CONCLUSION.

Inequality of pupils associated with thoracic aneurysm is usually due to inequality of blood-pressure in the ophthalmic arteries resulting from the abnormal vascular conditions.

Our best thanks are due to Dr. Mackenzie, Dr. Sansom, Dr. Kidd, and Dr. Head, and to Mr. Waren Tay, Mr. Mansell Moullin, and Mr. Furnivall for permission to record the cases quoted. The experimental work was done in the Gordon Laboratory at Guy's Hospital.

HISTORICAL BIBLIOGRAPHY.

1727. Pourfour de Petit (Mémoires de l'Académie Royale des Sciences, 1727, p. 1, and Histoire de l'Académie Royale des Sciences, 1727, p. 7) claimed that the sympathetic (intercostal nerve) took origin from the spinal cord and controlled the size of the pupil. He described the effect of division of the nerve in animals.

1839. Reid (Edinburgh Medical and Surgical Journal, vol. xlix., p. 132, January, 1838, and vol. lii., p. 38, August 30th, 1839), repeated and confirmed Petit's experiments and showed that division of the nerve led to contraction of the pupil upon the same side.

1846. Serafino Biffi (Omodei: Annali di Medicina, third series, vol. xxii., pp. 630 to 641, vol. cxviii. the Catalogue of the Library of the Royal College of Surgeons of England) demonstrated the effect of stimulating the peripheral and of the divided sympathetic.

1847. Hyrtl (Handbuch der Topographische Anatomie, p. 202) claims that vascular conditions cannot affect the size of the pupils for the following reasons: 1. Because the vessels of the head may be engorged and yet the pupil be large. N.B. The possibility of the size of the pupil varying inversely as the arterial tension has been discussed in the present paper and an attempt has been made to show that venous engorgement, being frequently associated with a fall of the arterial tension, may lead to enlargement of the pupils. 2. Because after death by decapitation the pupils may be small even though the blood has drained from the vessels. N.B. Hyrtl forgot that the cervical sympathetic must have been divided with the rest of the neck and that myosis of nervous origin would therefore be a probable consequence. Langley and Anderson (*vide infra*) accept Hyrtl's statement without further investigation. It is a well-known fact that if an animal be bled to death in a simpler way than by decapitation the pupils become large.

1853. Walshe (Diseases of the Lungs, Heart, and Aorta, p. 759) described inequality of the pupils in association with thoracic aneurysm but did not suggest an explanation.

1854. Brown-Séquard (Comptes Rendus de l'Académie des Sciences, 1854, tome xxxviii., p. 72) extended and completed Claude Bernard's researches.

1855. Gairdner (Edinburgh Medical Journal, August, 1855, p. 153) described a case of thoracic aneurysm which at the necropsy was found to have involved the inferior cervical ganglion of the sympathetic in which during life the pupil on the same side had been the smaller of the two and which did not dilate on shading nor completely on the instillation of atropin. No mention is made of unilateral changes of temperature, sweating, enophthalmos, or ptosis, but the case seems to have been one of some sympathetic paralysis due to the growth of a thoracic aneurysm.

1856. Waller (Comptes Rendus de l'Académie des Sciences, 1856, tome xliii., p. 659) described the spiral or zigzag structure of the vessels of the iris as seen by the microscope in albino rabbits and showed that whether straight when the pupil was small, or coiled when the pupil was large, their calibre did not vary.

1858. Ogle (Transactions of the Royal Medical and Chirurgical Society, 1858, vol. xli., p. 397) wrote on the influence of the sympathetic on the eye and its appendages. This paper is the *locus classicus* for the clinical aspect of the question. Ogle collected 27 cases in which there was some abnormality of the pupils in association with aneurysms, either thoracic or cervical, or with malignant growths in the thorax or neck, or with inflammatory processes in the neck or with injuries of the cervical cord. In some of these there can be no doubt but that there was sympathetic paralysis or interference with the cilio-spinal centre; in others the evidence is not so clear and Ogle is forced into the explanation that at times there may be an irritation of the sympathetic acting at times directly on the trunk and at times on the sympathetic filaments supplied to the sac wall of an aneurysm. It is noteworthy that in the cases where this explanation is necessary there is no record of any sign, beyond inequality of the pupils, of implication of the sympathetic. Since the publication of Ogle's paper all text-books, both English and foreign, seem to have accepted his theory as sufficient to explain the anisocoria associated with thoracic aneurysm.

1875. Grünhagen and Samkowy (Archiv für die Gesammte Physiologie, x., p. 165) thought that dilatation of the pupil was caused by action of the sympathetic which acted either (1) by decreasing the quantity of blood in the iris so that it shrinks; (2) by contraction of the longitudinal coats of the radially-disposed arteries; or (3) by inhibition of the sphincter iridis.

1892. Langley and Anderson (Journal of Physiology, 1892, vol. xiii., p. 554) in a long and important paper discuss the mechanism of the movements of the iris and conclude that in addition to the sphincter iridis there is a radially-disposed contractile substance, not necessarily muscle though for convenience it is called the dilator muscle. With regard to some of the points discussed in the present paper they hold that the myosis which results from tapping the anterior chamber may be due to the fact that owing to the reduction of tension the ciliary region of the iris is allowed to come forward. We have suggested that it may be partly due to the reduction of the external pressure round a set of spiral vessels in which there is a positive internal pressure. Langley and Anderson accepted Hyrtl's views and thought that variations in blood-pressure could not normally affect the size of the pupil. They found that by injecting blood and warm saline fluid into the carotid no alteration of the pupil could be obtained in a living animal; if, however, the injection was made in a dead animal and with a carmine injection mass myosis resulted. These experiments agree with our own observations which we have attempted to explain as due in the first case to the free anastomosis of the circle and in the second case to an obstruction in that anastomotic ring. Langley and Anderson, on the other hand, consider that the phenomenon is best explained on the supposition that it is due to stimulation of the sphincter iridis. In addition, they confirm Waller's account of the structure of the vessels of the iris and give figures showing how during dilatation of the pupil under atropin or stimulation of the sympathetic the vessels become zigzag and retain their normal calibre.

PRELIMINARY NOTE ON THE CHEMICAL AND THERAPEUTIC PROPERTIES OF LACHNANTHES TINCTORIA.

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LAST December, at the request of Dr. P. W. Latham of Cambridge, we undertook to investigate the chemical and therapeutic properties of the herb lachnanthes. Our investigations were considerably delayed at the outset by the facts that it was impossible to obtain either in England or in America more than a few pounds of the plant for nearly three months and that we experienced great difficulty in obtaining really virulent cultures of tubercle bacilli. At the present moment we are hampered by the fact that so small a quantity as 10 pounds of the plant has practically exhausted the available supply in England. Comments have been made on this delay and we think it well to issue a statement of the results which we have so far obtained.

The lachnanthes used by us was first submitted for examination to Mr. E. M. Holmes, the curator of the museum of the Pharmaceutical Society of Great Britain, who kindly undertook this duty for us and who certified that the specimens were genuine. The plant was then forwarded to Messrs. John Bell and Co. of Oxford-street in order that an extract might be prepared, and we are glad of this opportunity of expressing our indebtedness to them for the trouble they took in the matter and for the amount of time they gratuitously gave us. The lachnanthes was thoroughly exhausted with 70 per cent. alcohol and the alcohol was then completely distilled off the solution *in vacuo* and without the aid of heat. The solution obtained in this manner was employed in our experiments.

REPORT BY MR. GARDNER.

The extract made by Messrs. Bell and Co. from seven and a half pounds of lachnanthes herb contained 2·88 per cent. of solids. The whole extract, free from alcohol, was precipitated with lead acetate; the precipitate was then washed and decomposed by sulphuretted hydrogen. The aqueous filtrate yielded on evaporation a syrup which was soluble in alcohol and also in acetone. The solution in acetone was deep-red and on spontaneous evaporation yielded no crystalline matter but dried to a deep-red brittle shellac-like solid. The lead sulphide precipitate was dried and extracted with ether. This ethereal extract deposited a small amount of a red solid, whilst the residue on treatment with acetone yielded a further small amount of a yellow deliquescent substance. The mother liquor on spontaneous evaporation left a red syrup which constituted the bulk of the extract.

After extraction with ether the lead sulphide precipitate was extracted with 94 per cent. alcohol, and this extract yielded on spontaneous evaporation two or three grammes of a red crystalline solid, whilst the mother liquid dried to a red tarry matter, soluble in acetone, but which as yet has shown no signs of crystallisation. This constituted the bulk of the extract.

The filtrate from the lead acetate precipitate was now precipitated with lead subacetate. The precipitate thus obtained was decomposed by sulphuretted hydrogen as before and filtered. The aqueous filtrate contained the bulk of the resinous matter set free; it was evaporated and the residue exhausted with alcohol. A small portion was, however, insoluble in alcohol and was re-crystallised from water. The alcoholic extract was evaporated and extracted with

water, when a small amount remained undissolved. The bulk dissolved and on evaporation yielded a brittle, yellow, deliquescent, amorphous solid which was, however, soluble in water and insoluble in chloroform. It contained no nitrogen, did not reduce Fehling's solution, and was unsaturated. There were about from four to five grammes of this.

The lead sulphide precipitate was extracted with ether and alcohol. These extracts yielded small deposits of crystalline matter, but for the most part dried to a red viscous substance.

The filtrate from the lead subacetate was treated with sulphuretted hydrogen, the lead sulphide filtered off, and the filtrate evaporated to a dark syrup which was not sweet. This syrup was treated with animal charcoal and the aqueous extract was evaporated. A syrup was obtained which on standing for some weeks deposited crystals. These were filtered on the pump and recrystallised from dilute alcohol. The mother liquor on evaporation left a syrup.

As soon as a sufficient supply of the necessary material can be obtained the nature of these various bodies will be ascertained, as far as it is possible to do so.

REPORT BY DR. SPITTA AND DR. ARTHUR LATHAM.

In these experiments the aqueous solution made by Messrs. Bell and Co. was used. The extract was not wholly dissolved, consequently the suspended matter was thoroughly shaken up before the injections were made. Guinea-pigs were the animals employed.

The difficulty experienced at the outset of the investigations in obtaining really virulent cultures of tubercle bacilli was overcome by employing the caseous glands—pounded up in sterile normal saline—of guinea-pigs which had been inoculated with fresh tuberculous sputum. These emulsions, which microscopically were very rich in tubercle bacilli, were employed in each series of experiments.

SERIES I.

The following Experiments were made to ascertain the Lethal Dose of Lachnanthes.

Guinea-pig.	Inoculation.	Result.
No. 1	1 cubic centimetre of the aqueous solution.	Intra-peritoneal injections. No effect.
,, 2	2 cubic centimetres.	,, ,, ,,
,, 3	3 ,,	,, ,, ,,
,, 4	4 ,,	,, ,, ,,
,, 5	5 ,,	Death in 48 hours.
,, 6	6 ,,	,, 24 ,,
,, 7	8 ,,	,, 12 ,,

Symptoms.—There was paralysis of the hind limbs, then of both the anterior and posterior extremities, with twitching of the muscles and spasmodic movements of the limbs. The animals were unable to stand and they fell on their sides. The muscles of the jaw were affected and there was twitching.

Post-mortem examination.—There was no hæmorrhage in the spinal cord. The gall-bladder was full. The peritoneum contained granules of pigment and the omentum was deeply pigmented. The phagocytes contained granules of pigment. (N.B.—This pigment represents the insoluble material deposited at the bottom of the bottle containing the extract.)

SERIES II.

Control Animals Inoculated with Tuberculous Material.

Guinea-pig.	Weight in grammes.	Inoculation.	Result.
No. 1	260	Inoculated subcutaneously at the knee with 0·5 cubic centimetre of emulsion, in normal sterile saline, of caseous glands of a guinea-pig dead from typical tuberculosis.	Death in six weeks from typical tuberculosis.
,, 2	276	The same.	Death in seven weeks and two days from typical tuberculosis.

Animals Inoculated with Tuberculous Material and Lachnanthes.

No. 3	261	The same plus three cubic centimetres of the solution of lachnanthes injected subcutaneously at the knee on the opposite side.	Death in five weeks and two days. Typical tuberculosis.
,, 4	268	The same.	Death in six weeks and one day. Typical tuberculosis.
,, 5	251	0·5 cubic centimetre of emulsion of bacillus tuberculosis as above. One cubic centimetre of the solution of lachnanthes was injected twice a week subcutaneously till death.	Death in 10 days. Nothing was found post mortem save enlargement of the inguinal glands and deep lumbar gland on the side inoculated with tubercle bacilli.
,, 6	250	The same.	Death in four weeks and four days. Typical tuberculosis.

SERIES III.

Control Animals Inoculated with Tuberculous Material on May 23rd, 1902.

Guinea-pig.	Inoculation.	Result.
No. 1	Inoculated with 0·5 cubic centimetre of emulsion of the glands from guinea-pig No. 1 in Series II. in normal saline.	Death in five weeks and two days from typical tuberculosis.
,, 2	The same.	Death in four weeks and three days from typical tuberculosis.

Animals Inoculated with Tuberculous Material and Lachnanthes.

No. 3	The same plus three cubic centimetres of solution of lachnanthes injected subcutaneously on the opposite site at the knee.	Death in five weeks and two days from typical tuberculosis.
,, 4	The same.	This animal was lost at the Jenner Institute.
,, 5	0·5 cubic centimetre of emulsion of bacillus tuberculosis as above. One cubic centimetre of solution of lachnanthes was injected subcutaneously twice a week.	Death in 19 days. Post mortem the inguinal and deep lumbar glands were enlarged on the inoculated side. The spleen was enlarged and studded with nodules. Tubercle bacilli were found. The retro-hepatic gland was enlarged. Neither liver nor lung was infected. The glands on the opposite side were not enlarged.
,, 6	The same.	Death in 25 days. Post mortem there was enlargement of the inguinal and the deep lumbar glands on the inoculated side. The spleen was enlarged and studded with nodules. Tubercle bacilli were found. The liver was infected; a few small scattered nodules were present. The retro-hepatic gland was enlarged and hard. No lung infection was seen. There was no glandular enlargement on the uninoculated side.

Conclusions.—It would appear from the above that lachnanthes consists largely of a resinous substance or substances and some body which is precipitated by lead subacetate and is soluble in water. Further, so small a dose as five cubic centimetres of an aqueous solution of the material obtained by alcoholic extraction of the plant is sufficiently powerful to kill guinea-pigs, whilst doses varying from one cubic centimetre to three cubic centimetres of the same solution do not exert any inhibitory action upon the progress of tuberculosis but rather seem to hasten it. Further experiments are being made and will eventually be published.

MEDICAL MEN AND CRICKET.—A cricket match was played at Exeter on July 2nd between "Doctors" and the "Exeter Home Team," which resulted in an easy win for the medical men, who scored 204 runs against their opponents' 47.