard, E. D. (1950). *Quart. J. Med.*, 19, 285.
 Lightwood, R. (1952). *Proc. roy. Soc. Med.*, 45, 401.
 — Payne, W. W., and Black, J. A. (1953). *Pediatrics*, 12, 628.
 Lignac, G. O. E. (1924). *Dtsch. Arch. klin. Med.*, 145, 139.
 Lowe, K. G., Henderson, J. L., Park, W. W., and McGreal, D. A. (1954). *Lancet*, 2, 101.
 McCune, D. J., Mason, H. H., and Clarke, H. T. (1943). *Amer. J. Dis. Child.*, 65, 81.
 Moncrieff, A., and Wilkinson, R. H. (1954). *Acta paediat. (Uppsala)*, 43, Suppl. 100, p. 495.
 Norman, A. P. (1954). In *Recent Advances in Paediatrics*, edited by D. Gairdner, p. 247. Churchill, London.
 Wylie, M. E. S. (1953). *Arch. Dis. Child.*, 28, 297.

ORDER AND DISORDER IN PULMONARY FUNCTION*

BY

W. MELVILLE ARNOTT, M.D., F.R.C.P.

William Withering Professor of Medicine, University of Birmingham

PULMONARY CIRCULATION

The fact that the pulmonary circulation and its regulation is vital to efficient respiration needs no emphasis. There are various avenues of approach to this circulation. It can be considered from the purely structural angle as a system of branching vessels discharging into a capillary network which drains into a converging venous system, or it can be regarded as a limbo into which blood vanishes from the right ventricle and from which it emerges purified in the left auricle, without any great interest being taken in the vicissitudes of its journey through the lungs. Up till comparatively recently such was the conventional attitude of many who devoted themselves to cardiology, an outlook which in its restriction was matched only by that of the chest physician, whose only reminder of the pulmonary (or bronchial) circulation was the not infrequent occurrence of haemoptyses. Another approach is to conceive of the pulmonary circulation as a series of dimensions and energy levels related to one another by physical laws. This is essentially the physiological approach, and one which is in the closest harmony with current attitudes in internal medicine. I make no apology for basing my

*The second Oliver-Sharpey Lecture for 1955, delivered to the Royal College of Physicians of London on March 22. The first lecture was published in our issue of July 30, p. 279.