The Rational Basis of Diagnosis in Internal Medicine

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At the time I started my medical studies in the early thirties, the era of morphological medicine had reached its zenith. This had started in the middle of the seventeenth century, and none other than Giovanni Battista Morgagni (1682-1771) in Padua was at its birth. Autopsies had been performed, secretly or publicly, for many centuries before. However, they served to describe the normal form and topography of various organs rather than to identify the causes of disordered health. Illness was believed to be a punishment from heaven, or possession by an evil spirit whose placation or expulsion would cure the malady. However, the classical description, by Sydenham (1624-1689) and others, of several of the then prevalent contagious illnesses, and some of the other common maladies of those days such as gout, angina pectoris, or hysteria, and the emancipation of the human mind from the scholastic chains of the Middle Ages excited curiosity about the possible changes in individual organs in diseases already known or being discovered. These studies received a further impetus when, in the lands of the Danube monarchy, the Empress Maria Theresa (1740-1780), influenced by her personal physician Gerhard van Swieten (1700-1772), ordered an autopsy on everybody who died in the university hospitals of her empire.

Napoleon’s physician Corvissart (1755-1821), in his Essai sur les maladies et lesions organiques du coeur et des gros vaisseaux (1806), and the great English Guy’s Hospital physician Richard Bright (1789-1858), in his Cases and observations illustrative of renal disease accompanied with the secretion of albuminous urine (1836), are further important figures on this road. After the microscope was added to the armamentarium of the pathologist the day came when the German Rudolf Virchow (1821-1901) was able to present a completed edifice of medicine based on pathology. A specific morphological and histological change in some organs or systems formed the basis for the various symptoms and signs presented by the diseased person. The task of the physician was to unravel from these various groupings of signs and symptoms a particular organic change in order to establish a diagnosis. This new approach had, in Virchow’s earlier days, little to offer to therapy, even if he himself suspected various external influences such as
climate, humidity, temperature. It was up to Louis Pasteur (1822-1895), Robert Koch (1843-1910), Emil Behring (1854-1917) and others to demonstrate that the causative agents of some of the greatest killers of the human race could be visualised by the microscope, grown in the laboratory, and fought by active or passive mobilisation of the body defences. Chemotherapy was still a dream (Paul Ehrlich, 1854-1915). X-rays gave physicians an opportunity to investigate the lungs, heart and skeleton. It seemed that medicine, previously based on empiricism, superstition and prejudice, had gained a scientific foundation on which to build.

The morphological changes discovered on post-mortem by the pathologist gave an adequate explanation for the dyspnoea, cough, purulent sputum and haemoptysis in pulmonary tuberculosis (responsible for over one-third of all deaths in Europe after the First World War). It was not difficult to understand the bleeding from a peptic ulcer or from oesophageal varices in cirrhosis of the liver where scars were deviating portal blood into dilated collateral channels. It was easy to see how a severe inflammation of the tonsils in scarlet fever could invade the middle ear, produce a mastoiditis or a cerebellar abscess. Also the intestinal perforation or bleeding in typhoid fever became understandable in the light of the morphological changes. The pseudo-membranous inflammation descending from the fauces to the larynx and trachea explained the dangerous diphtheritic croup, and the early discovery of the microbial toxins made it possible to understand the origin of the nervous paralyses. Pathological diagnosis became the coveted ideal of the clinician, and the pathologist his judge. The physician of those days was a frequent visitor to the autopsy room and I can still remember my first chief, the haematologist Professor Hynek, walking at least three times a week, surrounded by his assistants, downhill from the first medical clinic on Charles' Square in Prague to the Hlava Institute of Pathology on Albertov — a distance of one mile — to be shown, to the accompaniment of jokes and anecdotes by Professor Šíkl, all the errors committed by himself and his staff.

However, the pathological concept did not substantially alter the basic clinical approach to the problems of disease and its bedside diagnosis. It provided only an objective morphological correlation, verified by the microscope, to a certain grouping of symptoms and signs, i.e. to certain syndromes, on which the clinical diagnosis was based. This was achieved by the clinician of the morphological era in the same way as by the clinician of the pre-morphological times, namely by comparing certain symptoms and signs and their grouping found in a particular patient with similar patterns that he had become familiar with from past experience or from the literature. Apart from the history and physical examination, which had to remind him of a pattern seen or heard of before, the physician's laboratory and X-ray aids were limited. Bacteriology and serology were available for the diagnosis of infection. The three-lead ECG helped the diagnosis of myocardial infarction and cardiac arrhythmias. Proteinuria and a
raised blood urea revealed the presence of renal disease. The Van den Bergh and Takata reactions pointed to the presence of liver disease. Gastric achylia and the presence of Boas-Oppler bacilli suggested the possibility of stomach cancer, and an abnormal blood sugar curve diabetes mellitus. These and a few rarer tests were all a clinical laboratory could offer to support the clinical diagnosis. However, all these methods were used either to provide another stone for the diagnostic mosaic or to assess the extent of damage. In the same way as a hundred years earlier, clinical medicine was still a specialty in its own right, and the correct clinical diagnosis the outcome of considerable experience gained over many years and, therefore, almost inaccessible to young beginners. During the process of teaching, the student had to be shown a very large variety of patients in order, when faced years later by an analogous pattern, to recall that he had seen something similar before. He then had to be able to look up in his textbook the appropriate therapeutic steps. This necessitated large teaching clinical departments with many patients. I remember my visit to the department of medicine at Leipzig University in 1954. It had 650 beds and, in answer to my question whether such a department was not too large to be managed by one chief, Professor Max Bürger staggered me by saying that with less than 650 beds it was impossible to teach clinical medicine.

Other drawbacks of this morphological approach were no less serious. By the nature of an autopsy, the pathologist was forced to explain the course and origin of the disease from its end result – very often a hopeless task. Whereas the morphological basis was adequate to explain the rise in blood urea when the renal glomeruli were obliterated by disease, it could offer no explanation for the polyuria and salt-wasting of chronic renal failure. Understanding the hypertension of chronic renal disease was difficult, and Bright’s (1836) idea that a left ventricular hypertrophy was needed to propel blood through the rigid vessels of a diseased kidney was certainly incorrect. The connection between renal tubular cells overfilled with hyaline droplets and generalised oedema was not clear without modern knowledge of renal function and volume homeostasis. A still greater puzzle was provided in the early stages of essential hypertension, as no abnormality of any organ could be detected by the pathologist. And there was no explanation for – and, because of the absence of any morphological basis, no interest in – the majority of patients in medical out-patients suffering from a chronic anxiety state or disturbed autonomic balance. They were dismissed by the unsympathetic physician with the diagnosis of organ neurosis, neurasthenia, or even malingering. And yet these were, and are, really suffering people requiring a doctor’s help.

These and other similar examples, together with the tremendous advances in knowledge of physiology, biochemistry and immunology, and the introduction of electron microscopy about the time of the Second World War, are the reasons for the profound, revolutionary change that clinical medicine has undergone in the
Table 1. Differential diagnosis of breathlessness on functional grounds. The principal clinical manifestation of the pathophysiological disturbance is in brackets.

|                      | Dyspnoea on exertion | Orthopnoea | L. vent. failure (Cardiac asthma) | Pulmonary oedema on top of exercise | Low arterial \( \text{O}_2 \) pressure (Central cyanosis) | Past history of productive cough | L. vent. hypertrophy (Heaving apex beat) | R. vent. hypertrophy (Precordial pulsation) | Small stroke volume (Small pulse) | Atrial fibrillation | Complete arrhythmia (Angina) | Inconsistent history; cold moist hands | Extreme reduction of renal function | Pallor |
|----------------------|----------------------|------------|----------------------------------|-------------------------------------|-------------------------------------------------|---------------------------------|--------------------------------|--------------------------------|----------------|----------------|----------------|--------------------------------|----------------|----------------|
| I. Anxiety state     |                      |            |                                  |                                     |                                                  |                                 |                                 |                                 |                          |                |                |                                |                      |                |                     |
| II. Inadequate \( \text{O}_2 \) supply to tissues: |                      |            |                                  |                                     |                                                  |                                 |                                 |                                 |                          |                |                |                                |                      |                |                     |
| 1. Low partial \( \text{O}_2 \) pressure     | +                    | -          | +                                | -                                   | -                                               | -                               | +                               | -                               | -                     |                |                |                                |                      |                |                     |
| 2. Pulmonary disease  | +                    | +          | +                                | +                                   | +                                               | -                               | +                               | -                               | +                     |                |                |                                |                      |                |                     |
| 3. Pulmonary emboli   | +                    | +          | +                                | +                                   | +                                               | -                               | +                               | -                               | +                     |                |                |                                |                      |                |                     |
| 4. Fluid lung†       | +                    | +          | +                                | +                                   | +                                               | -                               | +                               | -                               | +                     |                |                |                                |                      |                |                     |
| 5. Chronic pulmonary congestion |                      |            |                                  |                                     |                                                  |                                 |                                 |                                 |                          |                |                |                                |                      |                |                     |
| (a) Mitral stenosis‡ | +                    | -          | -                                | +                                   | -                                               | -                               | +                               | -                               | +                     |                |                |                                |                      |                |                     |
| (b) Left-to-right shunt |                      |            |                                  |                                     |                                                  |                                 |                                 |                                 |                          |                |                |                                |                      |                |                     |
| 6. Left ventricular failure |                      |            |                                  |                                     |                                                  |                                 |                                 |                                 |                          |                |                |                                |                      |                |                     |
| (a) Hypertension     | +                    | -          | +                                | +                                   | -                                               | -                               | +                               | -                               | +                     |                |                |                                |                      |                |                     |
| (b) Aortic stenosis  | +                    | -          | +                                | +                                   | -                                               | -                               | +                               | -                               | +                     |                |                |                                |                      |                |                     |
| (c) Aortic incompetence |                      |            |                                  |                                     |                                                  |                                 |                                 |                                 |                          |                |                |                                |                      |                |                     |
| (d) Mitral incompetence |                      |            |                                  |                                     |                                                  |                                 |                                 |                                 |                          |                |                |                                |                      |                |                     |
| (e) Ischaemic heart disease |                      |            |                                  |                                     |                                                  |                                 |                                 |                                 |                          |                |                |                                |                      |                |                     |
| 7. Anaemia           | +                    | -          | +                                | +                                   | +                                               | -                               | +                               | -                               | +                     |                |                |                                |                      |                |                     |

* With emphysema heart cannot be palpated.
† Most patients have hypertension or severe left ventricular failure.
‡ Chronic bronchitis often associated.
last 30 years. It gradually became clear that, with the exception of sequelae of acute trauma, the changes found in organs and tissues by the pathologist are just another expression of the pathogenic agent (or agents) that led to the clinical symptoms and signs of the disease. The affected cell enzymes or organelles or the changed structure of tissues that can be seen by the microscope, especially since the introduction of the biopsy needle and of histochemistry and immunohistology, give rise to a subjective feeling of abnormality or to the appearance of an abnormal sign. It is the task of the physician to learn to interpret these in terms of disturbed physiology of certain cells, organs or systems. He must try to investigate the reason for this disturbance of function and, through a synthesis of these functional disturbances and their probable causes, he should arrive at the clinical diagnosis. From this aspect disease appears as an experiment of nature whose analysis, for causes and mechanisms, is the task of the clinician. Under such conditions, the sharp limit between physiology and clinical medicine is gradually vanishing. Clinical medicine is no longer a discipline in its own right but is gradually changing to bedside pathophysiology. The symptom or sign, whether it be physical, biochemical or haematological, is no longer a piece in the mosaic constituting the pattern of a nosological entity known from past experience but an expression of changed function.

For instance, such a common symptom as shortness of breath (Table 1) points to increased respiratory effort, which may be due to a ventilation disproportionately high for the actual metabolic needs in chronic anxiety states (suggested by numerous autonomic stigmata, and a multitude of inconsistent symptoms) or to an inadequate oxygen supply to the tissues. If we disregard the low partial pressure in high altitudes, the reasons for this may be an inadequate or faulty oxygenation of blood in the lungs or a disturbed transport of oxygen from the lungs to the tissues. Any disease of the respiratory pathways that obstructs the passage of air to the alveoli, any reduction of the respiratory surface by lung disease, fluid in the alveoli, or disease of the thorax, may lead to breathlessness. A past history of productive cough or wheezing points towards lung disease. Breathlessness on effort combined with nocturnal attacks of dyspnoea is an unmistakable sign of left ventricular failure and suggests hypertension, valvular disease overtaxing the left heart, or ischaemic heart disease. Dyspnoea on effort, increasing gradually over years without episodes of cardiac asthma but occasionally leading to pulmonary oedema during exertion, is typical of a chronic pulmonary engorgement in conditions interfering with the outflow from the lungs, or left-to-right shunts. An altered quality of the pulse (due to a changed filling of the left heart), the presence or absence of atrial fibrillation (pointing to damage to the atrial muscle by overstretching in mitral stenosis, ischaemia in coronary heart disease, or metabolic disturbance in thyrotoxicosis), and other expressions of changed haemodynamics help to differentiate between these. A history of oliguria with overfilled pulsating neck veins in acute or chronic renal
failure is suggestive of a fluid-lung. On the other hand, lassitude and pallor may indicate anaemia as a cause of breathlessness. The colour index and the past history usually afford clues to its cause.

It is obvious that such an approach requires an entirely different kind of training in clinical medicine. The pathophysiological meaning of every symptom and sign has to be taught. The students must be trained how to gain information by questioning and by thorough physical examination. They must be shown how to extricate the necessary clues from the ballast of many words and how to manipulate the important information.

In the analysis of symptoms or signs, only those that have a limited number of interpretations can serve as clues and lead to a solution. General symptoms such as lassitude, headache or insomnia are, as a rule, useless. One part of what is called the art of medicine is the acquisition of skill in detecting the proper clues in the history and physical examination, their correct analysis in pathophysiological terms and their synthesis, which lead to diagnosis.

It is clear that laboratory investigation — biochemical, histological, electro-microscopical, immunological and, above all, clinico-physiologicals— must provide data on correlations between a change of function and its clinical manifestation, be it a subjective symptom, an objective sign, or a change observable in the clinical laboratories. These data must become the property of a modern clinician. The final diagnosis, rather than being a word that automatically brings to mind a list of therapeutic procedures confirmed by past experience or blessed by belief, should contain information on the causative agent and the mechanisms by which it produced damage. The resulting therapeutic plan should attempt to remove the causes, to disrupt the pathogenetic chain of events and, eventually, to correct the disturbed function or to protect the whole organism from its consequences. It is, of course, clear that some acute diseases require urgent therapeutic action before a full diagnosis can be established. Thus, the acute abdomen necessitates surgical intervention even if its cause is still obscure; the recognition of dehydration calls for its immediate correction. These group diagnoses are based, as before, on the recognition of a certain complex of symptoms and signs. However, their interpretation is different: they translate a certain change of function which the physician must try to correct through a physiological approach.

Physiology also penetrates into the laboratory, where it helps to interpret the data. Thus, the ECG abandons empirical description and, based on electrophysiology and vectocardiography, follows the whole process of activation of the myocardium. Many such examples could be quoted and it is no exaggeration to say that there is almost no organ or system that cannot be studied in the laboratory. Modern radiology helps to identify changes of motility, i.e. function of the gastrointestinal tract, the efficiency of the venous system, the patency of the arteries and the flow of blood in the various cavities of the heart. Endoscopy allows direct inspection of practically any hollow viscus and biopsy of its mucosa,
and makes registration of its contractions, i.e. function, feasible. Biochemistry has
given to modern clinical medicine a vast number of methods and, again, the
physiological approach has enhanced their application. The various indices and
constants of the past have been replaced by the reflection of a certain change in
function in their biochemical expression, e.g. the blood sugar curve, the change of
the blood level of transaminases in the course of liver disease, and so on. Their
largest contribution is possibly in nephrology, where biochemistry and physiology
make it possible to penetrate deeply into the function of an organ completely
hidden from inspection and palpation. The discovery of the cardiac catheter by
Cournand and Richards marked a new era in cardiology. Spirometry allows an
estimation of the residual air and of pulmonary function. Many of these
techniques were further simplified by nuclear medicine, which also gives better
information on thyroid function than any previous method and allows the study
of pulmonary, hepatic, and renal blood flow, and cardiac output by non-invasive
procedures. Ultrasound can trace abnormal borders of an organ or a mass and
assess the function of the heart muscle and valves.

Fascination with the present-day possibilities of laboratory methods often
leads to their unselective application. Some believe that this makes their approach
more scientific. Others do it in the unwarranted hope that the patient may benefit
from a mass of data and that a serious later disease may thus be prevented. The
technically and electronically minded even hope that the day is not too remote
when the computer, fed with as much heterogeneous data on the patient as
possible, may provide them, within seconds, with the correct diagnosis and
treatment. Some of these considerations are certainly correct in preventive
medicine. One must, of course, be strictly selective and recognise the limits.
Screening for the early stages of mass diseases — tuberculosis, hypertension,
ischaemic heart disease, gynaecological and prostatic carcinoma, diabetes mellitus
— can be done relatively simply and inexpensively. However, it must be
remembered that changed biochemical and electrocardiographical parameters
reflect a change in function, and such changes do not necessarily make a patient
ill. How many of those, in addition, have no preventive value, can be seen from
the following analysis of the findings in 200 patients seen consecutively in general
medical out-patients (Table 2). In all of these the routine analysis of blood
included (apart from the ESR and blood count) sodium, potassium, bicarbonate,
chloride, calcium, phosphate, bilirubin, plasma protein and electrophoresis, urea,
creatinine, cholesterol, glucose, GOT, GPT, alkaline phosphatase and uric acid.
The cholesterol, glucose, uric acid and liver enzymes were abnormal in 4 to 13.3
per cent of otherwise healthy individuals. The other 10 parameters exceeded their
usual range in only 0 to 1 per cent of subjects not suffering from an obvious
disease in which their abnormality could be anticipated. However, the cost of
achieving this not unexpected result was DM 12,400. It is also important to
remember that once the pathophysiological significance of a patient’s symptom or
Table 2. Results of the survey of laboratory tests routinely carried out in 200 medical outpatients. The first column indicates the total percentage of the abnormal results. The second column shows the percentage of abnormal results in patients in whom such an abnormality would not be expected and where its finding had a preventive value. The cost of the unjustified investigation amounted to DM 12,400.

| Abnormal % | Abnormality not expected: preventive % | Cost DM |
|------------|---------------------------------------|---------|
| Na"        | 2                                     | 0       | 1,240   |
| K"         | 8.5                                   | 1.0     | 1,240   |
| Cl"        | 4.0                                   | 1.5     | 1,240   |
| HCO₃⁻      | 16.0                                  | 0.5     | 1,240   |
| HPO₄²⁻     | 0                                     | 0       | 1,240   |
| Ca"        | 4.0                                   | 1.5     | 1,240   |
| Bilirubin  | 1.0                                   | 0       | 1,240   |
| Urea       | 8.5                                   | 0.5     | 1,240   |
| Creatinine | 7.0                                   | 0       | 1,240   |
| Protein    | 2.5                                   | 1.0     | 1,240   |
| Uric acid  | 21.3                                  | 13.3    | 848     |
| Cholesterol| 27.0                                  | 10.5    |         |
| Glucose    | 8.5                                   | 4.0     |         |
| GOT        | 9.5                                   | 7.0     |         |
| GPT        | 12.0                                  | 8.0     |         |
| Alkaline phosphatase | 6.0 | 4.0 |         |

sign has been recognised it is not necessary to verify it again by experimental investigation. Thus, it is unnecessary to measure the oxygen content of the arterial blood in order to recognise its undersaturation in a patient with central cyanosis, nor is it necessary to study the pressure in the pulmonary capillaries to diagnose its elevation in the presence of a paroxysm of nocturnal dyspnoea. To avoid a misunderstanding on this point, I must stress that I am not opposed to the use of even expensive and elaborate techniques of investigation if they form part of a planned research programme that may lead to advances in clinical medicine, even if the particular patient does not benefit from them. But I am against their indiscriminate use for the aims mentioned above because of the discomfort they may cause the patient and because of the unnecessary cost.

Computer analysis of data from clinical or other investigations and in epidemiology is of undisputed value. Computer models of various biological systems make a detailed study of complicated relationships possible and allow formulation of important predictions. Routine use of the computer in the chemical laboratory is more doubtful. The promise of an effective service with prompt delivery of laboratory results leaves much to be desired: contact with
laboratory staff is lost, the patient becomes a number, and the whole service impersonal; vital information about the patient is frequently delivered late and, occasionally, not at all; without warning, the physician in charge of the patient discovers that the specimen has gone astray. A computer as a machine for clinical diagnosis appears to me, in spite of its promising appeal, to be a step in the wrong direction. The results may be more accurate and the list of possibilities more complete, including all sorts of rarities the programmer discovers in the world's literature. This is true even if the computer is programmed in such a way that it actually carries out the analysis in terms of pathophysiology as outlined above. However, it bypasses the physiological analysis in the mind of the physician, which revolutionised the clinical medicine of our day, and restricts therapeutic thinking to a list of recommended procedures. It would lead to a degeneration of the medical brain, would reduce the physician to the role of a feldscher, and would introduce an inhuman trait into clinical medicine, disastrous both to the profession and to the patient. The computer in industry has possibly rationalised manufacture of a product, put many employees out of work, and almost certainly increased the costs of the product. The danger of the computer making the doctor redundant is not real because he would still be needed to extract from the patient the symptoms and signs that have to be fed into the computer, and to administer treatment. The expense would, therefore, be considerably increased by the cost of the equipment and the computer would, by its impersonal and unfounded diagnosis, produce so much anxiety that hundreds of additional doctors would be required to dispel it.

Physiology has taught us that mental stress can produce profound changes in the function of the cardiovascular or alimentary system and in metabolism. It should not surprise us, therefore, that an anxiety state, or mental stress in general, may produce symptoms and signs that make the sufferer feel ill. To dismiss them as functional and, therefore, uninteresting and unimportant, is wrong. This attitude does not help the patient and such ‘functional’ changes may eventually produce an ‘organic’ disease; for example, essential hypertension, or peptic ulcer. Every physician should try to gain insight into the symptoms of his patient from this aspect and he should not relegate the task to the psychiatrist unless the problem proves too difficult for him to solve. It is important to realise that the attitude of the patient to his disease and to his surroundings may be an important element in the aetiology and an important factor in determining the speed of recovery or the further course of the disease. To obtain this insight one must gain the confidence of the patient. Careful listening to the patient’s complaints, interest, and sympathy are the basic requirements and this is one more reason, possibly the decisive one, why I am certain that a computer will never be able to replace the physician and why I hope that the era of such a medical robot will never dawn.

In busy clinical practice the critical and detailed evaluation of every symptom and sign in terms of pathophysiology is more time-consuming than draining blood
for laboratory investigation or applying some measuring apparatus. It is, therefore, necessary that this is properly appreciated by insurance companies, who are still ready to pay a substantially higher honorarium for meaningless and superfluous laboratory data than for a painstaking history. However, by avoiding much of this extra cost, such an approach will eventually reduce the astronomical growth of expenditure on health care, as the following examples may demonstrate.

A female patient, aged 64 years, had been suffering for the past 34 years from rheumatoid arthritis. She was treated on repeated occasions by corticoids, gold, and analgesics. In 1973 her left knee-joint was replaced by a prosthesis and she had to undergo further surgery because of infection. In 1976 she became tired and breathless on exertion, but slept comfortably lying flat. Her skin then became pale and yellow. The diagnosis of anaemia was confirmed by a blood count (haemoglobin 6.4 g per cent, haematocrit 17 per cent, erythrocytes 1.9 million, reticulocytes 23.6 per cent). Blood loss was suspected and, because of the previous therapy with corticoids and anti-inflammatory agents, gastrointestinal bleeding was suspected, although there was no history of melaena or haematemesis or of any gastrointestinal discomfort. Yet, because of this suspicion, a barium meal and a barium enema were administered and a gastroscopy was carried out—all with negative results. The costs involved were DM 104. A physiological way of reasoning would have avoided this unnecessary expense: a high colour index practically excludes a chronic blood loss and the high reticulocyte count should under these circumstances have led at once to the recognition of a chronic haemolytic anaemia. The yellow colour of the skin and the detection of urobilinogen with Ehrlich's reagent would have taken a few seconds, cost nothing, and would have confirmed this conclusion. In addition, the examination of faeces for occult blood, costing DM 5, would have confirmed that no bleeding has taken place, avoided at least three days of hospital stay and DM 750 in expense (Table 3).

Table 3. Cost of the investigations of the patient with severe haemolytic anaemia.

| Description                          | Cost DM |
|--------------------------------------|---------|
| 1. Barium meal neg.                  | 28.00   |
| 2. Gastroscopy (with biopsy) neg.    | 48.00   |
| 3. Barium enema neg.                | 28.00   |
|                                      | **104.00** |
| 1. Occult blood in faeces            | 5.00    |
| 2. Urobilinogen in urine             | 2.10    |
| 3. Bilirubin in blood                | 6.20    |
|                                      | **13.30** |
A 45-year-old patient with a past history of pleural effusion 17 years previously and of a varicose ulcer present for two years, gave a 10 months' history of severe dyspnoea on exertion, orthopnoea, oedema of the legs, and increased abdominal girth. On admission to another hospital, peripheral cyanosis and pulsating neck veins were noted. The lungs were physically and radiologically normal. He had a marked precordial pulsation, a fixed splitting of the accentuated 2nd pulmonary sound and a systolic murmur heard over the sternum. The pulse was regular 92/min, and blood pressure was 115/90 mm Hg. The liver was markedly enlarged; ascites was present and he had large varicose veins. An ECG showed right ventricular hypertrophy and right ventricular and atrial strain. X-ray confirmed the enlargement of the heart and large pulmonary arteries were seen. Congenital heart disease, possibly a pulmonary stenosis, was suspected. A phonocardiogram, mechanocardiogram and the measurement of pressure in the right heart by a floating catheter were performed, with inconclusive and partly misleading results. The costs involved were DM 175 (Table 4).

Table 4. Cost of the investigations of the patient with multiple pulmonary emboli.

| Investigation                      | Cost DM |
|-----------------------------------|---------|
| Phonocardiogram                   | 17.50   |
| Mechanocardiogram                 | 17.50   |
| Floating R. heart catheter        | 140.00  |
|                                   | 175.00  |
| Right heart catheter              | 140.00  |

There were, however, several clues in the history and physical findings: dyspnoea of the type described was obviously of pulmonary origin, yet the absence of cough and the normal chest findings argued against a primary parenchymatous lung disease. There was no pulmonary congestion to suggest mitral stenosis nor a left-to-right shunt to explain the shortness of breath. A pulmonary stenosis was unlikely as the pulmonary component of the 2nd sound was easily audible, both pulmonary arteries were dilated, and the dyspnoea could not be accounted for. These, together with the strongly accentuated 2nd pulmonary sound, suggested pulmonary hypertension which, in the absence of a primary parenchymatous disease or pulmonary congestion, must have been due to the obstruction of the pulmonary vascular bed by blood clots. Their origin was suggested by the varicose ulcer and was actually visualised by phlebography in the deep leg veins. The nature of the pulmonary disease was confirmed by scan. The systolic murmur, increased in intensity on inspiration, was obviously due to a relative tricuspid incompetence resulting from an enlarged right ventricle. The
correct interpretation of the loud 2nd pulmonary sound was documented by measuring the pulmonary artery pressure by a heart catheter; the pulmonary vascular resistance amounted to $1840 \text{ dyn } 10^{-1}$. It is obvious that a physiological interpretation of the physical signs would have avoided this procedure and saved a further DM 140.

These are two examples of many that each one of us could probably quote. They show that the revolutionary changes in the pathophysiological basis of medicine may strengthen the contact of the physician with his patient and give a safe diagnostic approach for young and relatively inexperienced physicians. The pathophysiological approach provides a more rational basis to therapy and, in addition, can be more economical.

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**GARDENER EXTRAORDINARY**

For most Londoners Upton Park means football and the ‘Hammers’. Two centuries ago it meant a botanical garden that rivalled Kew. Its creator was Dr John Fothergill who managed to be young, famous, rich and generous all at the same time. Linnaeus named a genus of shrub after him. Searching for a convenient country retreat in which to indulge in botany, Fothergill came across Rooks Hall in the tiny village of Upton. He bought the hall in 1762, renaming it Upton Park. There he made the finest private botanical garden in Europe. He spent endless hours with ships’ captains in the nearby docks, teaching them how to collect and transport plants and seeds from far away places. His magnolias were magnificent and his tea trees flourished. He employed four artists to paint his specimens. Not content with his world-wide knowledge of botany, he played an active part in prison reform, was interested in resuscitation from drowning and, naturally, in the use of vegetable remedies, spurning the lancet and the purge.

At his death a 15 foot high coffee tree was left to Dr Lettsom and his 2,000 paintings of plants were bought by the Empress of Russia. Many of his dried specimens had been given to his friend, Sir Joseph Banks, President of the Royal Society, and they eventually went to the British Museum. Upton Park fell into a state of neglect but now forms the municipal park of West Ham.