T H E S I S

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"T H E P O I S O N O U S E F F E C T S O F

. F R I C A N B O X W O O D

O N M A N."

By

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THE POISONOUS EFFECTS OF AFRICAN BOXWOOD ON MAN.

After being in the General Practice of Medicine for a good number of years, it is easy to get out of touch with University methods of teaching and writing, and the greatest difficulty is found, in the first place, in selecting a suitable subject for the thesis, and, in the second place, in arranging and marshalling facts in the proper way.

A great field of study is open to the General Practitioner, and if his mind can be kept clear and free from the rut of ordinary cases, and his powers of observation bright and active, many strange cases can be found, that are not mentioned in books. To keep a record of these is the great difficulty. Time, or rather the want of time is a serious factor. The absence of facilities, especially in the country, for experimental and research work is another deterring factor. Strange phenomena, that the General Practitioner cannot explain are seen, but through lack of time and possibly energy, a mental note is taken, and there the matter ends.

My attention was attracted 23 years ago to certain cases apparently of asthma, which differed in several ways from cases of ordinary asthma. On watching these cases carefully and on making enquiry into the history before, during, and after an attack, the conclusion was forced upon me, that here was a new Industrial Disease, which had not been described before, and which was evidently due to the poisonous effects produced by the inhalation of the dust of a certain wood - Gonioma Kamassi or African

Boxwood - used in the making of shuttles for weaving.

It occurred to me that a paper on this subject might meet the requirements for my thesis. I was strengthened in this view, when I thought that, apart from any slight originality the paper might contain, it would be a small contribution to that great section of modern medicine- preventive and industrial medicine.

Dust is the enemy of the workman. Many of the Industrial Diseases are caused by the inhalation of dust, which may be organic or inorganic, soluble or insoluble. Only particles which are insoluble in the fluids of the body, when carried into the air passages remain as foreign bodies either to stimulate the ciliated epithelium to over-action for their expulsion, or if they gain access to the lymph channels, to give rise to a proliferation of connective tissue. If the dust is soluble it may cause poisoning. It is with the latter that this paper has to deal, as an endeavour will be made to show that the dust of African Boxwood contains an alkaloid, soluble in the fluids of the air passages, sweat etc. to such an extent that poisoning takes place.

BOTANICAL FEATURES:--

Gonioma Kamassi or African Boxwood is a member of the poisonous order of Apocynaceae, and is known also as Knysna Wood - Knysna being the place from which it is shipped.

The order of Apocynaceae (1) is divided into the

following species:-- genera?

(1) Carissa.

(2) Acocanthera Venerata.

(3) Ranwolfia.

(4) Pacypodium.

(5) Tabernaemontana.

(6) Gonioma.

(7) Strophanthus.

These are trees, shrubs or herbs often yielding milky latex or bitter poisonous juice. With the exception of Gonioma, none of the species are of commercial value and only Acocanthera Venerata is mentioned as having any medicinal value. Smith (2) mentions this as a medicine used by the natives to cure snake bite, and describes the method, but at the same time warns against its use, and mentions cases where it proved fatal. He also states that with Euphorbia juice it was formerly used for poisoning arrows. With its attractive flowers, foliage and berries, it is perhaps the most dangerous poison South African forests contain, and a case is on record in which fatal results followed the use of a skewer of the tree used to turn meat over a camp fire, though the natives believe that its introduction into the blood is more dangerous than into the stomach.

Sim in his book "The Forests and Forest Flora of Cape Colony" gives the following description:--

"GONIOMA KAMASSI OR AFRICAN BOXWOOD is an evergreen tree about 20 feet in height, and seldom more than 12 or 14 inches in diameter, having usually a clean,

straight stem, and a small compact crown. Leaves are opposite or in threes, lanceolate, 2 to 3 inches long, ½ inch wide, acute at apex, tapering to the base, entire, thinly coriaceous, glabrous, shining deep green above, paler below, exstipulate, - Cymes terminal, few flowered; Flowers yellowish white, scented. Corolla cup shaped with five blunt lobes. Corolla tube ½ inch long, pubescent inside with sessile stamens inserted about half way up; Corolla limbs spreading, rotate 2 inches wide, the lobes twisted in aestivation. Nectary not present. Pistil shorter than Corolla tube, with an apparently single two celled sub-glubose ovary, a slender style and a capilate stigma."

This tree grows abundantly in the lower forests of the Midland Conservancy of Cape Colony, extending sparingly near the coast, as far east as East London. It is reserved in all the Conservancies except the Transkeian, where it is not known to occur.

The timber is yellowish in colour, dense, close grained, very hard, and weighs 58 lbs. per cubic foot. As a comparison it is interesting to note that oak wood weighs 48 lbs. per cubic foot. This shows the great density of African Boxwood. Very little attention seems to have been paid to this tree, until its hard wood was found to be able to be worked and turned easily. It was formerly used for fencing-poles in the district in which it grows, but it is now too valuable for that. Considerable quantities of the wood are now sent to Europe under the name of Boxwood, and it is considered equal to Buxus for Engraver's work, and for

all purposes for which Box is generally used.

The juice of the tree is watery and bitter.

BOXWOOD AND SHUTTLEMAKING:--

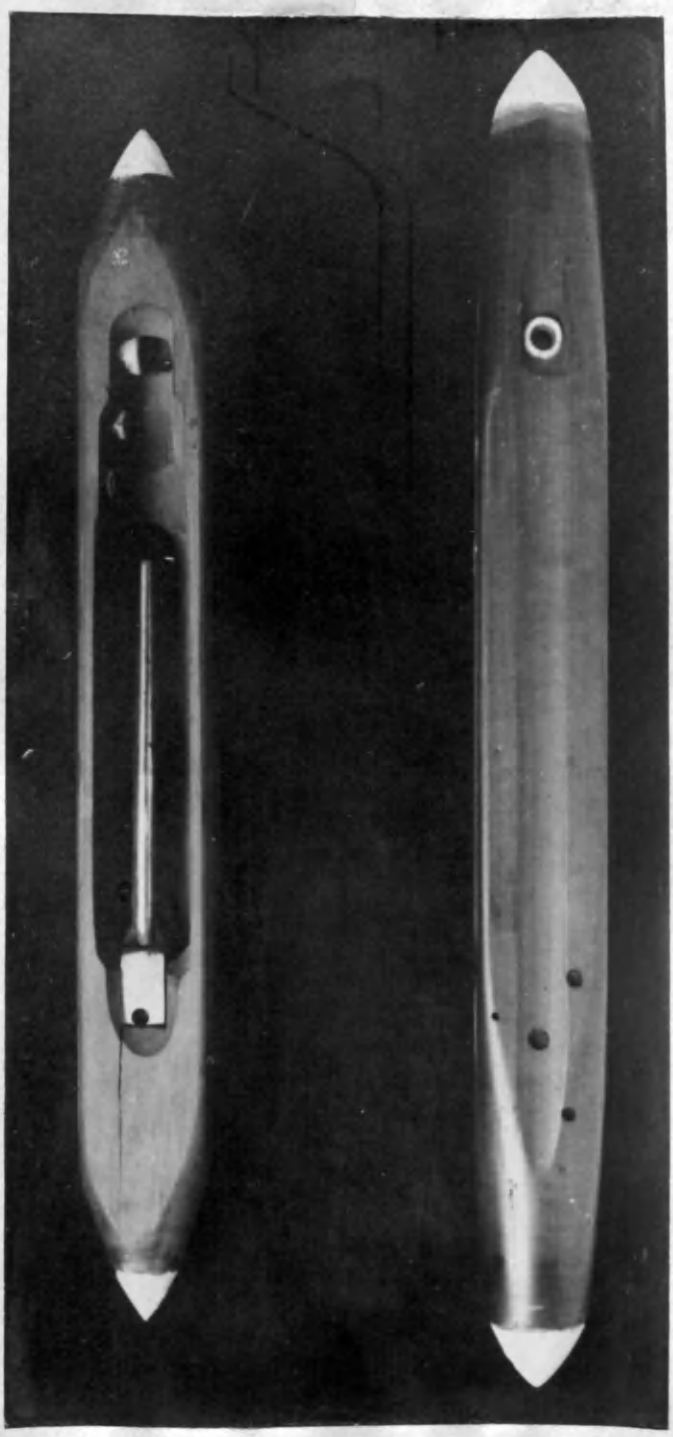
The shuttle carries the weft across the warp in the making of cloth. It is cigar shaped and so far as African Boxwood shuttles are concerned, they vary from 11 inches to 15 inches in length, and from 1½ inches to 2 inches in breadth. They are steel tipped, with an excavation in the centre for holding the spool of weft.

The kinds of wood used for making weaving shuttles are Persian Boxwood, Persimmon, Cornel or American Dogwood, and Beechwood. African Boxwood was gradually introduced into the shuttle making industry about 30 years ago to replace Persian Boxwood, which was becoming scarce and expensive. It made an excellent shuttle, almost, but not quite so good as that made from Persian Boxwood, which made the best shuttles. It was hard and durable, having twice the life of Persimmon, had few knots, was cheap and easily worked. A shuttle made from African Boxwood weighed on an average 2 oz. heavier than a shuttle made from Persimmon or Cornel, and owing to the hardness of the wood and the absence of knots, a very smooth surface could be produced, so lessening friction and tearing of the warp. The shuttles were so smooth and strong that African Boxwood shuttles were used in the best Bradford trade, in the Cotton trade of Lancashire, and in all silk mills, where there was a very delicate warp and weft used.

5A

PHOTOGRAPH OF AFRICAN BOXWOOD SHUTTLE.

HALF NATURAL SIZE.



Shuttle making is a very dusty occupation. The wood is hard and fine, and clouds of dust, like smoke, rise from the various machines as the wood is step by step gradually fashioned into a shuttle.

The wood working processes in shuttle making are:--

(1) Sawing the logs across.

(2) Cutting the blocks to lengths.

(3) Dressing up the edges.

(4) Boring and tipping.

(5) Body making viz:-- sawing out the interior of the block.

(6) Turning so as to form the pointed ends.

(7) Finishing and rubbing down the ends with sand paper, known as"hustling".

Until the introduction of African Boxwood no complaint of illness or ill health was made by the workers except that they were constantly in a cloud of dust. Beyond being disagreeable, this did not seem to affect them much.

ALKALOIDS:--

If the conclusion, arrived at from clinical evidence, that the disease from which these men were suffering was caused by the inhalation of the dust of African Boxwood, was to be maintained, it would be necessary to show that the dust of this wood contained some poison, probably an alkaloid, which on contact with the mucus of the air passages and of the lungs, or with the sweat of the hands dissolved, and entering the blood caused the symptoms from

which they complained.

It seemed quite clear that these cases were not ordinary cases of Asthma caused by the irritation set up by the inhalation of dust. Before the introduction of this wood, no such irritation had been caused.

It was obviously impossible in an ordinary private practice to examine the wood for an alkaloid, but as the cases which had been seen, and which are described later, pointed to the wood as being the cause, the Shuttlemakers Society referred the examination of the wood to Professor Harvey Gibson.

Professor Harvey Gibson (3) in the Liverpool University Laboratory set about the examination of the wood for an alkaloid in the following manner:--

> A kilogram of the dust was extracted with four litres of water, at a temperature of 70 - 80° C. To this was added 100 C.C. of concentrated hydrochloric acid, the whole being agitated and digested for four hours. The liquor was then filtered, and the ligneous material well washed. The combined filtrate and washings were concentrated down to two litres, such resinous matter as was present, and which had separated out was filtered off and the clear brown solution was precipitated, by an excess of Potassium - bismath iodide. A voluminous orange-brown precipitate was obtained, (a double compound, alkaloid - bismath - iodide) which was collected and well washed with water. The precipitate was then decomposed by an

excess of a 10 per cent. solution of caustic soda, in order to liberate the free alkaloid, and the mixture was extracted twice with about 100 C.C. of freshly-distilled chloroform. A certain amount of emulsification was unavoidable. After settling, the chloroform extract was washed with water, and finally all traces of moisture were removed by filtration. The chloroform solution, which was deep brown in colour, was then distilled on a water bath to remove most of the chloroform, the last traces being removed by heating at 80 - 90°C. in an open glass dish. A thick dark brown syrup remained over, consisting of the free alkaloid which, on cooling, solidified into an amorphous brittle glassy solid. It weighed 0·7 gr. representing 0·07 per cent. of alkaloid in the wood. Assuming that it had been possible to extract all the alkaloid, the wood may be taken as containing 0·1 per cent. of the alkaloid.

The alkaloid was then converted into the hydrochloride by digestion with dilute hydrochloric acid (5 per cent.) the whole being evaporated to dryness on a water bath. The residue after evaporation was then dissolved in water and filtered from about 0·2 gr. of resinous insoluble impurity, and the filtrate was diluted so as to contain 0·7 per cent. alkaloid hydrochloride. The alkaloid when examined in detail was found to be very soluble in chloroform, and in alcohol (though less so), sparingly soluble in water, but the hydrochloride was readily soluble in water,

and salt solution. On heating, it decomposes, chars, and gives off a vapour with a peculiar and penetrating odour. On adding caustic soda or Na_2CO_3 to a solution of the hydrochloride the free alkaloid is thrown down as a yellowish amorphous curdy precipitate. It was found to be impossible to obtain it in the crystalline form by dissolving it in hot water and cooling. The alkaloid give the following reactions:--

(1) Bismath iodide in potassium iodide gave a bright orange precipitate even in very dilute solutions.

(2) Iodine in potassium iodide gave a dirty brown precipitate coagulating in dark brown masses.

(3) Nesslers solution gave a whitish - yellow precipitate.

(4) Tannic acid gave a gelatinous white precipitate

(5) Picric acid gave a yellowish precipitate.

(6) Platinic chloride gave a yellowish precipitate. in strong solutions.

(7) Phosphomolybdic acid, gave a thick yellow precipitate".

He summed up his conclusion by saying that the wood contained a considerable amount of alkaloid, probably artirin or an allied product, and that the substance was readily soluble in common salt solutions.

The important point with regard to the alkaloid extracted by Professor Harvey Gibson was its easy solubility in saline solutions. It seems quite feasible that the alkaloid contained in the fine dust could be readily dissolved by the saline mucus of the air passages, and lungs, and so taken

into the blood.

It now remained to test the physiological effect of the alkaloid on the mammalian heart. This was done on the instruction of Professor Harvey Gibson in the Thompsom Yates Physiological Laboratory of the University of Liverpool. The solutions used for experimental purposes were:--

(a) A 1% solution of the alkaloid in absolute alcohol, diluted to ten times its volume with Ringer's solution.

(b) A 0·7% solution of the hydrochloride in water.

The heart used was that removed from a recently killed cat, and perfused with a salt solution prepared according to Ringer's formula at body temperature. The flow through the heart was maintained by means of oxygen pressure.

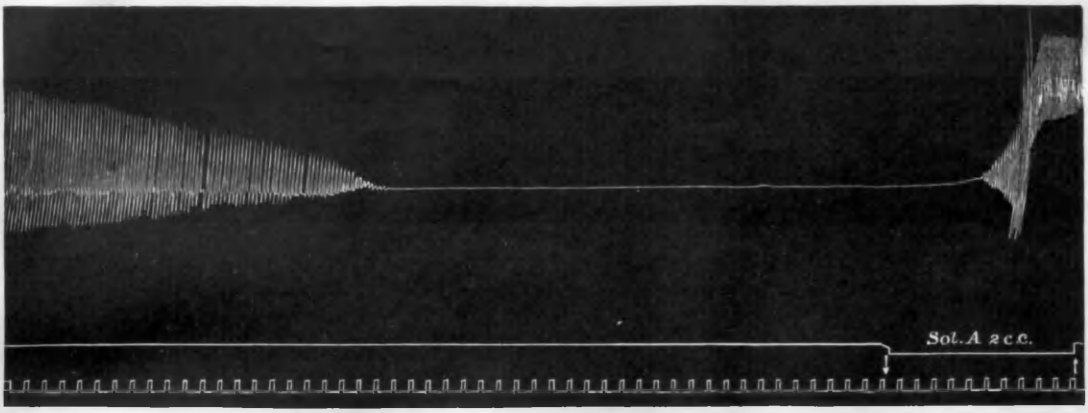
EXPERIMENT 1. (WITH SOLUTION A.) (3)

(a) CONTROL EXPERIMENTS:-- In using solution A it was necessary to know what share in the results obtained was due to the presence of alcohol in which the alkaloid was dissolved, so that control experiments were first of all carried out before any of the alkaloid was injected. Three such controls were recorded, and it was found that (using 7C.C. of alcohol) at the first and second injections, the heart beat was almost instantly stopped, but for a short time only; at the third injection the heart had become accustomed to the dose, and the effect was masked.

(b) Observation 1. (Fig. 1.) - 2 C.C. of solution "A" were next injected by means of a hypodermic syringe into the perfusion tube, about 3 feet away from the

heart, after it had regained its normal beat. The solution"A" was thus well mixed with the perfusion fluid. The immediate effect was a slowing of the

FIG. 1



Tracing from cat's heart after injection of 2 c.c. of solution A. See text, Experiment I, Observation 1. The tracing is to be read from right to left. Time record in 5 sec. intervals.

heart, and a rapid reduction to zero. The time of injection lasted fifty-five seconds. Ten seconds after the injection was begun, the slowing of the heart beat followed, and twenty seconds later had entirely ceased. The heart remained quiescent for about 180 seconds or about 2½ minutes after the injection had ceased. The heart then commenced beating very feebly, and with a much slower rhythm, gradually increasing in vigour, and still more gradually in speed.

Observation 2. When the heart had again regained a normal but slower beat, 5 C.C. of solution"A" were injected in the same way as before, the time of injection lasting rather over one minute (70 seconds.) Within half a minute of the first injection, the heart began to slow, and decrease in vigour, and finally at

the end of the injection period, came to a standstill. The cessation was permanent for about 7 minutes, when the heart began to show feeble attempts at contraction, and a minute later more or less regular, but very slow beats. (about one beat every five seconds.) The heart showed no signs of permanent recovery.

EXPERIMENT 2 (WITH SOLUTION "B".)

Observation 1:-- Solution "B" was diluted to 1 in 10 with Ringer's Saline and 8 C.C. of the mixture was slowly injected (the period of injection lasting two minutes 45 seconds.) A few seconds after injection commenced, the vigour of the beat rapidly fell to one-sixth of the normal, and in about half a minute fell to nil, the heart remaining quiescent for half a minute after the injection has ceased. It then began slowly to recover, the beats being at first very feeble and slow, but increasing both in strength and rhythm, until, about three minutes after, the beat was again fairly normal, though not quite so rapid as at first.

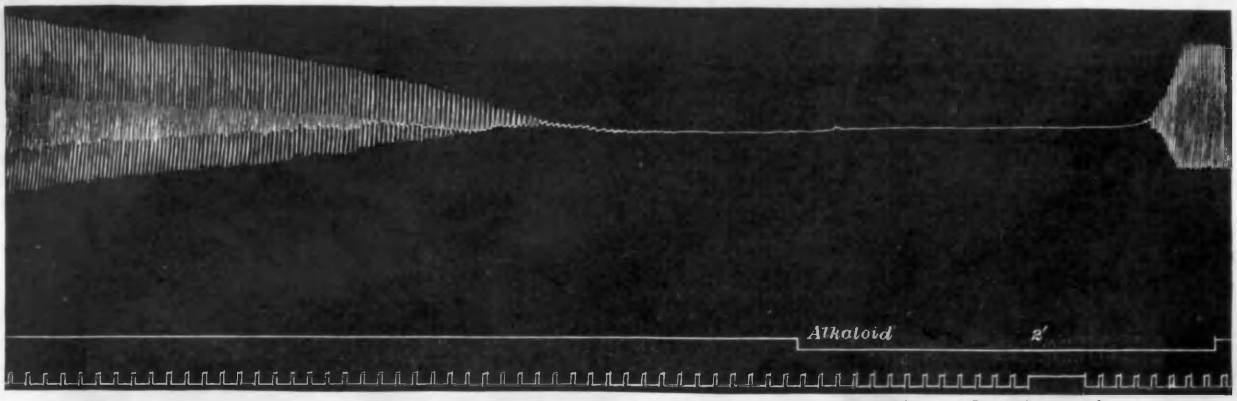
Observation 2 and 3. - Short injections of 10 C.C. of the fluid escaping from the heart produced only a slight effect.

(b) Control Experiment 4. At this stage 10 C.C. of Ringer's saline without alkaloid were injected, but no effect was produced.

(c) Observation 5 (Fig. 2) The solution "B" was again used, but this time diluted with Ringer's saline to one part in five of the saline. Of this fluid 5 C.C.

were injected.. The beat rapidly slowed down and ceased twenty five seconds after the injection had been begun. The injection lasted 2 minutes, during

Fig. 2

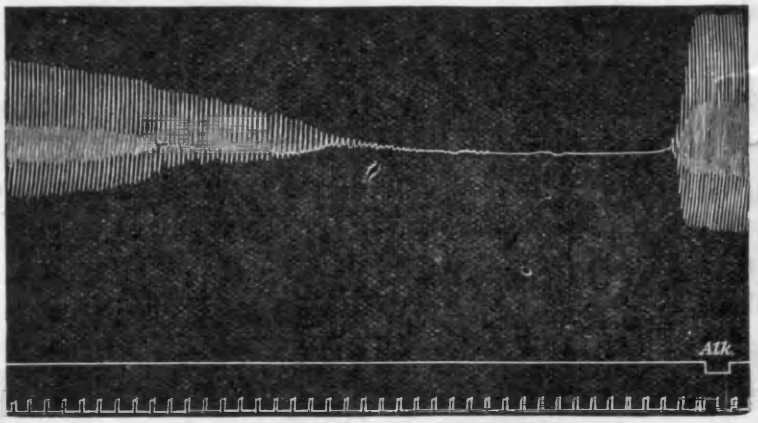


Tracing from cat's heart after injection of 5 c.c. of solution B. See text, Experiment II, Observation 5. Tracing to be read from right to left. Time intervals, 5 secs.

which time, and for 60 seconds longer the heart was entirely quiescent. Then followed a slow and gradual recovery, the rhythm, however, never reaching the speed of the original heart beat. (It is of interest to note in this relation that several of the workmen suffering from action of the wood dust, also showed a very slow pulse.)

Observation 6. (Fig. 3.) In this experiment 2 C.C.

Fig. 3



Tracing from cat's heart after injection of 2 c.c. of solution B lasting 10 secs. See text, Experiment II, Observation 6. Tracing to be read from right to left. Time interval, 5 secs.

only were injected, but the recovery was very rapid viz; under ten seconds. The effect was almost instantaneous, the heart ceasing to beat within about five seconds, and remaining practically quiescent for 1½ minutes, when very slow and feeble pulsations recommenced gradually, but very gradually increasing in vigour and rapidity to the normal once more.

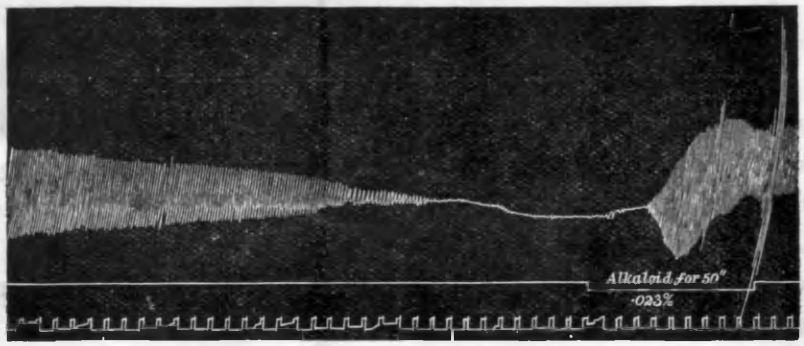
All the observations hitherto recorded were carried out by the syringe method of delivery in order to economise the material, which, as will have been seen from the description of the method of preparation, was obtained only by a long and laborious process. The syringe method permits of only approximate estimation of dosage, and hence, in the experiments yet to be described, the more exact method of administering the dose in full stream from a flask, containing a mixture of solution "B" and Ringer's saline made up before-hand to the required strength, was adopted. The flask used was similar to that containing the normal Ringer's saline and was under the same Oxygen pressure, and the change from normal saline to drugged saline and back again was effected by means of a system of three way taps, connecting either flask with the delivery tube immediately before the delivery tube enters the heart.

EXPERIMENT 3. (WITH SOLUTION "B").

Observation 1 (Fig. 4.) In this experiment carried out as above described solution "B" was diluted to 0·023 per cent, and administered for fifty seconds. In all 33 C.C. of the fluid passed through the heart. The effect was a rapid slowing, and final stoppage

within thirty seconds of the beginning of the in-

FIG. 4



Tracing from cat's heart after injection of 33 c.c. of solution B. See text, Experiment III, Observation 1. Tracing to be read from right to left. Time intervals, 5 secs.

jection; quiescence continued for about a minute after injection had ceased, when the heart began to slowly recover both in vigour and in rhythm.

Observation 2. The same degree of dilution of solution "B" was employed but the fluid was administered for six minutes, five seconds, 142 C.C. in all passing through the heart. In this case within half a minute the heart had ceased to beat continued quiescent, during the entire period of injection, and for several minutes afterwards, and, though recovering very feebly and slowly it appeared to be permanently injured.

EXPERIMENT 4. (WITH SOLUTION "B")

Solution "B" was diluted to 0·0077 per cent. and administered for one minute 45 seconds. The beat rapidly slowed and decreased in vigour, reaching a standstill, with occasional spasmodic flickers, before the end of the injection. The tracing showed that the heart never recovered, and only evinced occasional

spasmodic contractions of feeble power, and most irregular rhythm. The heart was, undoutedly permanently injured.

EXPERIMENT 5.

Solution "B" was diluted to 0·0026 per cent. and administered for four minutes thirty seconds, 48 C.C. of the fluid in all passing through the heart. The beat declined very gradually, disappearing by the end of three minutes. Recovery was very imperfect, and even when they recommenced, the beats were very much slower, and most irregular.

EXPERIMENT 6.

The solution "B" was still further diluted viz:-- to 0·0013 per cent., and administered for about eight minutes, when the solution began to give out. The beat was very slowly retarded, and became gradually feebler; recovery was fair, but never became complete."

The actual result of all these experiments shows that African Boxwood contains an alkaloid, easily soluble in saline solution, which acts as a cardiac poison, gradually slowing the heart beat, and causing diminution of vigour in the contractile tissues of the heart. The experiments shew that the effect of the alkaloid is cumulative, finally causing a cessation of the heart beat, under long exposure to its influence.

TOXIC ACTION.

Men working African Boxwood, complained with peculiar unanimity of a very definite set of symptoms. These were running at the eyes and nose, headache, feeling of sleepiness or doziness, difficulty of breathing, nausea or sickness and faintness or weakness. Usually three or four of these symptoms were complained of by the same individual.

Local Symptoms.

With the exception of running of the eyes and nose there were no local symptoms. The eyes were red and swollen, and looked as if the patient had been weeping for some time. A clear fluid ran from the eyes and nose. The nose appeared sore during the attack, owing to the patient constantly drying it, and the complaint was made that the nose "felt twice the size it ought to do." The mucous membrane was swollen and red, but there was no ulcerative condition present.

No man working this wood suffered from any dermatitis, or from any irritation of the skin.

General Symptoms. The constitutional symptoms complained of were:--

(1) HEADACHE. This is of a violent and persistent type, and, coming on over the eyes and spreading to the temples, lasts for several days after the workman has left work.

(2) FEELING of SLEEPINESS. This was described as a feeling of doziness, and in one instance the feeling was so overpowering that the man, a sawyer, had to exert great effort to resist it, or he would have fallen off the bench.

(3) DIFFICULTY of BREATHING. The condition of the chest was described as being "fast." The trouble was apparently expiratory. Inspiration seemed to be fairly easy, but the forced muscles of expiration had to be used to empty the chest. One case in particular was so bad that every moment looked as if it were going to be his last. The difficulty of breathing was such that he had not time to speak. He could only jerk out a word or two in answer to questions, and swallowing any thing was out of the question.

On auscultating the chest the inspiratory sounds were fairly normal, but the expiratory sounds were prolonged and piping.

(4) NAUSEA and SICKNESS, were almost always present. The longer the man stayed at his work, the more violent the retching became, Complaint was also made of a bitter taste in the mouth, and when the retching was violent a peculiar almost camphor like odour of the breath was felt.

(5) FAINTNESS and WEAKNESS were marked symptoms, especially if the workman had tried to stick to his work. The patient looked pale, with a slightly greenish tint, and was covered with a cold clammy perspiration. He was in the peculiar position of feeling that he must lie down to rest, but could not do so owing to the difficulty of breathing. He cried for fresh air and sat leaning forward on his knees gasping for breath.

CARDIAC SYMPTOMS.

Slight praecordial pain and uneasiness were complained

of by men working this wood. The heart sounds were normal, but in one or two instances the effect on the pulse was peculiar. One workman, after he had been working the wood for a little time, complained of a feeling of weakness and difficulty of breathing. On examination his pulse was found to be very slow - 45 per minute. If this man went on with his work and had a bad attack with all the usual symptoms of difficulty of breathing, retching etc., his pulse rate was found to have risen to about 100 and sometimes over, and it was very soft and easily compressed. Owing to his serious condition, he was taken home, and after a day or two away from his work, and with rest in bed, the pulse rate again became very slow, and it was only after he had been away from his work for a week or two that his pulse came up to what was evidently normal for him - 68 per minute

Dr. Legge, (4) H.M. Chief Medical Inspector of Factorie examined 112 men out of 164 employed in certain factories working African Boxwood. The symptoms complained of to him are tabulated below:--

SYMPTOMS.	NUMBER.	PERCENTAGE.
Headache.	27	24·1%
Feeling of Sleepiness.	10	9·0%
Running of the Eyes.	13	11·6%
Running of the Nose.	28	25·0%
Breathing Affected.	34	30·4%
Nausea or Sickness.	13	11·6%
Faintness or Weakness.	11	9·8%

Recorded below are the notes of six cases seen by me.

Case (1) is still alive, age 57, well and hearty and with no difficulty of breathing or cardiac trouble. African Boxwood has not been used in the Factory in which he works, for a good number of years, and incidentally my supply of "cases" has disappeared. At any rate he is now, so long as African Boxwood is not used, a perfectly healthy man for his age. I saw him first in 1901. He was then 33 years of age.

CASE 1. F.R. AGED 33.

Previous History and Health. His previous health was good, until 1897 or 1898, when the symptoms from which he complains, began. The symptoms were at first vague and indefinite. Occasionally he felt "wheezy" in his chest, and thought he had cold, and was becoming bronchitic. His family history is good. Both his father and mother are alive - the latter has occasional epileptic attacks.

Present Illness. I saw him first in 1900 when the illness was well developed. African Boxwood has only been worked, so far as he remembers, in the Shuttle Factory since 1895 or 1896, and that only occasionally. It has never, since they began using it, been worked continuously, but only occasionally with varying periods of time elapsing. At first he worked the wood a good deal "dressing up" and he did not notice any bad symptoms, or any injurious effects on himself for about 3 years. Then the symptoms from which he now suffers,

when they begin to use that special wood, began.

History of an Attack:-- The attack began with running of the eyes and nose, sneezing, and a feeling of suffocation. He had a feeling of nausea and sickness, then retching began. He felt faint and done up, so much so that he felt he must lie down, only he could not, on account of the difficulty of breathing. He complained of a slight pain and uneasiness over the cardiac region, and broke into a cold clammy sweat, with large drops of perspiration on his forehead. His breathing gradually became worse, more rapid and difficult, so that he could neither speak nor swallow anything for want of breath. When he got into the fresh air his symptoms seemed to him to be at first aggravated, and then gradually to pass off. The duration of the attack depended on the length of time he had stayed at work. If he stopped now at his work, when they were using this wood, for say ten minutes, he would take two or three hours to recover, but if he stayed at his work one or two hours, he would take two or three days to recover. Lately it has begun to affect him more quickly than it used to do. If they were using that wood now and he went to work, he would be retching violently in about ten minutes. At times he has been working in one of the upper rooms of the workshop, where he could not see, and did not know what wood was being sawn up. Yet as soon as the dust began to work its way up, his symptoms began. After

one very severe attack he was three weeks at home, and three weeks at Ilkley Convalescent Home to recruit, and finally felt quite well. He returned to his work, but unfortunately they were using this wood, and that same day he was as bad as ever. Now that they have not been working this wood at this workshop for a long time, he is quite a healthy man, strong and active, and has not broken any time.

Physical Condition during the Attack. He was seated upright in a chair, with the door of his house wide open, gasping for breath. He had a somewhat livid appearance, and the skin was cold to the touch, and covered with a cold clammy perspiration. His temperature was normal. He could not lie down, and the difficulty of breathing was such that he could just jerk out a word or two in answer to questions. His eyes were red and somewhat swollen, and both his eyes and his nose were running. There was no ulcerative condition of the inside of his nose, but the mucous membrane was swollen, and he complained of his nose feeling twice the size it ought to do. He kept constantly retching and trying to vomit, but could get nothing up from his stomach.

Circulatory System. He complained of slight cardiac pain and uneasiness, and dyspnoea was marked. Pulse was frequent and about 100 per minute. It was regular, but soft, small and easily compressed. The apex of the heart was in its normal position, and on palpation could scarcely be felt. On auscultation the valve

sounds were normal in character, but weak and muffled, and altogether gave the impression that the heart was rapidly failing. During recovery from the attack the pulse rate gradually fell to 52 per minute, and it was usually over a week before it regained its normal speed of 67 per minute.

Respiratory System; Respiration was quick and laboured. The dyspnoea was marked and of the expiratory kind. He had a great deal of difficulty evidently in emptying his chest, and had to sit up in his chair, with his hands on his knees, and use his forced muscles of respiration. There was no dulness on percussion or increased resonance. On auscultation the inspiratory sounds were fairly normal but expiration was prolonged and piping. Beyond the piping expiratory sounds no rhonci were heard.

Digestive System:-- This seemed normal, with the exception that he complained of a bitter taste in his mouth, and of the violent retching.

All the other organs were normal and there was no albumen in the urine.

Diagnosis: When I first saw him during a severe attack I was quite at a loss to account for his symptoms. The attack looked somewhat like an ordinary attack of spasmodic asthma caused probably by the inhalation of dust, yet I had never before seen an attack of asthma cause so much cardiac depression in such a short time. On the other hand it did not quite conform to the ordinary type of cardiac dyspnoea -

there was more difficulty with the expiration than is usual with such attacks, and there was no evident cardiac valvular lesion. The attack seemed to come between an ordinary attack of asthma and one of cardiac asthma.

This man was seen by me in several attacks, and when careful enquiry was made into the history of the attacks, it became evident that they were associated with something which happened at his work. The attacks always came on at work, never when he was at home. On going over his day's work with him after several of such attacks, it was found that invariably an attack came on when African Boxwood was being worked in the Factory.

The following are the short histories of five other cases, all suffering in the same way, but to a lesser degree:--

CASE 2. A. B. S. AGED 35. He has worked all his working life in a shuttle factory and was quite healthy up to 1901, the year when this case was seen. He complained of headache over the eyes and temples, of running at the eyes and nose, and of a bitter taste in his mouth. He felt "fast" in the chest and was "dozy." Soon he began to retch and vomit. He felt he had to get out into the open air. He was never so bad as Case 1, and could on most occasions come to see me.

On examination his eyes were red and suffused; his nose was running. The nasal mucous membrane was red and swollen. Examination of his chest showed inspiratory sounds to be normal but the expiratory

sounds were difficult, long and piping. The cardiac valve sounds were normal, and the pulse rate varied according to the severity and stage of the attack from 45 to 104.

He complained that the smell of African Boxwood dust upset him, and he found that if he stayed long, working the wood, the attack as described above would come on.

Later he used a cotton wool respirator, with all sorts of inhalants in it, whilst at work with this wood, and he thought it "kept out the smell," and that by using it he could ward off an attack. However, as more of this wood began to be used, he got gradually worse.

The man is at present 59 years of age, and, since the use of the wood was stopped in the shop in which he works, he breaks no time and is healthy, with the exception of a slight tightness of the chest when he gets a "cold," due probably to the mechanical irritation of ordinary wood dust.

CASE 3 E.B. AGED 38, a sawyer, complained of running of the eyes and nose, frontal headache, and "fastness of the chest." His pulse was 56 per minute, cardiac sounds were normal, but he felt "weak and tired." Inspiratory sounds were normal, expiratory sounds piping, prolonged, and dry.

These symptoms came on only when African Boxwood was worked in the shop in which he was employed. When the wood was not being worked, he was quite

normal, and had a normal pulse of 65 per minute.

CASE 4 F.M. AGED 40, a sawyer in a Shuttle Factory in Bradford, complained of "fastnes of the chest, and doziness" when working African Boxwood. If he was long exposed to the dust of this wood, he started retching and vomiting, and felt "weak and done." African Boxwood was only used in this Factory at irregular intervals, and when it was not being used the man was quite well, although he was continually in a cloud of dust from other woods. On examination during an attack, and he was never so bad but what he could get about, his pulse was 58 per minute on several occasions, heart sounds were normal, and he had difficulty in emptying his chest. Expiratory sounds were prolonged and dry, and he had to use his muscles of forced expiration.

His normal pulse rate averaged from 65 to 68 per minute, and when the attack was not on, his respiratory sounds were quite normal.

CASE 5. T.D. AGED 40, a "dresser up" in a Shuttle Factory said that he had always been a healthy man up to about 3 years after African Boxwood began to be used. For about 3 years after its introduction he felt no bad effects on his health.

He now complained that when working this wood his eyes and nose after a short time "began to smart" and "run," his breathing became difficult and he felt "faint and weak."

He associated his illness with the "smell" of African Boxwood, and its accompanying bitter taste.

As more of this wood came to be used in his workshop, and he was consequently more frequently and for longer periods exposed to its dust, the attacks from which he suffered, came on more quickly and took a longer time to pass off.

He was quite convinced in his own mind that this wood was the cause of his illness, as, when it was not being used in the factory, he was quite well and healthy. He moved his work from one shuttle factory to another shuttle factory trying to find one where African Boxwood was not used, but failed.

On examination during the time he was feeling ill, his eyes were red, his nose was swollen inside, and both were running, and the tears "smarted" on his face. He breathed with difficulty, and had asthma of the expiratory type. He was pale and his breath had a camphor like odour.

On auscultating his chest the inspiratory sounds were quite good, but expiratory sounds were prolonged and noisy. He had great difficulty in emptying his chest. His pulse 54 per minute, was soft and easily compressed. His heart sounds appeared normal, but were weak and not very distinct. His pulse rate struck me as being peculiar owing to its slowness, as from his general appearance and distress, and his feeling of faintness, I expected to find a rapid weak pulse.

CASE 6 J.J. AGED 40, who tipped and turned down the

shuttle, and sometimes planed them, complained of Asthma and a feeling of weakness and faintness. These symptoms appeared when African Boxwood was being used, but as he had a financial interest in the Factory, he would not admit that this wood had anything to do with his asthma. Treatment on ordinary lines for his asthma, "Tucker's Asthma Cure" etc., were of no avail.

The attacks passed off when the use of the wood was discontinued in that Factory.

Diagnosis:-- The attacks of shortness of breath and "fastness" of the chest, occurring in these cases, associated with signs of rapid cardiac failure, were the principal features to be noticed.

Patients suffering from Cardiac or Renal Asthma do not present the features of laboured expiratory dyspnoea so marked in these cases. The breathing of cardiac asthma is of a gasping or panting kind, an air hunger and the respiration rate is generally much increased. The slow pulse rate, in cases of African Boxwood poisoning, seen before a severe attack developed; the rapid pulse with signs of cardiac failure, as shown by the slightly livid appearance, the cold and clammy skin, during an attack; and the return, when in a few days the attack had passed off, to a slow pulse before in a week or two, regaining the normal speed, all points to something other than cardiac asthma. As Professor Harvey Gibson showed in his experiments on the mammalian heart, the alkaloid contained in African

Boxwood acts as a cardiac poison, gradually slowing the heart beat, and causing diminution of vigour in the contractile tissues of the heart.

In renal asthma occurring in Chronic Interstitial Nephritis the attacks came on as a rule every night, and the difficulty of breathing is more of the panting kind. The presence of albumen in the urine, the high blood pressure and the hypertrophied heart all help to distinguish this kind of asthma.

The asthma, from which workers in African Boxwood suffer, differs from ordinary asthma, or the asthma due to the inhalation of dust, in that the difficulty of breathine was of the expiratory kind. In ordinary asthma the breathing is slow and laboured, the obvious difficulty being in forcing the air in and out of the chest - the difficulty being inspiratory as well as expiratory. In ordinary asthma again there are very rarely signs of a failing heart.

If associated with expiratory asthma, with a marked tendency to cardiac failure, you have a patient complaining of running of the eyes and nose, of a bitter taste in the mouth, with headache over the eyes and temples, with probably a feeling of doziness or sleepiness, and who complains of nausea and sickness; who works in a factory where he is exposed to the dust of African Boxwood, and who only suffers from these symptoms when he is so exposed, then the conclusion must certainly be arrived at that the patient is suffering from African Boxwood poisoning. Especially must this be the case, when it is known that the patient, when not suffering from these symptoms, has no trace of heart

or kidney disease, and who, when the attack was over, and he was not in contact with the wood, was a perfectly healthy and normal individual.

In recent work on asthma, great stress has been laid on sensitization and anaphylaxis. (5)

On looking at the purely clinical picture of African Boxwood poisoning, and leaving out of account the results of the actual experiments, which were made with the alkaloid found, on the mammalian heart, there seems to be a great similarity between the history and symptoms of African Boxwood poisoning, and the history and symptoms of sensitization and anaphylaxis.

This wood was worked at irregular intervals. It is quite conceivable (6) that a protein from the dust gained entrance to the blood through the respiratory tract, that the men thus received a sensitizing dose; but so long as the dose was repeated within the incubation period no symptoms of anaphylaxis occurred. If, however, on some occasion the wood was not worked for ten days or so and the incubation period, whatever it was, had passed, then when the men were again exposed to the dust, the anaphylactic condition became demonstrable - running at the eyes and nose, headache, asthma, sickness, vomiting and prostration. When the men were away from work and so from exposure to African Boxwood dust, they had no symptons. Immediately they were exposed to it again the attack began. One case of mine was ill for three weeks getting over an attack, and went to a Convalescent Home for three seeks to get quite well. He went back to his work feeling absolutely fit, but as that wood was being sawn

up in the Factory that day he became so ill that he had to be taken home within a quarter of an hour of going. It looks as if this man had become so sensitive to the poison that the slightest exposure to it brought on anaphylactic phenomena.

Other hard woods used in trade, are known to be toxic to a certain extent. At the meeting of the British Medical Association in 1902, Dr. C. Young of Birkenhead, described certain symptoms which he had observed in men working Marcaibo Boxwood, used for making rulers . The tree is known as Tabebuia Pentaphylla of the order of Bignoniaciae. The men complained of dryness of the throat, inflammation of the eyes and dilatation of the pupils, which lasted two or three days.

Joiners who saw and chip Seguoia Wood, (7) complain of a running at the nose, frequent fits of sneezing, smarting sensation in the eyes, irritation in the throat and bronchi accompanied by a cough, laboured breathing and quickened pulse, followed by a sense of oppression at the stomach. The symptoms usually last a day or two. The seguoia tree is a conifer and grows in California.

Cocobola Wood (8) used in the manufacture of handles of tools, bowling balls, walking sticks etc., evolves a very pungent and irritating dust causing inflammation of the eyes and skin, and bronchial trouble. The factory Inspector in Berlin,(9) observed an undue prevalence of diseases of the respiratory organs in those working this wood, and insisted on the introduction of fans for removal

of dust.

Sabicu Wood grown in Cuba, and Japanese Hard Wood "tagayasa" when worked in factories produce a snuffy dust causing running at the eyes and nose, the latter also causing dermetitis, and a dark brown gunpowder staining of the skin. The toxic action is attributed to a substance akin to Chrysarobin, and is said to injure the digestive and renal functions.

Satinwood. The chief Medical Inspector of Factories for Great Britain 1904, draws attention to a few cases of a peculiar inflammation of the skin, affecting cabinet workers engaged in handling "Satin wood" panels for decorative purposes. The dust from the wood (Choroxylon Swientenia) affected only the unprotected portions of the body, face, hands, arms. An intense irritation was produced, followed by redness, swelling and pain. Later the skin became moist and peeled off. Nestler (10) found that the active principle was a stearin like substance soluble in ether.

Teak Wood dust is said to produce constitutional symptoms, such as nausea and vomiting.

It will be observed that the irritating and poisonous properties of the various woods described, expend themselves mostly in creating catarrhal symptoms of the eyes and nose, and in causing dermatitis. Constitutional symptoms are rare and, with the exception of Seguoia wood, may be neglected. Seguoia wood dust in addition to catarrhal symptoms caused difficulty of breathing, quickened pulse and a sense of oppression in the stomach, but

these symptoms passed off in a day or two without any cardiac weakness, and never became severe.

The ordinary hard woods used in shuttle making, are Cornel or Dogwood, Persimmon and Beechwood. These were introduced as well as African Boxwood to replace Persian Boxwood, the supply of which is running short. Persian Boxwood is a harder wood even that African Boxwood, and made the most durable shuttles. The workers of all these woods, with the exception of African Boxwood, do not suffer from Asthma or any other deleterious effects, although the dust must be inhaled in large quantities.

The alkaloid contained in the dust of African Boxwood appears to have a cumulative action. There is no history of any case occurring at once. All the cases so far reported had been working the wood for a considerable time, a year, two years, three years etc., before any deleterious effects were felt. The cases described in detail in this paper, had all been working this wood for over three years before becoming ill. Of course in the factories in which they were employed, African Boxwood was not worked continuously, but only occasionally with varying intervals of time elapsing.

When once the symptoms were established, the men became more and more susceptible to the poison. As described in Case 1. after he had acquired the disease in 3 years, ten minutes exposure now put him hors de combat., and so with the other cases.

Dr. Legge (11) in his report describes several cases. One of these, a sawyer aged 63 employed in the trade 30

years, commenced cutting the wood in quantity in June 1904, and continued to do so for 12 months without inconvenience. During the following three months he became affected with running at the eyes, sleepiness and difficulty of respiration. For the last four weeks during which time he has given up working on this wood, his condition has improved. In another case a man employed 33 years began to complain of the usual symptoms after two years. The attacks gradually got worse for 4 or 5 years, and he had to stop working the wood. He took to metal peg making, and since then has had no attack. Several other cases are cited by Dr. Legge, and in all of them it took some time for the symptoms to show themselves, in all, the attacks began coming on more quickly, were more severe, and lasted longer. In every one of the cases cited, whenever work was stopped on that wood, the attacks ceased. It took from three to six weeks for the symptoms to pass off in severe cases, and for the man to feel quite well. In some of these cases also, a resumption of work on this wood brought on an attack the same day.

IDIOSYNCRACY and TOLERANCE, also play a part. It is difficult to estimate even roughly the amount of dust these men inhaled or to estimate the time it took to make each one sensitive to the poison, The African Boxwood was never worked continuously but only at irregular intervals, so that the dosage was gradual. Yet some men became more quickly affected than others. Some men were never affected at all. Dr. Legge saw one sawyer, aged 63, who stated that

he had sawn over 100 tons of African Boxwood continuously, without any exhaust draught applied and had experinced no symptoms.

Two deaths, so far as their history goes, are attributed to the action of the dust of this wood. One, a finisher, aged 52 is reported to have had symptoms exactly similar to these herein described. The death certificate was signed in November 1904, "Cardiac Incompetence." His medical man informed Dr. Legge that it did not occur to him that this was brought about by any direct action on the heart, but that it was due to Chronic Bronchitis, bronchiectasis and emphysema. General anasarca was present. He remembered that the family attributed the symptoms to a certain wood, and the man's wife said that when he first had the attacks, he got better quickly, and that when he went back to work he soon got worse.

The other, a sawyer, aged 50, was stated to have shewn the same symptoms of Chronic Bronchitis and attacks of Dyspnoea during life. His death certificate, however, was signed " diarrhoea one month."

Treatment. None of the drugs ordinarily used in asthma or cardiac weakness, had the slightest effect either during an attack, or in those cases where they had just begun to complain of shortness of breath etc., All they seemed to desire, when an attack was on, were rest and cool fresh air. If their comfort in this way was attended to, the attacks gradually subsided and in from three to six weeks according to the severity of the attack, they were quite well again.

The great thing to be aimed at was to prevent these men from inhaling the dust. Two cases of mine wore respirators, with cotton wool as a filter, but they felt suffocated and awkward in them, and discarded them.

Exhaust ventilation applied in the various stages of the manufacture, so as to suck off the dust at the moment it is made, appeared to me to be the remedy. If this failed then the use of the wood should be prohibited.

4. Industrial Medicine.

Case 1. in the context was seen by me in 1901, and was instrumental in drawing the attention of the Shuttle Makers Society to an apparent danger to which their members were exposed. The attention of the Home Office was drawn to the Report made by Professor Harvey Gibson on his examination of the wood. Enquires were at once started, and Dr. Legge, H.M. Chief Medical Inspector of Factories, made a tour of the various shuttle factories of the Country.

I was asked to give him a report of a case, and this was used by Professor Harvey Gibson who was giving a lecture on African Boxwood in Blackburn, in December 1905. The report of this case, and the result of Professor Harvey Gibson's examination of the wood, were published in the Annual Report of the Chief Inspector of Factories for 1905.

I received a notice from the Home Office to attend on 1st November 1906, before the Committee appointed to enquire, and report what diseases are due to industrial occupations, and which can properly be added to the diseases enumerated in the Third Schedule of the Workmen's Compensation Act 1906, in order to give evidence as to the Alkaloidal

poisoning from African Boxwood in shuttle making. Professor Clifford Allbutt was the Chairman. As a result of this enquiry, poisoning by Gonioma Kamassi (African Boxwood) was added to the Third Schedule of the Workman's Compensation Act 1906, as one of those industrial diseases in which the workman would get compensation if disabled while using African Boxwood.

The employers were also compelled to instal exhaust ventilation by hoods and ducts in such a way as to catch the dust as near as possible to the paint where it is produced.

Conclusion.

An attempt has been made to present such facts regarding African Boxwood that may give the reader some idea of the history, source, general uses and poisonous qualities of this wood. As many employers, since the inclusion of the workers of this wood in the Workmen's Compensation Act, fight shy of using it, and those who continue working it are compelled to use exhaust ventilation, the supply of Clinical data has almost ceased.

Still here is a case of a new disease appearing in the routine work of a general practice, and by a process of exclusion and by the observation of the workers themselves, suspicion is thrown upon African Boxwood as the cause. An alkaloid, akin to Digitalin is found in the dust of the wood. This alkaloid is found to be soluble in normal saline solution, so that it could readily be dissolved and absorbed through the lungs, and air passages. This alkaloid is found to be a cardiac poison. Doses injected into animals produced death in a very short time, and

these animals died of syncope. Numerous experiments on a cat's heart showed that the alkaloid was a cardiac poison causing gradual slowing of the heart beat, and diminution of vigour of the contractile tissue of the heart, that the effect of the alkaloid was cumulative, finally causing a cessation of the beat under long exposure to its influence. These experimental data, are supported by clinical evidence. Cases are reported that show that workmen, working this wood, suffer from a peculiar train of symptoms, and that those affecting the heart bear out the experimental data. The heart under a certain dose of the poison slows down, and in some cases quoted, the pulse rate falls as low as 45 per minute. As the dose was increased by the man sticking to his work, the heart became rapid and feeble, and shewed signs of failing. If the man was taken away from his work, the signs of cardiac failure disappeared in a day or two, the rapid heart beat gave place to a slow one, and after a week or two the heart resumed its normal speed. The effect clinically also was evidently cumulative. It took gradual doses, spreading over from one to three years, and the wood was only worked at intervals, to cause the symptoms to arise. When the man had got a certain amount of the poison in his blood, he became peculiarly susceptible to it, and the effects of it took usually several weeks to pass off.

That it was the dust of African Boxwood that caused these symptoms, and not the dust of any of the other woods used in the shuttle factory, is proved by the fact that it was only when this wood was being worked that the men

complained, that if they were withdrawn from work, the symptoms gradually disappeared, and that they could work all the other woods with impunity. As soon, however, as they began cutting this wood, the symptoms became evident. Now that in the Shuttle Factory here, this wood is not used, none of the workmen suffer from the symptoms.

In the Report of the Chief Inspector of Factories for 1907
there is a "Special Report" by John Ney M.D who was
accompanied by Dr. J. M. Legge & who examined 79
men engaged in working "South African Boxwood"

REFERENCES.

(1) The Forests and Forest Flora of Cape Colony by Thomas R. Sim F.L.S. etc.

(2) Smith.. A Contribution to South African Materia Medica

(3) Biochemical Journal Vol. 1 No. 1.

(4) Annual Report of the Chief Inspector of Factories and Workshops for Year 1905.

(5) Asthma by Frank Coke.

(6) A Manual of Immunity. Fraser

(7) Diseases of Occupationby Thomas Oliver.

(8) Diseases of Occupation and Vocational Hygiene by Kober and Hanson.

(9) Neiser Internat Ubersicht Über Gewerbe Hygiene Berlin 1907.

(10) Nestler Promethus Berlin 1913.

(11) Dr. Legge Annual Report of the Chief Inspector of Factories 1905.

Also in Report for 1907 there is a Special Report on Shuttlemakers + dust of wood from "South African Boxwood"