# Clinicopathological Conference

## A Case of Thromboembolic Pulmonary Hypertension

DEMONSTRATED AT THE ROYAL POSTGRADUATE MEDICAL SCHOOL

### Clinical History

Professor SIR JOHN MCMICHAEL: This patient (Case No. 296136; P.M. 11281) was aged 61 at the time of his death. He was a company director who had lived in Kenya since 1949. He was well until March 1962, four years before his death, when he experienced a sudden right-sided chest pain, which was worse on breathing, and this was associated with haemoptysis. He was admitted to hospital in Nairobi, where he was found to have the signs of a right basal pneumonia, which was confirmed by *x*-ray. Though *Streptococcus pneumoniae* was grown from his sputum he responded slowly to the appropriate antibiotic therapy. Three weeks after the beginning of his illness he developed signs of congestive heart failure, and was found to have a venous thrombosis in the left calf. He was given anticoagulants and digitalis. He made a good recovery from this illness but had diminished exercise tolerance, though he was not in congestive heart failure.

Two years later, in 1964, he was readmitted to hospital in Nairobi on account of several episodes of nocturnal dyspnoea. On examination he was cyanosed, with cold extremities and swelling and tenderness of both calves. He had signs of right and left heart failure with engorged neck veins and a tender enlarged liver, and bilateral crepitations in the lungs. There was also an apical pansystolic murmur. His blood pressure was 170/100 mm. Hg.

The chest *x*-ray film showed some pleural thickening at the right base, but the heart was of normal size. The electrocardiogram showed secondary R waves in AVR and V4R and inverted T waves in leads II, III, AVF and V1–V4 (Fig. 1). At that time he was treated as though he had had a myocardial infarction, and was given anticoagulants, digitalis, and diuretics. In spite of this marked ascites collected, and subsequent chest films showed increasing right ventricular hypertrophy with engorgement of the hilar vessels. He had to sleep propped up with several pillows and remained on the verge of gross failure with severe ascites.

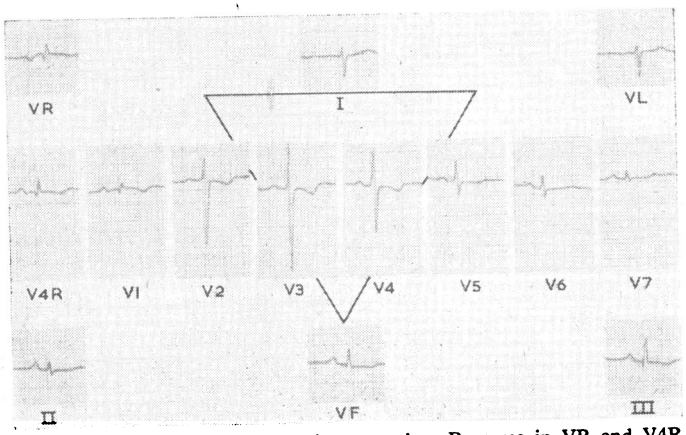



FIG. 1.—Electrocardiogram showing secondary R waves in VR and V4R and inverted T waves in leads II, III, VF, and V4R to V4.

### Physical Findings

In 1964 he was referred to Hammersmith Hospital. He was very short of breath even at rest. On examination he was found to be a wasted and cyanosed man with cold extremities. He had dilated arm veins, and the right cephalic and both long saphenous veins were thrombosed. The neck veins were engorged to the angle of the jaw. His pulse was 90/min. and regular, and the blood pressure was 135/90 mm. Hg. There was a marked parasternal heave suggesting right ventricular hypertrophy and a pansystolic murmur at the left sternal edge and apex, increasing on inspiration.

On examination of the respiratory system there were signs of pleurisy at the right base. There was gross ascites, and a hard liver edge could be felt just below the costal margin. The spleen was not felt.

The investigations showed a haemoglobin of 15.8 g./100 ml., with a packed cell volume of 50%. The blood urea was 57 mg./100 ml. The liver-function tests showed a bilirubin of 1 mg./100 ml., alkaline phosphatase 28 King–Armstrong units, albumin 3.3, globulin 3.5 g./100 ml.

The chest film showed a pleural reaction in the right costophrenic angle. The heart was a little enlarged. The peripheral pulmonary arteries—particularly in the left lung—were rather small compared with the main pulmonary arteries. The electrocardiogram showed evidence of right atrial hypertrophy and right ventricular hypertrophy.

Cardiac catheterization showed the right ventricular pressure to be 70/10 mm. Hg, pulmonary artery pressure 74/33 mm. Hg. The cardiac output was 2.7 l./min. and lung-function tests showed alveolar overventilation with a large physiological dead space.

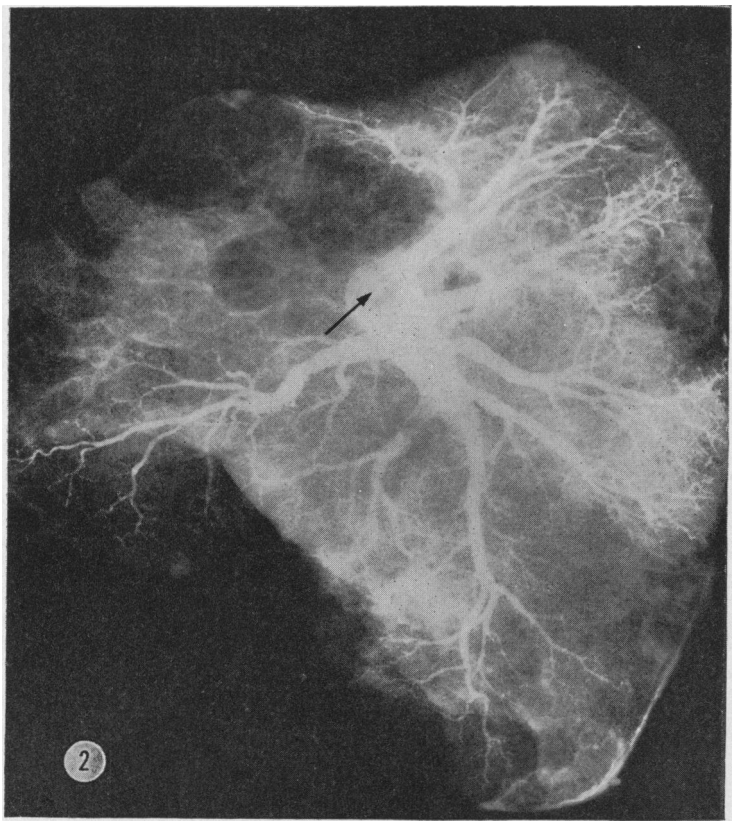
It was felt that these findings were compatible with a diagnosis of thromboembolic pulmonary hypertension. He was treated with digitalis, diuretics, and anticoagulants, and was allowed to leave hospital. Some months later he was readmitted for reassessment, and he was at that time complaining of increasing cramp in his legs. The clinical signs were very much as before, as was the chest film and electrocardiogram. While in the ward he had a sudden cardiac arrest from which he could not be resuscitated.

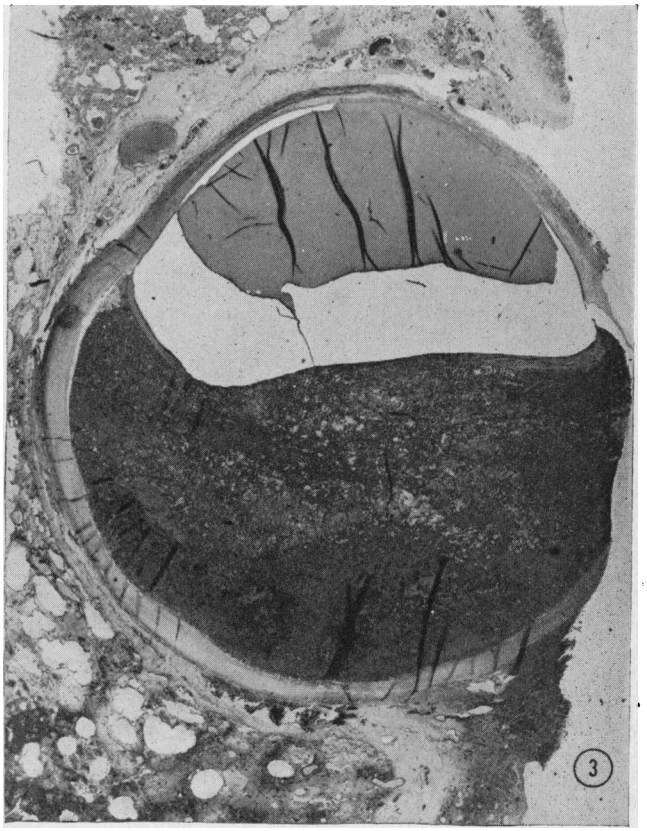
### Clinical Diagnosis

(1) Thromboembolic pulmonary hypertension, cause unknown.

### Post-mortem Findings

Dr. E. G. J. OLSEN: The body was that of a thin but well-nourished deeply cyanosed man, weighing 10 st. 2 lb. (64.5 kg.), with petechiae over the anterior chest wall. Bilateral gynaecomastia was present.





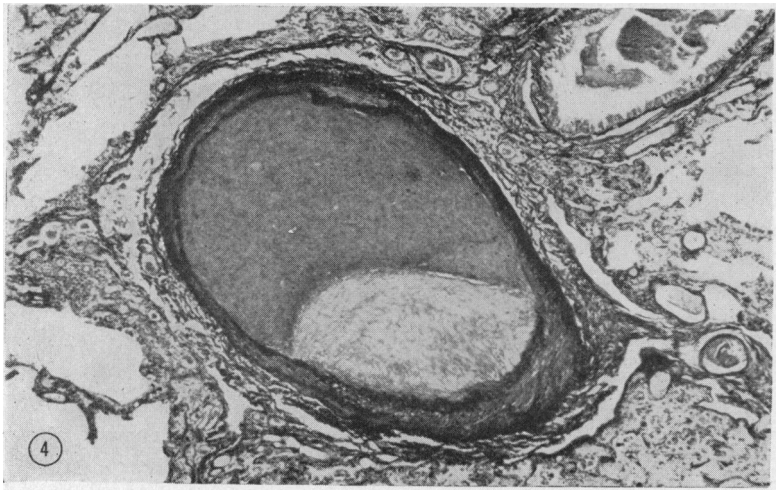


FIG. 2.—Post-mortem pulmonary arteriogram of right lung showing several large areas which have not become injected. This is due to pulmonary artery occlusion. Some of the small injected vessels end abruptly for the same reason. The large organizing thrombus shown in Fig. 3 can be seen here (arrow) as a filling defect (approximately one-third natural size).

FIG. 3.—Section of right pulmonary artery showing great reduction in lumen by laminated thrombus. The paler material in the lumen is injected medium (see arrow in Fig. 2; H. and E. ×7.5.)

FIG. 4.—A large muscular pulmonary artery containing a pale-staining partially organized thromboembolus. (Elastic–Van Gieson. ×40.)

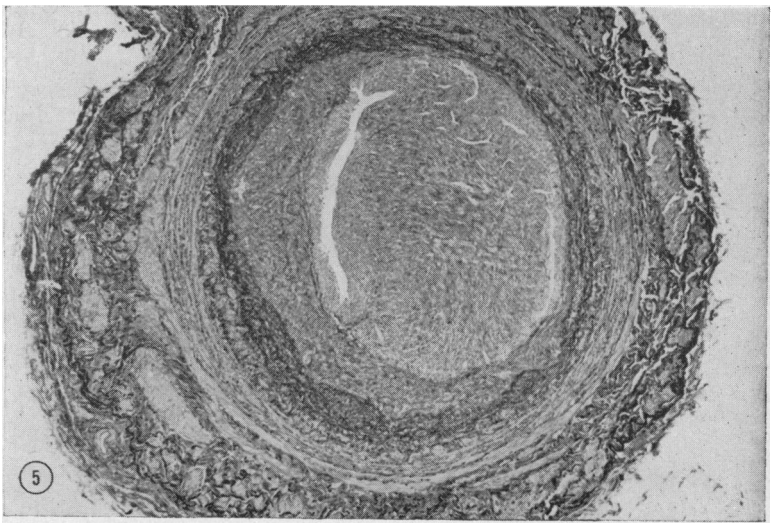


FIG. 5.—Right long saphenous vein almost occluded by old organized thrombus. (Elastic–Van Gieson. ×40.)

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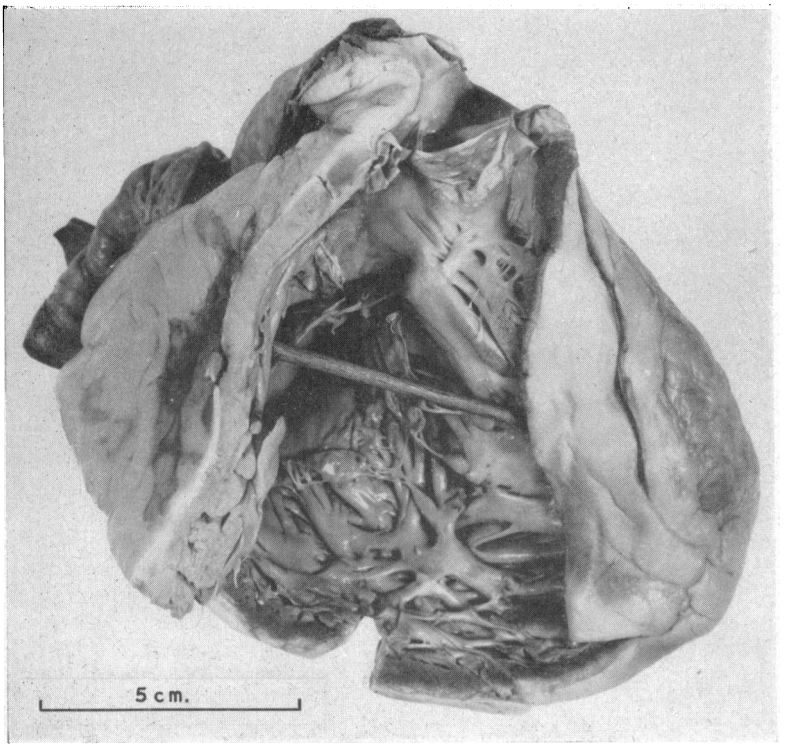


FIG. 6.—Heart showing right ventricular hypertrophy.

FIG. 7.—Breast showing gynaecomastia with proliferation of connective tissue and ducts (H. and E. ×40.)

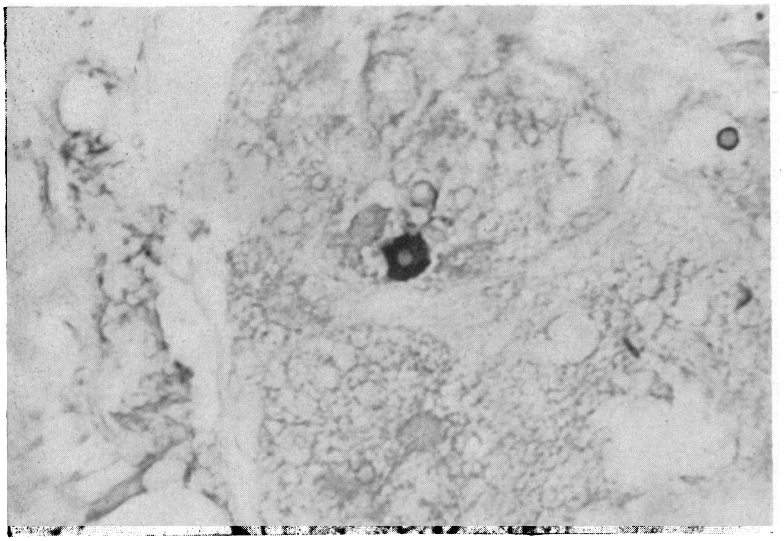

FIG. 8.—Darkly stained laminated "spironolactone" body in adrenal cortex. (Sudan Black. ×1,000.)

The *pleural cavities* contained 50 ml. each of straw-coloured fluid and the peritoneal cavity 1,500 ml. Numerous ribs were fractured.

The *pleura* was patchily thickened over both lungs. A few old adhesions were present. The *left lung* weighed 950 g. (N=400 g.). Some oedema and multiple infarctions were present with numerous recent and old thrombi occluding vessels down to a size just visible to the naked eye. The pulmonary trunk contained a laminated thromboembolus extending into the right and left pulmonary arteries and narrowing the lumina by about 40%. The *right lung* weighed 1,110 g. (N=450 g.). It was injected with Raybar cream, and *x*-ray films showed extensive infarction in both upper and lower lobes (Fig. 2). The main pulmonary artery was dilated, and it, as well as many larger arteries (5,000 $\mu$–2,000 $\mu$), showed irregular narrowing of the lumina; some showed total occlusion, which was particularly severe at muscular artery level (66 $\mu$ and less).

Histology of both lungs showed a whole spectrum of widespread vascular occlusion at all levels of the arterial tree (Fig. 3, 4), varying from very recent thrombi and early organization to abundant "septal organization" consisting of a few fibro-elastic bands dividing the lumen of a previously occluded vessel. In other arteries eccentric intimal fibrosis was seen. The thrombus at the bifurcation of the pulmonary trunk showed layering of very old thrombus (many months) to recent thrombus (days) near the lumen of the vessel. Evidence of pulmonary hypertension consisting of concentric intimal fibrosis and medial hypertrophy (to double its normal thickness) was present, particularly at the muscular artery level (600 $\mu$–100 $\mu$) and in the arterioles.

The pulmonary veins were normal, but old and recent infarction was confirmed.

Thrombosis with total occlusion was found in the right cephalic, right long saphenous (Fig. 5), and left femoral vein, and severe narrowing by organized thrombus was present in the left long saphenous vein and the splenic vein.

Histology showed thrombi of varying ages. The venous walls appeared normal.

The *heart* weighed 425 g. (N=380 g.). Right ventricular hypertrophy (Fig. 6), 9 mm. at conus (N=3 mm.), and some dilatation was present. The left ventricle was normal. The *valves* were also normal, including the tricuspid valve, 130 mm. (upper limit of normal).

Histology confirmed muscular hypertrophy and showed patchy fine fibrosis.

The coronary arteries showed confluent atheroma but widely patent lumina. There was moderately severe patchy atheroma in the thoracic part of the aorta and severe atheroma with calcification and ulceration in the abdominal part.

The *liver, spleen,* and *kidneys* showed mild congestion only.

Both *breasts* showed gynaecomastia, which on histology (Fig. 7) showed an increase in dense collagen tissue, loose periductal tissue, and ducts, some of which showed branching.

The *adrenal glands* each weighed 6 g. (N=6 g.), and showed "Spironolactone" bodies (Fig. 8) in the zona glomerulosa but no other changes.

There was a hydrocele of the cord and a spermatocele on the left side. The *testes* were normal.

## Pathologist's Diagnosis

(1) Thromboembolic pulmonary hypertension. Right ventricular hypertrophy.

(2) Peripheral venous thrombosis.

(3) Congestion of liver, spleen, and kidneys.

(4) Gynaecomastia.

## Incidental Findings

(5) Hydrocele of the spermatic cord and spermatocele.

(6) "Spironolactone" bodies.

## Discussion

Professor SIR JOHN MCMICHAEL: There is nothing much to add so far as the gross findings are concerned. They were recognized in life. I don't apologize for having diagnosed tricuspid incompetence, because in its developing stages it comes and goes. This disorder cannot always be diagnosed at necropsy, for the degree of dilatation of the tricuspid ring is a living phenomenon. The heart can undergo some degree of rigor mortis, and this may abolish the evidence of dilatation. The whole course of this illness was relentless, and we were not able to influence the outcome.

The use of anticoagulants in venous thrombosis is quite justified. It is generally believed now that the beginning of a thrombus, particularly on an artery, is usually by platelet conglutination on an atheromatous plaque which has ulcerated. This process of platelet conglutination is not influenced by anticoagulants. One thing anticoagulants may influence is the subsequent propagation of a clot. Clots in veins tend to grow almost like seaweed from a root out into the bloodstream; you often see great long clots from the femoral veins embolizing the pulmonary arteries, coiled up like a big worm. It is hoped that anticoagulants may stop this secondary clotting process but they do not stop the initiating platelet thrombus. This may explain why anticoagulants are not much good in the arterial side of the circulation, where very little clotting tail is seen, but they can be of benefit on the venous side. They are worth trying, but in spite of anticoagulants there was evidence here of recent clots which had formed while he was on his treatment, which had been well maintained by a former colleague. Note also that in spite of this continuous thrombosing process in his veins he had extensive confluent atheroma in his abdominal aorta and also in his coronaries, but he had no thrombi on the arterial side of the circulation. If change in the clotting tendency of the blood is responsible for arterial thrombosis, then this patient should have developed complicating arterial thrombosis as well. This is a very important and interesting negative. Professor Goodwin has been very much interested in this condition for a long time; I am sure he would like to say something.

## Baffling Disease

Professor J. F. GOODWIN: This disease is a very baffling one. It tends to present either in this way with obstruction to large vessels, or with obstruction to arterioles, so that the onset is insidious and not usually marked by the symptoms of venous thrombosis or pulmonary embolism. We will neglect that group for the moment. This patient, I think, was very interesting, because he showed one of the features well known with recurrent pulmonary embolism: that the signs of venous thrombosis may appear after the pulmonary embolism and thrombosis have arrived.[1 2] He seems to have had a considerable amount of emboli and developed heart failure before his first obvious venous thrombosis occurred. I think that is very important. In assessing a patient who has unexplained heart failure, particularly unexplained hyperventilation, this disease ought to be considered. The physical signs are very interesting in these patients, and we have found that many of them, when they reach this stage of the disease, have delayed pulmonary valve closure owing to prolonged ejection by the right ventricle, which is very dilated.[3] This may lead to erroneous diagnosis, and sometimes even constrictive pericarditis may be suspected because of the high end-diastolic pressure in the right ventricle which can occur in right ventrieular failure. Medical treatment, as Sir John said, is often unsatisfactory, probably

because in many cases the diagnosis is made too late. I think heparin has some advantage over phenindione, but it is difficult to give over long periods, and osteoporosis may result from prolonged use. I have been very reluctant to embark upon surgical treatment, such as ligation of the inferior vena cava, which is practised in the United States quite extensively. The reason for being conservative may perhaps be seen from this morning's demonstration of occlusion of small arterioles and arteries; preventing further emboli would not necessarily cure the disease. But there obviously are some patients in whom this is worth thinking about, and last year Moser and his colleagues[4] in Washington removed large thrombi from the main pulmonary arteries of two patients with this disease. It is interesting that they were able to pull out a number of tails of clot from vessels in which I would have thought thrombi would have been completely organized and adherent. It is, then, extremely important to bear this form of therapy in mind in some of these patients, but unfortunately the disease is often so widespread that such treatment is unlikely to succeed.

## Fibrinolytic Activity

While trying to discover the underlying cause of the tendency to thrombosis we investigated[5] fibrinolytic activity in a group of these patients and found that it was normal, except in those who had repeated pulmonary infarcts but no pulmonary hypertension. In these patients fibrinolysis was defective—I really don't know what this means! But more recently Hirsch and McBride[6] have studied platelet adhesiveness and platelet turnover in this type of patient. I don't think the tests were actually done on this particular patient, but they have been performed on a number of such patients, and increased stickiness has been found in all. I don't know whether this is the cause of the repeated thromboses—it might merely be the result. The possible therapeutic implications are being studied.

Dr. M. CAMPBELL: I would like to emphasize a clinical point. Thromboembolic hypertension should be suspected if a patient is found to have a low $P_{CO_2}$ which persists or gets worse during exercise. The mechanism of the overbreathing is obscure.

Professor R. E. STEINER: Can I just ask Professor Goodwin to enlarge his account of the group with micro-embolism, where there is small-vessel occlusion?

## Pulmonary Hypertension in Young Women

Professor GOODWIN: This, of course, is the other type. It has been recognized for many years, since Castleman and Blane[7] published their original cases. There is progressive right ventricular failure from micro-embolism in the arterioles of the lungs. The syndrome occurs usually in young women after a normal pregnancy. They develop progressive dyspnoea and often syncope on exertion, followed by progressive and relentless right ventricular failure. When we examined[8] and investigated these patients we found obliterative pulmonary hypertension with no obvious cause for it, and (if I could poach on Professor Harrison's ground for a moment) the arterioles of the lungs at necropsy showed evidence of exactly what Dr. Olsen has shown us—thrombosis, presumably on an embolic basis, with recanalization of vessels without an obvious preceding arteritis, no involvement of the large pulmonary arteries, and no source for embolism. It has been postulated, but many people argue with this, that these patients develop during or after pregnancy repeated or continuous micro-emboli, perhaps arising from the pelvis, which gradually choke up the pulmonary arterioles. A possible alternative explanation is that these patients lack some factor which normally keeps their pulmonary arterioles clear. Perhaps we all have small pulmonary emboli from time to time but have an efficient mechanism for disposing of the emboli, which these patients do not have. Animal work by Allison *et al.*[9] has shown rapid reduction in the size of pulmonary emboli in dogs. It is very interesting that even a large pulmonary embolus in an otherwise normal person may resolve completely. But we don't really know the answer to this, and in many of these patients the diagnosis of the cause of the obliteration of arterioles is inferential until a histological examination is made. Such patients do resemble very closely those with idiopathic, solitary, or lone pulmonary hypertension, but they can be distinguished by the association with pregnancy. This disorder is almost always confined to women, there is no family history, and it does not occur in children. In "primary" pulmonary hypertension there is commonly a family history, the patients are often male children, and I think that Professor Harrison will again agree that the arterioles show medial hypertrophy only, or may even be amazingly normal, and show no evidence of organic obstruction.

Professor C. V. HARRISON: Yes, that far I agree.

## Source of Emboli

Dr. CELIA OAKLEY: I think it is arguable whether the group of patients without demonstrable major pulmonary arterial occlusions have had thromboemboli at all. It's probably true to say that there are no males in this group, except in the rare instances when they were young children and might be examples of true primary pulmonary hypertension or else they had a familial incidence of idiopathic pulmonary hypertension. The majority are young women who have recently been pregnant. Might the disease not be a response to amniotic fluid or trophoblastic embolism? One could hardly expect other emboli to be so sex discriminating.

Professor MCMICHAEL: I must confess I've some reservation about this. We used to talk about primary pulmonary hypertension as something like arterial hypertension. An effort has been made to ascribe the findings to occlusion by emboli of finer vessels, but if one gets too refined, one makes a diagnosis on very speculative assumptions.

Professor STEINER: This patient had massive occlusion of large pulmonary arteries. If one compares the arteriogram with that of a patient with arteriolar occlusion, the latter shows good filling of the pulmonary arteries well out to the peripheral border without major occlusion. In fact, this is the distinction we make between the two types. Although some of the large arteries can be very tortuous, obliteration seems to be right out in the very small branches and arterioles. There seems to be quite good correlation between the angiographic appearances and the morbid anatomical findings.

Professor GOODWIN: This is the condition which occurs in those patients who after pregnancy get fainting attacks and breathlessness and are often dismissed as anaemic or neurotic—until the disease is irreversible. It is terribly important to diagnose the condition, whatever the actual underlying cause may be.

Professor MCMICHAEL: I must say I think we're not very successful in treating these patients.

Professor GOODWIN: No, we're very unsuccessful, and I think it's because we get these patients too late. A patient in whom the disease has really been reversed was diagnosed quite early because she fainted pushing the pram, and this was naturally unusual for her. Her practitioner spotted some signs of pulmonary hypertension, which led to the disease being detected and anticoagulants started.[10]

## Is it Embolic?

Dr. C. T. DOLLERY: Can I suggest that neither of these diseases are necessarily embolic? I never have believed that "small vessel" pulmonary vascular disease is embolic, and I

wonder how much of the large vessel disease is embolic. We diagnose pulmonary emboli fairly frequently, and yet this kind of disease is quite rare. Looking at the pathology, it seems as if there must have been hundreds of distinct embolic episodes. Surely some of these would have been recognized clinically. I know this man had peripheral vein thrombosis at one stage, but it does seem to me that there is much more to this than embolism.

Professor MCMICHAEL: You don't even accept this one today?

Dr. DOLLERY: Not necessarily, no. We've been studying the experimental effects of platelet emboli. These cause a very transitory blockage of small vessels. Even vascular occlusion by blood clot is lysed remarkably quickly in animals. It cannot necessarily be inferred that this would happen if vessels were bombarded day after day, but it does suggest one ought to look further than simple infarcting embolism.

Professor GOODWIN: I agree with you—this is exactly the reason why one has the feeling that there's something going on locally in the lung, either some kind of failure of an enzyme, or some structural change which we don't recognize, which keeps the process going after perhaps one pulmonary embolism or a calf vein thrombosis.[11] In 999 people out of a 1,000 this will resolve, within two weeks probably, but the thousandth person will go on to progressive thrombosis. Now you can't deny that what we see here is a blood clot in the pulmonary artery, and I think it's very likely that it is in the small vessels too. But I agree that there is probably a failure of the normal mechanism of disposing of clots in the lung. I suspect that as we're sitting here many of us are having a few small pulmonary emboli, but we're all able to deal with them.

Dr. OLSEN: Under the microscope we are unable to recognize any consistent changes in vessel walls, be it large vessels or small vessels. Various authors have previously pointed out that changes could be seen. A peculiar form of arteritis which has usually disappeared when the patient comes to necropsy has been postulated. Gilmour and Evans from the London Hospital pointed out medial thinning. Now neither of these changes can be found consistently, and, as Professor Goodwin and Dr. Dollery pointed out, there must be something else, but this we cannot see with light microscopy.

Professor J. P. SHILLINGFORD: Systemic hypertension is a very common condition, and it is unlikely that emboli cause this. Is it not possible that pulmonary hypertension occurs without emboli in some cases as a result of primary changes in the arterioles?

Dr. OAKLEY: This may account for some of the familial cases. Can I raise a point about sticky platelets in the absence of Dr. McBride?—sticky platelets are simply juvenile ones, and they reflect an increase of platelet production due to utilization of platelets in thrombi.

Dr. M. NOBLE: The clinical picture can be produced by trophoblastic emboli,[12] and I think it's important to exclude this in women by doing quantitative gonadotrophin studies, because this type of case can be successfully treated.

We are grateful to Professor J. P. Shillingford and Dr. E. D. Williams for assistance in preparing this report, and to Mr. W. Brackenbury for the photomicrographs.

## REFERENCES


1. Stevens, A. E., *Lancet*, 1961, **2**, 1005.
2. Thompson, E. N., and Hamilton, M., ibid., 1962, **1**, 1369.
3. Shapiro, S., Clark, T. J. H., and Goodwin, J. F., ibid., 1965, **2**, 1207.
4. Moser, K. M., Houk, V. N., Jones, R. C., and Hufnagel, C. C., *Circulation*, 1965, **32**, 377.
5. Ellison, R. Curtis, and Brown, J., *Lancet*, 1965, **1**, 786.
6. Hirsh, J., and McBride, J. A., *Brit. med. J.*, 1965, **2**, 797.
7. Castleman, B., and Bland, E. F., *Arch. Path.*, 1946, **42**, 581.
8. Goodwin, J. F., Harrison, C. V., and Wilcken, D. E. L., *Brit. med. J.*, 1963, **1**, 701, 777.
9. Allison, P. R., Dunnill, M. S., and Marshall, R., *Thorax*, 1960, **15**, 273.
10. Wilcken, D. E. L., MacKenzie, K. M., and Goodwin, J. F., *Lancet*, 1960, **2**, 781.
11. Goodwin, J. F., in *Proceedings of a Symposium on Pulmonary Embolic Diseases* held Boston 1964, ed. A. A. Sasahara and M. Stein, 1965. New York.
12. Bagshawe, K. D., and Noble, M. I. M., *Quart. J. Med.*, 1966, **35**, 39.


# Approved Names

The first supplement to the November 1966 consolidated list of Approved Names is printed below. Communications relating to Approved Names should be addressed to the Secretary, British Pharmacopoeia Commission, General Medical Council, 44 Hallam Street, London W.1.

| Approved Name | Other Names | Action and Use |
|---|---|---|
| Amiloride .. | *N*-Amidino-3,5-diamino-6-chloropyrazinamide<br>MK-870 is the hydrochloride | Diuretic |
| Bisoxatin .. | 2,3-Dihydro-2,2-di-(4-hydroxyphenyl)benz-1,4-oxazin-3-one<br>La-271a, Wy-8138 and Laxonalin are the diacetate | Laxative |
| Bupivacaine .. | 1-Butyl-2-(2,6-xylylcarbamoyl)piperidine<br>AH 2250 is the hydrochloride | Local anaesthetic |
| Cellacephate .. | A partial mixed acetate and hydrogen phthalate ester of cellulose | Enteric coating |
| Cephaloglycin .. | 7-[D(−)-α-Aminophenylacetamido]cephalosporanic acid<br>Kefglycin | Antibiotic |
| Clofluperol .. | 4-(4-Chloro-3-trifluoromethylphenyl)-1-[3-(4-fluorobenzoyl)propyl]piperidin-4-ol<br>R.9298 | Neuroleptic |
| Clothiapine .. | 2-Chloro-11-(4-methylpiperazin-1-yl)-dibenzo[b,f][1,4]thiazepine | Tranquillizer |
| Cromoglycic Acid | 1,3-Di-(2-carboxy-4-oxochromen-5-yloxy)-propan-2-ol<br>FPL 670 is the disodium salt | Treatment of allergic airway obstruction |
| Desolone .. | 11β,17α-Dihydroxypregna-1,4-diene-3,20-dione<br>R.D. 20,000 is the 17-propionate | Corticosteroid |
| Dichromium Trioxide .. | Chromium sesquioxide | Diagnostic aid |
| Dopamine .. | 2-(3,4-Dihydroxyphenyl)ethylamine | Sympathomimetic |
| Emepronium Bromide | Ethyldimethyl-1-methyl-3,3-diphenylpropylammonium bromide<br>Cetiprin | Anticholinergic |
| Flumedroxone .. | 17α-Hydroxy-6α-trifluoromethylpregn-4-ene-3,20-dione<br>Demigran is the acetate | Treatment of migraine |
| Fluprofen .. | 2-(3′-Fluoro-4-biphenylyl)propionic acid<br>R.D. 17345 | Anti-inflammatory; analgesic |
| Hydroxyurea .. | Hydroxyurea<br>Hydroxycarbamide (I.N.N.)<br>Hydrea | Antineoplastic agent |
| Hypromellose .. | A partial mixed methyl and hydroxypropyl ether of cellulose | Laxative |
| Meladrazine .. | 2,4-Di(diethylamino)-6-hydrazino-1,3,5-triazine<br>Lisidonil is the (+)-tartrate | Polysynaptic inhibitor |
| Minepentate .. | 2-(2-Dimethylaminoethoxy)ethyl 1-phenylcyclopentanecarboxylate<br>UCB 1549 | Treatment of the Parkinsonian syndrome |
| Mitoclomine .. | *NN*-Di-(2-chloroethyl)-4-methoxy-3-methyl-1-naphthylamine | Cytotoxic agent |
| Mitopodozide .. | *N′*-Ethylpodophyllohydrazide<br>SPI | „ „ |
| Nifuratel .. | 5-Methylthiomethyl-3-(5-nitrofurfurylidenamino)oxazolidin-2-one<br>Macmiror | Treatment of trichomoniasis |
| Octaverine .. | 6,7-Dimethoxy-1-(3,4,5-triethoxyphenyl)-isoquinoline | Antispasmodic |
| Oxypurinol .. | 1-*H*-Pyrazolo[3,4-d]pyrimidin-4,6-diol<br>B.W. 55-5 | Xanthine oxidase inhibitor |
| Pentagastrin .. | t-Butyloxycarbonyl-β-alanyl-L-tryptophyl-L-methionyl-L-aspartyl-L-phenylalanine<br>BOC-β-Ala.Try.Met.Asp.Phe.$NH_2$<br>I.C.I. 50,123; Peptavlon | Gastrin-like peptide |
| Pramindole .. | 5-(3-Dimethylaminopropyl)-6,7,8,9,10,11-hexahydrocyclo-oct[*b*]indole<br>Iprindole (I.N.N.)<br>Wy-3263 is the hydrochloride | Antidepressant |
| Tetracosactrin .. | Synthetic β 1–24 corticotropin<br>Synacthen | Synthetic corticotrophin |
| Tiemonium | 4-[3-Hydroxy-3-phenyl-3-(2-thienyl)-propyl]-4-methylmorpholinium iodide | Antispasmodic; anticholinergic |
| Trifluperidol .. | 1-[3-(4-Fluorobenzoyl)propyl]-4-(3-trifluoromethylphenyl)piperidin-4-ol<br>R.2498; Triperidol | Neuroleptic |
| Virginiamycin .. | An antibiotic produced by *Streptomyces virginiae*<br>Virgimycin (I.N.N.) | Antibiotic |