Mrs. "Ford," aged 65 in 1926, an old lady whose father, daughter, and grandson also had haemolytic icterus, illustrates the frequent association of cholecystitis and cholangitis with this condition, and, when from age or severity of symptoms, both gall-bladder and spleen cannot be operated upon at the same time, the importance of deciding which operation should have priority. This patient had in her youth mild jaundice, varying in degree and probably of haemolytic origin, for her spleen was known to be enlarged. As time wore on, the jaundice picture altered and suggested cholecystitis. At the age of 51, in 1912, the gall-bladder was drained and calculi were removed. Thereby the pain disappeared, but jaundice persisted. The unwisdom of not removing the large spleen shortly thereafter is obvious. A few years later, when aged about 65, haemolytic anaemia in the shape of breathlessness and palpitation made itself manifest, and the blood picture showed 3,384,000 red cell count, the fragility was 0.6 for commencing haemolysis, the van den Bergh test showed a negative direct and a positive indirect reaction, and there was no bilirubin in the urine. A year later the jaundice increased, the van den Bergh direct reaction became positive, and bile pigment appeared in the urine; henceforth the case resembled more the picture of cholangitis. The red cell count was now 3,050,000, and the reticulocytes only 0.6 per cent., showing that there was but little fight left on the part of the bone marrow. Finally, it was decided to operate on the cholangitis; this was done, but, as a preliminary, after every care in typing, blood transfusion was performed. There followed a gradual deepening of the jaundice to a dark olive-green colour. Death ensued. The patient would have been better without the transfusion. This occurrence of severe jaundice following transfusion again finds illustration in the next case.

Mrs. "Bass."—Aged 44, admitted on January 11th, 1928, under Dr. Leyton, for whose permission I am indebted. There was here a doubtful history of icterus early in life; at the age of 13 the patient had been treated for chlorosis. She had had fourteen children, of whom thirteen died at or soon after birth. The last and fatal illness, at the age of 44, lasted nearly six months, and was characterized by increasing anaemia, an icteric tint, failure of appetite, and later loss of flesh. The spleen was enlarged nearly to the umbilicus; the liver was just palpable. Lungs clear; heart, soft systolic murmur at base; blood pressure 140/75; small haemorrhages in right fundus; urine cloudy with albumin; urobilin ++; x-rays of bones, normal.

TABLE VII.—"Mrs. Bass"

Date	R. B. C. c.mm.	W. C. c.mm.	Hb %	In ² ex	Small Lympho- cytes %	Reticulo- cytes %
11/1/28	1,600,000	8,000	33	1.03	31.0	30.0
17/1/28	1,600,000	9,000	34	1.06	20.5	43.4
23/1/28	1,600,000	8,560	32	1.0	27.5	65.2
4/2/28	1,400,000	9,360	28	1.0	29.0	
26/1/28	2,000,000	10,500	40	1.0	31.0	51.4
5/3/28	1,600,000		35			
8/3/28	1,900,000	11,500	39	1.02	9.0	48.5
11/1/28	33 normoblasts in counting 200 white cells					
4/2/28	78 normo., 8 megal., 5 micro. in 200 w. cells					
26/2/28	14 normo., 4 megal., in 200 white cells					
8/3/28	41 normo., 16 megal., in 200 white cells					
18/1/28	Van den Bergh reaction: Direct negative. Indirect positive.					
14/2/28	Strong biphase reaction after first transfusion.					
5/3/28	Strong biphase 4.8 units.					
5/3/28	Fragility reached 0.82. Wassermann reaction negative.					
5/3/28	Cholesterol: 257 mg.					
5/3/28	Test meal: Free HCl absent. Total acidity 0.22.					

The patient received three blood transfusions during the last sixteen days of her life: (1) 350 c.cm., (2) 600 c.cm., and (3) 500 c.cm. The blood group was No. 2. Each transfusion was followed by pyrexia (up to 104° F.), vomiting, diarrhoea, and deepening jaundice. Towards the end there was increased anuria, and two days before death (March 28th, 1928) only three ounces of urine were passed. This anuria has been shown by Baker and Dodds²⁹ to be due to the blocking of the kidney tubules by masses of acid haematin pigment.

Here, then, is a second case which suggests caution in the employment of transfusion of blood in this disease. It will be noted also how some of the severe cases are almost identical in their pictures to pernicious anaemia (for example, Labourne and Bass).

[The list of references will appear at the end of Lecture II.]

PSEUDO-ARGYLL ROBERTSON PUPILS WITH ABSENT TENDON REFLEXES

A BENIGN DISORDER SIMULATING TABES DORSALIS

BY

W. J. ADIE, M.D.ED., F.R.C.P.

PHYSICIAN, CHARING CROSS HOSPITAL AND ROYAL LONDON
OPHTHALMIC HOSPITAL; PHYSICIAN TO OUT-PATIENTS,
THE NATIONAL HOSPITAL FOR NERVOUS DISEASES,
QUEEN SQUARE

I wish to draw attention to a benign symptomless disorder characterized by pupils which react on accommodation but not to light, and by absent tendon reflexes.

Five of the six cases I am about to describe came under my notice in the course of a few weeks; the condition therefore cannot be very rare. Though harmless in itself it merits recognition because it is often mistaken for a manifestation of syphilis of the nervous system, with unfortunate consequences for the patients and their families.

CASE I

A woman, aged 36, was admitted to the Hospital for Tropical Diseases under the care of Dr. G. Carmichael Low for an "overhaul" on her return from abroad. Physical examination and routine laboratory tests revealed no evidence of disease apart from the neurological signs that concern us here. There was nothing in the family or personal history to explain these signs. Ten years ago she noticed that her pupils were unequal. On examination I found pupils of moderate size, the right just larger than the left, which was slightly oval; neither reacted to light, direct or consensual; both contracted fully on convergence, but the movement was remarkably slow; after the effort to converge was relaxed they remained small for several seconds, then dilated very gradually to their original size. All the tendon reflexes in the upper and lower limbs were completely abolished. There were no other signs of organic nervous disease. I knew that this myotonic pupillary reaction had nothing to do with syphilis, but had never seen or heard of it in association with absent tendon reflexes. I reported as follows: "A most unusual case; I prefer not to make a diagnosis; the condition is benign, and should not prevent her from returning to her work abroad." After her discharge, Dr. Low kindly allowed me to consult the hospital notes, and I found that Wassermann's test had been done on the blood and cerebro-spinal fluid with negative results.

CASE II

A woman, aged 23, attended hospital because her brother, an optician, had found that she had Argyll Robertson pupils. She was admitted to the National Hospital for investigation. She knew "what they thought," and was greatly distressed. With the first case in mind I promised her that she should leave the hospital with the stigma removed. Apart from the special signs, nothing of importance was discovered in the course of a thorough routine investigation. The following observations were made: the pupils were unequal, right $3\frac{1}{2}$ mm., left 3 mm.; the right was irregularly oval with the long axis vertical, the left regularly oval with the long axis horizontal. The reaction to light was completely absent in both; the reaction on convergence was present in both, but was abnormal; the contraction was delayed and proceeded slowly until the pupils reached pin-point size. When the effort to converge was relaxed they dilated very slowly to their original size. The knee- and ankle-jerks

were completely absent. These observations were confirmed repeatedly by myself and my colleagues. The Wassermann reaction was negative in the blood and cerebro-spinal fluid. The report on the fluid was as follows: clear, colourless; no cells seen; total protein 0.035 per cent.; Nonne-Apelt and Pandy reactions negative; Lange's colloidal gold test, no change (Dr. J. G. Greenfield).

CASE III

A young man, now aged 32, was brought to me twelve years ago by his sister, a medical student, who discovered that he had Argyll Robertson pupils. I found that his knee-jerks were absent, and thought that he was a case of congenital tabes. He came to see me recently about another matter, and I went into his family and personal history and made a complete physical examination. Nothing apart from the neurological signs suggested syphilis, congenital or acquired. His general health was good. The pupils were moderate in size and unequal, right larger than left. The right was totally inactive to light, the left reacted very feebly. On convergence both pupils contracted very slowly to pin-head size, then dilated still more slowly when he looked into the distance. He had noticed himself that the pupils varied in size from time to time. All the tendon reflexes in the upper and lower limbs were absent. There were no other neurological signs. He has submitted to several tests of the blood and cerebro-spinal fluid, all with negative results.

CASE IV

A woman, aged 45, attended the Royal London Ophthalmic Hospital for glasses and was referred to me by Mr. Foster Moore, who had noticed the abnormal pupils. There was nothing worthy of note in the family or personal history. Her general physical condition was good. Vision improved to 6/9 right, 6/18 left; no optic atrophy (Mr. Foster Moore). The pupils were unequal; right 3 mm., left 2½ mm. The left pupil did not react to light; on convergence it contracted slowly but fully, and maintained its smaller size long after convergence had ceased; it then dilated very gradually. The right pupil contracted feebly to light, slightly better on convergence; the contraction was not slow or unduly maintained. The knee-jerks were easily obtained and equal, but the ankle-jerks were completely absent. The Wassermann reaction in the blood was negative. The cerebro-spinal fluid has not yet been examined.

CASE V

A girl, aged 17, was referred to me by Mr. Foster Moore and admitted to the National Hospital for investigation. She noticed about two years ago that her pupils were unequal, and that the left pupil varied in size from time to time. Four months ago the left pupil became permanently large; since then she has not been able to use it for close work. Otherwise she has always been in perfect health. Examination revealed no other signs except the following. The pupils were unequal; right 2½ mm., left 8 mm. They were both inactive to light; on convergence the right pupil contracted slowly to pin-point size, and when convergence ceased it again dilated very slowly. The left did not contract on convergence. The knee-jerks were brisk; for a patient of her age, and compared with the active knee-jerks, the ankle-jerks were certainly abnormally sluggish. The Wassermann reaction was negative in the blood and cerebro-spinal fluid. Report on the cerebro-spinal fluid: clear, colourless, 1 cell per c.mm.; total protein 0.03 per cent.; Nonne-Apelt and Pandy reactions negative; Lange's colloidal gold reaction 0001100000 (Dr. J. G. Greenfield).

CASE VI

In an article on the myotonic pupil in Wilbrand and Saenger's *Neurologie des Auges*, I found a reference to a case described by Gehrecke in which eye signs like those in my cases were found in a patient with "imperfect stationary tabes." The following is an extract of the case history: A woman, aged 45; right pupil inactive to light, very slow contraction and relaxation on conver-

gence; ankle-jerks absent. There were no other signs of organic nervous disease. The family history was not given. The Wassermann reaction was negative in the blood and cerebro-spinal fluid. The Nonne-Apelt, Weichbrodt, and Pandy reactions were all negative; no increase of cells; pressure normal. Nevertheless, because the ankle-jerks were absent the diagnosis of tabes was made. This is the only case resembling my own that I have been able to find in the literature. I have not yet completed my search. (See note at end.)

COMMENTARY

It is not surprising that all of these patients with "Argyll Robertson pupils" and absent tendon reflexes were thought to be suffering from syphilis of the nervous system, congenital or acquired. The correct diagnosis can be made with certainty by closely observing the contraction of the pupil during the act of accommodation for near objects. The true Argyll Robertson pupil reacts promptly and fully, often excessively, on convergence, and dilates again as soon as the effort to converge the visual axes is relaxed. In these cases the pupils show the so-called myotonic reaction; they do not respond to light; they contract very slowly through a wide range during a sustained effort to converge; often remain small long after the effort ends, and, when they dilate again, do so slowly. They differ in other ways from the true Argyll Robertson pupil, but the above features are sufficient to distinguish them. This myotonic reaction is well known to ophthalmologists, and it has been firmly established that syphilis plays no part in its production. Mr. Foster Moore has described seven cases under the title "Non-luetic Argyll Robertson pupil," and has told me of several others he has seen. The characteristics of his cases are, he says, the complete or substantially complete inaction of the pupil to the light stimulus, the leisurely manner in which it contracts with convergence, and in which it again dilates after relaxation of convergence; the frequency with which it is unilateral; the integrity of accommodation; the absence of syphilis; the presence of knee-jerks, and the absence of signs of any nervous disease even after many years.

It seems to me more than probable that some of his cases with non-luetic Argyll Robertson pupils but normal tendon reflexes are examples of a milder form of the same benign disorder that I have described here. I think, too, that my cases are related to those described by Mr. Gayer Morgan and Dr. C. P. Symonds under the titles "A series of cases with rapid onset of unequal pupils and failure of accommodation: a forme fruste of encephalitis lethargica," and "Internal ophthalmoplegia with absent tendon reflexes." In their cases the defect was most often unilateral, the affected pupil was dilated, and reacted not at all or incompletely both to light and on convergence; further, accommodation was partially paralysed, so that visual symptoms were produced. In some of their cases the tendon reflexes were diminished or lost.

My fifth patient seems to me to provide evidence that links the three groups. In one eye her pupil was dilated and fixed, with paralysis of accommodation, as in the cases described by Mr. Morgan and Dr. Symonds; in the other eye accommodation was normal, the light reflex was absent, and the reaction on convergence was myotonic as in the non-luetic Argyll Robertson pupils of Mr. Foster Moore. My fourth case also showed a myotonic pupil on one side and a partially fixed pupil on the other. I have reason to believe that a large fixed pupil is sometimes the forerunner of a myotonic pupil. These and other more academic aspects of the subject I hope to deal with at another time. My object now is to make it known that pupils conforming to the prevailing loose definition of an Argyll Robertson pupil, and easily mistaken for the true

Argyll Robertson sign, may be found associated with loss of tendon reflexes in patients with a benign disorder that has nothing to do with syphilis whatsoever.

Note.—After this was written, Mr. Foster Moore kindly allowed me to read the typescript of his paper on the non-luetic Argyll Robertson pupil, which he read at the recent ophthalmological congress. In one of his fifteen patients with this abnormal reaction of the pupil, the knee-jerks were absent: in another they were obtained with reinforcement only.

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ACUTE MASSIVE COLLAPSE OF THE LUNG FOLLOWING LIPIODOL INJECTION

BY

A. J. SCOTT PINCHIN, M.D., F.R.C.P.

PHYSICIAN TO VICTORIA PARK CHEST HOSPITAL; PHYSICIAN, WEST
LONDON AND HAMPTSTEAD GENERAL HOSPITALS

AND

H. V. MORLOCK, M.C., M.D., M.R.C.P.

PHYSICIAN TO OUT-PATIENTS, VICTORIA PARK CHEST HOSPITAL,
MILLER AND HAMPTSTEAD GENERAL HOSPITALS

In view of the more general use of lipiodol injection of the bronchial tree as an aid to the diagnosis of pulmonary disease and of the increasing importance which collapse of the lung is assuming in the etiology of acute pulmonary conditions, this case is of special interest.

The patient, a healthy-looking young man, aged 18, was sent to us because of a pain in the side, which he had had for two months and which his doctor suspected as a pleurisy. The pain was sufficiently severe to prevent him breathing deeply. There were no physical signs except feeble breath sounds. He was admitted to hospital for further investigation to exclude the possibility of fibrosis with bronchiectasis. A simple skiagram of the chest showed no abnormality. A lipiodol injection of the bronchial tree was done by the crico-thyroid route. To suit the convenience of the hospital this procedure was carried out on the x -ray table. The following points are to be noted:

1. The injection was done on the x -ray table, the film being in position, and the time from the injection to record of the skiagram was considerably less than five minutes, probably only three minutes.
2. At the time of the collapse the patient showed only slight respiratory distress. The physical signs present were diminished movement, slight impairment of percussion note, and a considerable diminution of the air entry over the affected side of the chest.
3. The speed with which recovery took place according to the skiagraphic records.

Jacobaeus, Selander, and Westermarck,¹ in their paper on acute massive collapse of the lung, record four such cases in which the injection of lipiodol was followed by collapse of the lung. These were from a series of eight patients with normal bronchi whom the authors were injecting for purposes of investigation, and it is somewhat astonishing that they should have found so high a proportion in whom the injection was followed by massive collapse.

In our case the bronchi were normal, but in a previous investigation on the subject of dry haemorrhagic bronchiectasis we occasionally injected lipiodol into a patient with normal bronchi, yet this is the first case of massive collapse from this cause that we have seen. In a series of many hundreds of lipiodol examinations for many varying pulmonary conditions at Victoria Park Hospital no such case of massive collapse has occurred.

A point of considerable interest is the length of time between the injection and the collapse. In Jacobaeus's cases

ten to fifteen minutes elapsed between the injection and the skiagrams. In our case the time between the injection and the record by skiagram was probably not more than three minutes. That is to say, the collapse was practically immediate. Coryllos, Birnbaum,² and also Lee, Radwin, Tucker, and Pendergrass³ produced massive pulmonary collapse in animals by plugging a bronchus with a balloon. The collapse was not complete till six hours later. The latter authors also obstructed a bronchus with a solution of gum arabic, causing complete collapse in four hours. The time taken for the collapse to disappear in Jacobaeus's cases was from two and a half to nine hours; in our case there was considerable improvement in half an hour, and complete recovery in twelve hours.

ETIOLOGY OF MASSIVE COLLAPSE

Morison,⁴ in an instructive article reviewing massive collapse, groups the four main theories of etiology as follows:

1. Failure of the respiratory power of the lung playing an active part (Pasteur).
2. The mucus plug theory (Jackson, Lee, and others).
3. Reflex spasm of muscles of the bronchioles (Bradford, Sante, and others).
4. Inflammation of the crus and one-half of the diaphragm or of pleural membrane covering it (Charlton Briscoe).

Clinical experience goes to show that Group 1 probably has least influence in the production of the condition. A mucus plug, acting either as a complete obstruction or as a check valve (in which case the air may be exhausted much more rapidly), may indeed be a factor in the causation of post-operative collapse, but cannot cause this instantaneous collapse.

Reflex spasm, involving the walls of the bronchioles, is the only way in which the lung could be so rapidly emptied of its air. Jacobaeus put forward this view in explanation of his four cases following lipiodol injection, concluding that spasm of the bronchi and bronchioles squeezed out most of the air in the bronchial system, leaving only the alveolar air to be absorbed. In support of this view he claimed that in two cases of his the bronchi were seen to be distinctly smaller in the state of collapse than later when the collapse had passed off. This scarcely seems a fair contention, as one would expect that in a collapsed lung the bronchi would naturally be smaller.

Sante⁵ incorporates the first three views in his theory that the condition is due to simultaneous inhibition of the cough reflex by some toxic or reflex stimulus, with an impairment of the respiratory muscles, caused either by a defensive immobilization or by paralysis from a toxic neuritis. This permits secretion to accumulate and block the bronchus, atelectasis resulting.

In this explanation the mucus plug is the final cause of the atelectasis. As has already been recorded, an atelectasis produced by a mucus plug in animal experiments required four to six hours to develop, but in these animals the inhibition of the cough reflex and the impairment of the respiratory muscles were not present. In cases of immediate collapse, we would suggest that it is the inhibition of the cough reflex and the impairment of the respiratory muscles which produce a reflex spasm of the bronchi and bronchioles (as suggested by Jacobaeus), thus actively expelling the air from the bronchial system, while the mucus plug acts as a check valve, not allowing air to re-enter.

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