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THE

NON-BACILLAR NATURE

OF

ABRUS-POISON,

WITH OBSERVATIONS ON

ITS CHEMICAL AND PHYSIOLOGICAL PROPERTIES.

BY

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PREFACE.

The following pages embody the results of an inquiry into the existence of the so-called "bacillus of jequirity seeds," with observations on the nature of abrus-poison, its chemical properties, and physiological action. The practical application of the knowledge thus far acquired to the treatment of cases of abrus-poisoning is also indicated.

The opportune presence of Dr. Koch and the German Cholera Commissioners at the Medical College Hospital has enabled us to conduct the bacterial part of the research with a thoroughness which we could not otherwise have hoped to attain. And if our results conflict with those of so well known a pathologist as M. Cornil, our observations have the merit of having been conducted under the immediate superintendence of Dr. Koch, than whom there is admittedly no greater authority on the subject of bacterial pathology. We desire to express here our grateful thanks to Dr. Koch and also to Dr. Fischer for the valuable assistance which they so freely rendered us throughout this inquiry. To Major Waterhouse of the Survey Department we are indebted for the careful and accurate execution of the lithographic illustrations.

Calcutta, 1*st March* 1884.

CONTENTS.

INTRODUCTION.

PART I.

THE BACTERIAL THEORY OF THE ACTION OF ABRUS-POISON.

CHAPTER I.

CHAPTER II.

CHAPTER III.

CHAPTER IV.

CHAPTER V.

CHAPTER VI.

PART II.

THE CHEMICAL NATURE OF THE ABRUS-POISON.

CHAPTER I.

CHAPTER II.

CHAPTER III.

The Physiological Effects of Abrin.

CHAPTER IV.

The Management of Cases of Poisoning by Abrin.

APPENDICES.

ILLUSTRATIONS.

INTRODUCTORY.

Seeds used hypodermically in India for poisoning cattle, and occasionally for committing murder. Dr. Warden's published researches. The local inflammation attributed by M. Sattler to a special form of bacillus. M.M. Cornil and Berlioz extend this idea to account for the general toxic symptoms, which they assert are due to a specific bacillus contained in the seeds. The interesting bearings of this "discovery" on general pathology, as well as the medico-legal importance of the poison, rendered the subject worthy of further study. Manner in which the subject will be treated.

THE seeds of the Indian liquorice plant, the 'jequirity' of the Brazilians (1), have for several years been extensively used in India for poisoning cattle (2), and less frequently for destroying human life (3); but the manner in which the seeds operate in inducing a fatal result has remained highly problematical.

Taken by the mouth, these seeds, like the roots and leaves of the plant, may be ingested in considerable quantity with impunity. In Egypt, the boiled seeds form an occasional article of diet amongst the poorer classes, although accounted hard and indigestible (4). It was only when the powdered seeds were introduced

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(1) The botanical characters of the plant are given in Appendix I.

(2) Report of Commission on Cattle Plague, Calcutta, 1870. Annual Report of Chemical Examiner to the Government of Punjab, 1873. Also the Ann. Repts. of the Chem. Examrs. of Bengal and North-West Provinces from 1874 up to date—*Vide* Appendix II for description of mode of using seeds for poisoning cattle.

(3) Ann. Rept. of Chemical Examiner, Punjab, 1873; also Bengal Police Rept. for December 1880.

(4) BURNETT'S Botany, Volume II, page 654. DRURY'S *Useful Plants of India*, page 3, 1873—*Vide* Appendix III for evidence regarding harmlessness when taken by the mouth.

into the subcutaneous tissues that fatal symptoms were found to develop, death occurring in cattle within 48 hours after the administration of one and a half to two grains of the seed.

In view of the practical importance of the subject, Dr. Warden was led in 1880 to make a chemical analysis of these seeds, with the result of finding that they contained no alkaloidal principle or glucoside. A crystalline acid, which he called *abric acid*, represented by the formula $C_{21}\ H_{24}\ N_3\ O_4$, was isolated, but this proved to be inert under all circumstances (1). A small quantity of pungent volatile oil was extracted from the seeds, but this also was inactive. The results of this analysis, together with those of several experiments on cats, and historical notes on the seed, which were published in detail in the *Indian Medical Gazette* for 1882 (2), although clearing the way for future investigations, afforded no positive insight into the anomalous manner in which these seeds exercised their poisonous action.

Quite recently M.M. Cornil and Berlioz, in a communication to the Académie des Sciences, have alleged that the poisonous symptoms produced by the abrus-seeds are due to a generalised bacterial condition (3). It had long ago been known that the topical application of an infusion of the seeds had the property of exciting an acute inflammation of the conjunctiva (4). And Sattler (5), after a series of observations, concluded that the artificial inflammation excited by this infusion was an infective disease caused by an innocuous bacillus which was always present in the air, but which took on pathogenic qualities when growing in an infusion of abrus-seeds (6).

It was the idea thus suggested by M. Sattler regarding the local affection which led M.M. Cornil and Berlioz to undertake

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(1) *Vide* Appendix IV.

(2) Page 287 *et seq.*

(3) *Le Progrès Médical*, 1883. No. 44. Their paper is abstracted at some length in the *Lancet*, Volume II, 1883, page 600.

(4) In India it is sometimes used by malingerers in jails to produce conjunctivitis.

(5) *Wiener Mediz. Wochen*, No. 18—21, 1883.

(6) Dr. Center of Lahore several years ago remarked on the occurrence of swarms of bacteria in the wound in cases of abrus-poisoning—*Indian Medical Gazette*, page 319, 1882.

the investigation of the influence of this supposed bacillus upon the organism as a whole, and they allege as the results of their investigations that the poisonous action of the abrus-seeds is due to a specific bacillus—"the bacillus of jequirity." This bacillus they believe to be derived from the seeds, and, developing primarily at the seat of the injection of the infusion, ultimately pervades all parts of the organism, and is the cause of the death of the animal.

These startling observations of M.M. Cornil and Berlioz, if confirmed, would naturally tend to upset existing views on germ pathology, and would stimulate to experimental research in an almost unlooked-for direction. The *Lancet* is not slow to accept M. Cornil's results, and devotes a leader to their consideration, remarking that an argument of much validity is hereby afforded for the doctrine of specificity of disease (1). The importance therefore of these alleged results in their relations to general pathology rendered the subject deserving of further study. The present series of observations had, however, the further object of ascertaining definitely the true mode of action of a poison which was of much medico-legal importance in this country.

Our inquiry at the outset will lead us to test the accuracy of M. Cornil's observations, which credit abrus-seeds with the possession of such remarkable properties—so opposed to all previous experience of the action of vegetable poisons; and the first question which will present itself for consideration is whether or not bacillar formation is necessarily associated with the local action and toxic manifestations of the abrus-seeds. If this is found to be really the case, then we will have to consider the significance of the bacillus. Is it a variety special to these seeds? Or, is it a known form of pathogenic bacillus; or, is it one of the ordinary non-infecting bacilli which has taken on special qualities due to a special kind of disturbance excited in the tissues by the abrus-seed infusion? But if we find that the local action and poisoning symptoms are due neither to the presence of bacteria nor to the products resulting from their growth, then we shall have to resort to a more extended chemical

(1) Page 601, Volume II, 1883.

examination in the endeavour to ascertain the nature of the poisonous principle which will sufficiently explain the local and general action of the seeds on the animal economy.

PART I.

The Bacterial Theory of the Action of Abrus-poison.

THE BACTERIAL THEORY OF THE ACTION OF ABRUS-POISON.

CHAPTER I.

The alleged presence in the seeds of specific bacteria or their spores. Evidence against this is furnished by (*a*) Culture experiments with the seed in gelatine according to Koch's method, (*b*) by Inoculation and Hypodermic experiments with pure cultivations of the micro-organisms obtained from the seeds, and (*c*) by Microscopical Examination of sections of the seed.

If the peculiar properties of the seeds be due to contained bacilli, then the bacilli or their spores ought to be capable of demonstration by culture of the seed in gelatine or by microscopical examination of a stained section, for it may be regarded as certain that organisms do not originate spontaneously under any circumstances.

By cultivation in sterilised gelatine according to the beautiful method of Dr. Koch, the subsequent pure cultivations ought to afford the bacteria in endless numbers, and uncontaminated with the other constituents of the seeds or with other micro-organisms. And if the specific action of the seeds be really due to these bacteria, the characteristic symptoms ought to follow on the topical application of, or inoculation of, these bacteria when applied *en masse* to the conjunctiva or injected hypodermically.

The following experiments were made with the view of ascertaining these points : —

A few of the abrus-seeds (1) were deprived of their *testæ*, leaving the embryonic radicle and gemmule, together with the fleshy cotyledons, and pounded for a few minutes in a clean agate mortar. Of this two separate cultivations were made (2), one

(1) To test whether these seeds were active or not, ½ grain was injected into a cat's thigh, and death occurred in 19½ hours—*See* Exp. No. XXI.

(2) The cultivations were always made in nutrient gelatine with the full observance of all the precautions practised by Dr. Koch.

on a glass plate and one in a large test-tube. The cultivation made in the test-tube gave only three colonies of bacteria, and as they were widely separated and their growth not rapid, they were allowed to grow in the nutrient gelatine for two weeks. All three colonies proved to be micrococci, and were apparently of the same kind, each colony having a well-defined border of a faintly brownish colour.

Experiment I.—These three colonies were mixed together with a very small quantity of distilled water, and a large portion well applied over the conjunctiva of a cat. No effect followed—not even the slightest irritation.

Exp. II.—Another portion of the mixed colonies, containing many millions of micrococci, was mixed with 10 minims of distilled water and injected subcutaneously into the inner aspect of thigh of a chicken. No result (1).

Exp. III.—The remaining portion of the mixed colonies was inoculated beneath the skin over back of a house-mouse. No result.

The cultivation of the pounded seeds which was made on the glass plate yielded several colonies of bacteria. Most of these were micrococci, but one form of bacillus was also present.

It may here be stated that all the preparations were duly stained with methyl violet—the same colour which M. Cornil used, and examined with one of Ziess's microscopes fitted with an Abbe's condenser, the lenses used being a one-twelfth inch oil immersion objective, with Nos. 2 and 4 eye-pieces.

The form of bacillus found in this cultivation was small and slender. They grew in semi-transparent tuft-like colonies, and tended to liquefy the gelatine. Their length was about half the diameter of a red blood-corpuscle, and their breadth about one-sixth their length. The sides of the rodlets were straight, and their ends abruptly cut across. In multiplying they did not form filaments. Their general appearance was not unlike the septicæmic bacillus of mice. The following experiments were made with them :—

Exp. IV.—A pure cultivation of these bacilli was allowed to grow for about two weeks, and a quantity taken and moistened with a little water and smeared over the conjunctiva of a cat. No result.

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(1) It will afterwards be shown that chickens are very susceptible to abrus-poisoning.

Exp. V.—A quantity was injected hypodermically into a chicken No result.

Exp. VI.—A quantity was inoculated into a house-mouse. No result.

The micrococci found on the glass plate appeared similar to those of the test-tube used in Exps. I to III. The following experiments were made with these micrococci:—

Exp. VII.—A quantity mixed with a little distilled water was smeared over conjunctiva of cat. No result.

Exp. VIII.—A small quantity mixed with a little water was injected into a chicken, without any apparent effect.

These culture experiments therefore show that the seeds contain no specific bacilli or spores capable of developing in nutrient gelatine. In one of the specimens no bacilli at all were found, even after cultivation for two weeks. In the other the bacillus which was found proved to be inert, both when applied topically to the conjunctiva and also when inoculated and administered hypodermically. The micrococci found in both cultivations were also inert.

For collateral evidence, stained sections of the seeds were examined. If bacilli be present in the seeds, then sections of the seeds stained with methyl violet ought to reveal the bacteria *in situ*. But such an examination failed to show bacteria of any kind. The annexed engraving from a drawing by Dr. Cunningham shows the microscopic structure of the seeds. The protoplasm of adjacent cells freely anastomoses. The protoplasm is of a granular character; the mode of shading practised in the engraving by short interrupted straight lines was adopted merely as a convenient way of giving effect to the granular appearance exhibited by the cell-contents. No starch granules can be detected in the seeds.

Thus the processes of cultivation and staining furnish positive evidence against the presence in the seed of bacteria. And it is only in keeping with the researches of Dr. Roberts (1) and others to find that undecomposed vegetable tissue is free from micro-organisms.

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(1) *Phil. Soc. Trans.*, 1874.

PLATE I.

The Microscopic Structure of the Abrus-seed.

Fig. 1.—Cotyledonary parenchyma.

Fig. 2.—The same under a low power.

Fig. 3.—Vertical section through the seed coats. For detailed description *see* Appendix I.

Fig. 4.—Apearance of surface of the seed due to the structure of the peripheral extremities of the outer layer of cells.

Fig. 5.—An isolated cell from outer stratum.

Fig. 6.—Horizontal view of stratum No. 8.

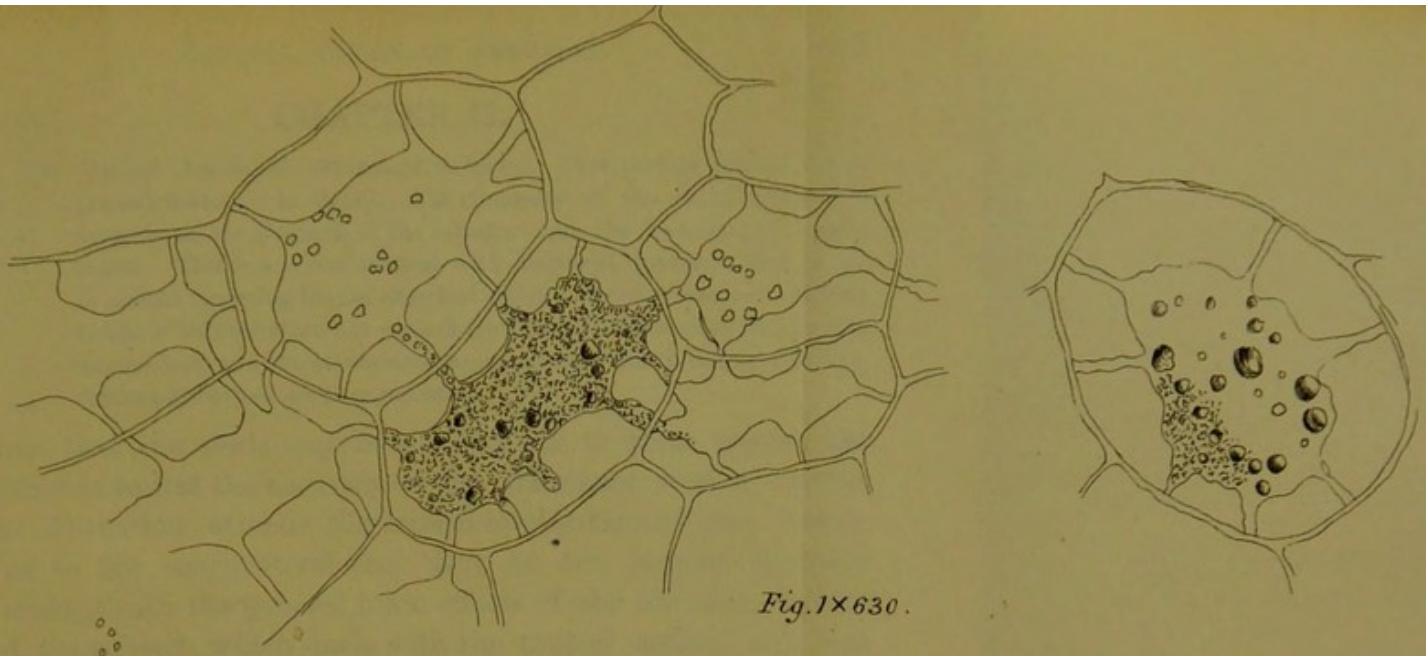

Fig. 1 × 630.

COTYLEDONARY PARENCHYMA.

Cells very thick walled separated from one another by narrow intercellular channels. Cell walls with numerous perforations by means of which processes of the protoplasm of different cells communicate with one another. Protoplasm granular with conspicuous oil drops and no starch grains.

Fig. 2 × 180.

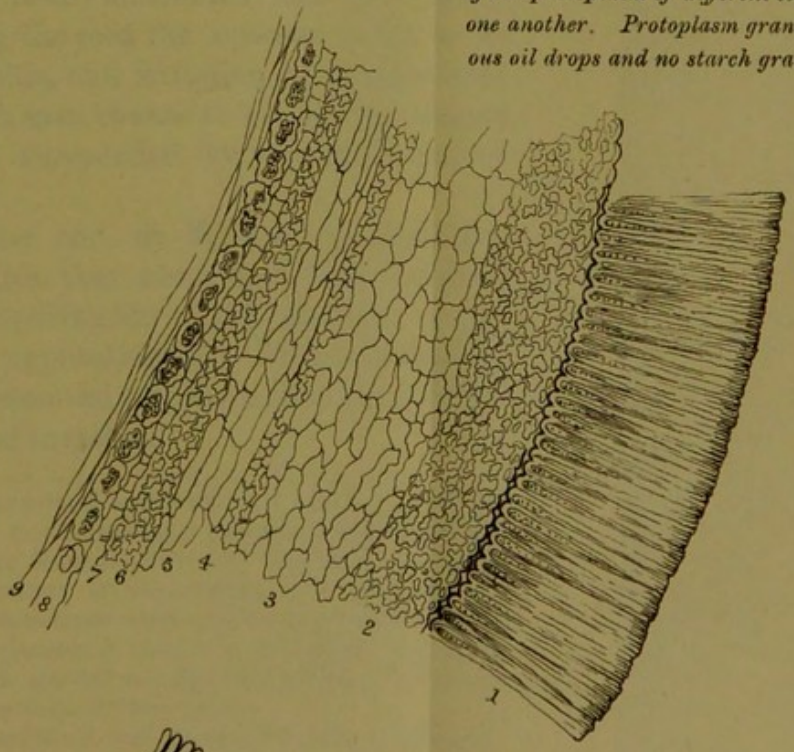

Fig. 3 × 110.

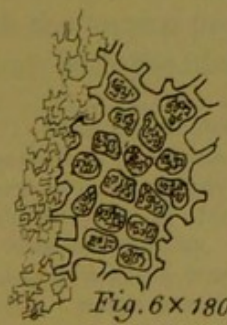

Fig. 6 × 180.

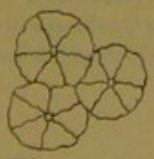

Fig. 4 × 520.

Fig. 5 × 180.

D. D. CUNNINGHAM, DEL.

CHAPTER II.

The Topical Action of abrus-seed infusion. This part of subject not at present taken up in detail. The intensity of the abrus ophthalmia depends on the strength of the infusion and the frequency of application. This fact is inconsistent with bacterial invasion, and is an argument favouring idea of chemical action. Mere presence of bacteria at site of inflammation not remarkable, for infusion used by Sattler was unsterilised, and the albuminous constitution of the infusion specially favours growth of micro-organisms.

FINDING that the seeds contain no bacteria or their spores, the next point is to test the accuracy of the statement that a specific bacillar formation attends the topical application of the watery infusion to the conjunctival sac. But as our inquiry interests itself mainly with the general toxic effects of the abrus-seeds, this part of the subject, which deals with the topical action, will not at present be taken up (1). There are, however, several points in connexion with this aspect of the question which may be profitably referred to in this place.

That an acute conjunctivitis follows the topical application of the infusion or powdered seeds is an undoubted fact (2). Even during the process of pounding the seed the operator is apt to be afflicted with sneezing, bronchitis, and irritation of conjunctivæ, and any cuts or scratches which may chance to be on his fingers become swollen, painful, and surrounded by an erythematous blush.

But although M.M. Sattler and de Wecker attribute the inflammation to a specific bacillus, they admit that the severity of the inflammation is directly proportionate to the strength of the infusion and to the number of applications (3). This is in keeping with the known properties of chemical poisons, and is quite inconsistent with the idea of bacterial invasion.

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(1) After the completion of our observations, and when just about to send our manuscript to the press, we find that in the February number of FRIEDLÄNDER'S "*Fortschritte der Medicin*" (Berlin, 1st February 1884) are two articles on abrus-ophthalmia—one by DR. C. S. SALOMONSEN of Copenhagen, and the other by DR. NEISSER of Breslau. The writers of both these articles are led to conclude that the ophthalmia resulting from the topical application of abrus-seed infusion is not due to bacteria. SALOMONSEN, it appears, was also led to make cultivations of abrus-seed infusions with results generally similar to those obtained by us.

(2) For the symptoms of abrus-ophthalmia and an account of the therapeutic value of abrus in eye-disease, *see* Appendix V.

(3) '*ophthalmie jequirîtique et son emploi clinique*, par H. SATTLER et L. DE WECKER, Paris, 1883.

M. DeWecker reports that the abrus inflammation is peculiar, in that it does not tend to spread to the cornea or other tissues, but is confined to the conjunctival sac to which it has been alone applied (1). And this is instanced by M. Cornil as being due to a want of absorption of the main agent in the causation of the inflammation, viz., bacilli. But numerous cases are reported where the inflammation spread to the face, neck, and upper part of the chest (2), and Dr. Moura, Brazil, found that the repeated application of an infusion (strength 1 in 20) produced in rabbits such intense inflammation as to result in suppuration of the eyeball and gangrene of the lids, and also inflammation of the submaxillary glands (3).

As the infusion used by Sattler was unsterilised, the presence of bacteria at the site of the inflammation is not remarkable, for the albuminous constitution of the infusion renders it an exceedingly favourable medium for the growth of micro-organisms.

CHAPTER III.

The Toxic Action of unsterilised abrus-seed infusion is not necessarily associated with a generalised bacillar formation. Difficulty of effectually sterilising abrus-seeds or their infusion. Fowls and cats were chiefly used in these experiments, their advantages over the rabbits and guinea-pigs employed by M. Cornil. With large doses death occurs too rapidly to be accounted for by bacterial invasion. Two experiments on fowls with filtered infusion; and two with solid residue, well-washed.—Rapid death.—No bacteria in blood. Eight experiments with powdered seeds to show effects of varying doses. Three experiments on cats with details of symptoms of abrus-poisoning and characteristic *post-mortem* appearances. The numbers and extent of distribution of any bacteria found are proportionate to the time which the animal survives, being least when the animal dies rapidly. The Essential Lesions of abrus-poisoning contrasted with the alleged bacterial lesions described by M. Cornil.

With the view of ascertaining whether or not a generalised bacterial condition was necessarily associated with the toxic action of the abrus-seeds, we proceeded to make hypodermic injections of an infusion of the seeds.

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(1) *Comptes Rend.* XCV, 299.

(2) *New Remedies*, June 1883, quoted in *Pharm. Jour.*, p. 687, 1883.

(3) *Annales d'Oculistique*, Bruxelles, 1882.

As it was found that a boiled infusion of the seeds was inactive (1), and that heat also destroyed the toxic power of the seeds, the prospect of sterilising the infusion of these hard seeds became a matter of great difficulty and of almost doubtful possibility. So in making the infusions, although every ordinary precaution was taken to ensure cleanliness, similar to those resorted to by M. Cornil, viz., by using distilled water which had been boiled and re-cooled, and scrupulously clean vessels, still the possibility of entry into the liquid of adventitious bacteria could not be considered as having been effectually guarded against.

In our experiments cats and fowls were mostly made use of, as it was found that they were readily acted on by the seeds. And by employing these animals, which are known to be less liable to infection by the commoner forms of bacteria likely to be met with in infusions, than guinea-pigs and rabbits, such as were employed by M. Cornil, one source of error was thereby avoided. The average weight of the cats used was 6½lb, and of the chickens 16 ozs. They were of as nearly the same size as possible, unless where otherwise stated.

In M. Cornil's experiments death took place in 36 to 60 hours. He used a weak infusion made by macerating 32 bruised abrus-berries (*sic*) for 24 hours in 500 grammes of warm distilled water, and of this he injected 1 to 2 cc. into the subcutaneous tissues of rabbits and guinea-pigs. We employed a stronger solution with the view of finding whether death might not be so hastened as to occur within a space of time too short to be attributable to bacterial infection. The results are as follow:—

Exp. IX.—2 ozs. of the seeds, deprived of their cuticle, were reduced to a fine powder by pounding in an iron mortar and passing through seives. The powder was then digested for about five hours with 4 ozs. of distilled water and filtered through two folds of filter-paper. The filtrate was of a faintly yellowish tinge, with a slight opalescent appearance. After standing for a time in the air it becomes more decidedly opalescent and of a light olive tint. It was strongly acid in reaction, and on boiling gave a copious white precipitate. Picric and nitric acids in the cold gave with it an abundant white precipitate.

(1) Although this fact at first sight might be construed as favouring the view that the active agent in the seeds was of a bacterial nature, it admits of quite another explanation, as will be shown afterwards.

Of this fresh filtrate 20 minims were injected subcutaneously into the inner aspect of a chicken's thigh. After injection the chicken ate a considerable amount of food. In eight hours it had become languid; did not move readily; its eyes were dull and watery. It then remained with its eyes closed in a sitting posture till death, when it fell on its side. There were no convulsions. Death ensued in 11 hours.

Post-mortem examination was made immediately after death. In the neighbourhood of hypodermic wound was slight œdema—this œdematous fluid contained a very few bacilli, only four or five in each slide; and these bacilli were not all of the same kind.

The vicinity of injection wound was not markedly hyper-vascular.

The blood was fluid, and no bacteria were present either in the cardiac or portal blood. The blood-corpuscles presented no distinctly abnormal appearance.

The heart was semi-contracted. Several small ecchymotic spots beneath the exo-cardial tissue at base and intense injection of vessels in the loose areolar tissue covering base of aorta and great vessels. Small quantity of clear fluid in pericardium.

The lungs presented numerous small points of bloody extravasation towards their attachment to chest wall.

The spleen is of apparently normal size and consistency. The liver is of a mottled appearance to the naked eye, but apparently free from hæmorrhages. Gall bladder turgid with fluid bile.

The sub-serous tissue on posterior and lower aspects of stomach is the seat of intense congestion, with numerous small hæmorrhages. In the sub-peritoneal layer of small intestine, at intervals of 1 inch or so, were small elevated points of extravasated blood about size of a small pin-head. These were opposite the attachment of the mesentery, and did not extend into muscular coat. The mucous membrane of small intestine was intensely congested with numerous little hæmorrhagic points, and the contents generally of a decidedly grumous character.

The mesentery presented several large extravasations in its capillary areas.

Exp. X.—Another chicken was injected with the fresh filtrate at the same time as the one in Exp. IX. Its symptoms were similar, and death occurred in 12½ hours. The *post-mortem* appearances were generally similar to the other chicken, and no bacteria were found in the blood.

Exp. XI.—The solid residue left in Exp. IX was washed several times with cold water, and 1 grain of it was rubbed up with about 10 minims of distilled water and injected into a chicken. Death occurred in 13½ hours. The *post-mortem* signs were generally similar to those in the two previous experiments.

Exp. XII.—A similar experiment was made at the same time in another chicken, death resulting in 14½ hours. No bacteria were found in either the cardiac or portal blood.

In the above experiments with the infusion death occurred in 11 hours and 12½ hours respectively—a space of time much too short to be attributed to bacterial infection; for in bacterial diseases the multiplication of the morbific organisms cannot take place so suddenly. Infective diseases have never been known to prove fatal within a less period than 17½ hours. (Koch.)

To find the precise amount of seed which produces death, and the effect of varying doses, the powdered seeds were rubbed up with a few drops of distilled water in an agate mortar, as it was found by Exps. XI and XII that the solid residue left after filtration of the infusion still retained a high activity; and this is the condition in which the seed is used for poisoning cattle.

Exps. XIII—XX.—The results of these experiments are summarized in the following table :—

Table showing effects on Chickens of injection of Abrus-seed in varying quantities.

Number of experiment.	Amount of seed injected.	Died or not.	Time in which death occurred.
XIII	$\frac{1}{900}$ gr.	No.	.....
XIV	$\frac{1}{600}$,,	,,	.....
XV	$\frac{1}{300}$,,	Died.	16 days.
XVI	$\frac{1}{100}$,,	,,	7 ,,
XVII	$\frac{1}{4}$,,	,,	42 hours.
XVIII	$\frac{1}{3}$,,	,,	22 ,,
XIX	$\frac{1}{2}$,,	,,	17 ,,
XX	2 grs.	,,	13 ,,

The powdered seeds were administered in a like manner to the following three cats:—

Exp. XXI.—Injected hypodermically into a medium-sized male cat ½ grain of powdered seed rubbed up with 10 minims of distilled water. Death occurred in 19½ hours. Acute abrus-poisoning is singularly free from striking symptoms. The animal becomes gradually exhausted, and dies quietly without convulsions. At first it seems unaffected, and may even eat little food, but after a few hours it becomes languid and disinclined to move. The eyes become dull and watery, and the conjunctivæ slightly inflamed: the excessive flow of tears form wet tracts on either side of nose. The flow of saliva is somewhat increased. It ceases to eat. Latterly, it crouches down, evidently through loss of power to support body. On being disturbed, it lifts its head in a one-sided sort of way, and the head shakes and is unsteady. Shortly before death it passes a few blood-stained

Symptoms of abrus-poisoning.

fluid stools with straining, and there may be slight prolapse of the rectum. This symptom is more marked in proportion to the time which the animal survives. The temperature falls considerably.

Post-mortem examination was made one hour after death. No evidence of decomposition. Commencing rigidity of limbs. Blood fluid.

Tissue at seat of hypodermic injection exhibits slightly increased vascularity, with a trace of œdema. A scraping from the tissue at the seat of injection shows a few large bacilli of a thick cylindrical form.

The superficial lymphatic glands at lower part of abdomen are very slightly enlarged, but not hæmorrhagic. Under the microscope the lymphatic glands are seen to contain no bacteria.

The cardiac blood, examined without re-agents, exhibits a great number of clusters of granular matter—the so-called '*blood-plates*' which are believed to be the broken-up protoplasm of white corpuscles. When stained with methyl violet not a single bacillus is seen, but a considerable number of those large dark masses which are believed to be the broken up nuclei of white corpuscles.

The pleural cavity contains a small quantity of clear serum. The lungs are of generally normal appearance.

The heart contains mostly fluid blood, but a few pale clots are present in both sides. Both ventricles are distended with blood. Over base minute extravasations in sub-pericardial tissue.

The liver not examined microscopically. Its general appearance is normal.

The speen is very slightly enlarged—about half over normal; but it is not softened: its surface presents a few relatively dark-coloured spots, apparently extravasations. Under the microscope it is seen to contain no bacilli.

Kidney fatty, but contains no bacilli.

The mucous membrane of small intestine is intensely congested, especially at its lower part and at caput cæcum. The hyperæmia is attended with abundant minute points of extravasation. The large intestine is less congested; its contents, together with those of the lower part of small intestine, are admixed with bloody mucus. The naked-eye appearance is not unlike that resulting from septicæmia.

Sections of intestine after hardening in alcohol showed under microscope numerous small capillary hæmorrhages in the papillæ. The capillaries were distended and crowded with red blood-corpuscles, but there was no evident breach in their walls. The extravasations appeared to occur by diapedesis. No bacilli were detected.

Neither the mesenteric nor any of the deep lymphatic glands were hæmorrhagic, or presented bacteria.

Exp. XXII.—To another cat, much larger and stronger than the one used in foregoing experiment, ½ grain of seed was given in a similar manner. Death occurred in 40 hours. The symptoms were similar to those of the other cat.

Post-mortem examination made five hours after death. Rigidity marked in both extremities. Hair over seat of injection can be pulled out on slight traction. The tissue at seat of injection is moderately injected, and a zone of œdema surrounds the seat of puncture. This œdematous fluid contains three kinds of bacilli, but none of them resembled the bacilli found at seat of injection in the case of the previous cat.

The superficial lymphatic glands are considerably enlarged, injected, but not softened. On section they present extensive hæmorrhagic extravasations into their substance. One or two bacilli, like one of the varieties found in the wound, are seen in the scrapings of one of these glands.

Minute hæmorrhagic points are also seen on the surface of most of the voluntary muscles in all parts of the body, and the extravasations extend into the muscular substance.

The upper surface of diaphragm also presents numerous extravasations.

The blood is fluid. The cardiac blood contains in one slide one bacillus of same variety as seen in the lymphatic gland. The blood of portal vein contains two of the same bacilli in one slide. Fewer blood-plates are present than in blood of previous cat.

Lungs are thickly strewn with hæmorrhagic points—not located to margins, but throughout substance; and they are generally darkly congested in the rest of their extent.

The pleura and pericardium contain a trace of clear serous fluid.

The heart exhibits at base, and chiefly towards posterior aspect, numerous large extravasations into sub-pericardial tissue.

Peritoneal cavity contains no fluid. The peritoneum much injected, but its surface free from exudation.

Liver darkly congested and slightly mottled. Gall bladder turgid.

Spleen much enlarged, and has numerous dark extravasations of considerable extent.

Kidneys pale, and evidently fatty.

The mesentery is highly injected. Its smaller glands near attachment of intestine are enlarged and very darkly coloured. The large mesenteric glands are much enlarged, darkly congested, and present extravasations into their substance.

The peritoneal covering of small intestine presents several small, dark, swollen points projecting beyond surface. They are situated along the free border, opposite the attachment of the mesentery, and do not extend inwards beyond the sub-peritoneal coat. No blood escapes on incising them.

Exp. XXIII.—$\frac{1}{3}$ grain was injected under the same conditions into a smaller cat. Death in 23 hours.

The symptoms and *post-mortem* appearances were generally the same as those in the other two cats. No bacilli were found in the portal blood, but a very few, and all of one form, were discovered in the cardiac blood.

In these three cats death took place in 19½, in 40, and in 23 hours respectively, under the same dose of $\frac{1}{3}$ grain of the seed,

the second cat being a much larger and stronger animal than the other two. Bacilli were found in the neighbourhood of the seat of injection in all three; in two, bacilli were discovered in the cardiac blood, and in one only did the portal vein contain bacilli.

The numbers and extent of distribution of the bacilli bore a definite relation to the period which elapsed between the time of injection and the death of the animal. Thus, in the animal which died in 19½ hours, the numbers of bacilli in neighbourhood of injection-wound were few, and there were none at all in the blood. In the animal which died in 23 hours there were more at the seat of injection, and a very few in the cardiac blood—an average of two per slide, but none in the portal blood. While in the cat which survived for 40 hours the bacilli were very abundant at the seat of injection, and traces of bacilli were found in the portal as well as in the cardiac blood.

The Characteristic Anatomical Lesions in Abrus-poisoning.

These have already been detailed in the *post-mortem* reports of the fatal cases. The principal morbid appearances are found in the wound, in the blood, and in those tissues and viscera which are highly vascular, viz., in the lymphatic glands, voluntary muscles, mucous membrane of stomach and small intestines, omentum, sub-serous tissue (visceral), lungs, liver, and spleen.

At the seat of the hypodermic injection and in its neighbourhood slight œdema of the subcutaneous tissue is found when the animal has survived for over 24—30 hours. This œdematous fluid contains bacilli, the characters and significance of which will be considered at some length hereafter.

The principal changes in the blood are the enormous numbers of 'blood-plates,' and of those larger, dark, granular masses which are usually believed to be the broken-up nuclei of white corpuscles.

The lymphatic glands, without being evidently enlarged or softened, are hyper-vascular, and present numerous minute hæmorrhages into their substance. Similar hæmorrhages occur into the substance of the voluntary muscles of chest and extremities. No bacteria existed at the seat of these capillary hæmorrhages.

The mucous membrane of stomach and intestine is highly injected; the hyperæmia is most marked towards the lower

part of small intestine and caput cæcum. Numerous small hæmorrhagic points are seen on the surface of the mucous membrane extending into the sub-mucous tissue. These are not specially confined to Peyer's patches, but are generally diffused. And the small intestine and colon contain a large quantity of blood-stained mucus. Microscopic examination shows that the capillary areas of the intestinal villi are frequently the seat of hæmorrhages. The mucous and sub-mucous tissue is infiltrated with red corpuscles, and the capillaries are distended by crowds of red corpuscles, but there is no apparent breach in the walls of the vessels. The red corpuscles appear to have escaped by diapedesis. No bacteria were found at the seat of these hæmorrhages. In the sub-serous layer of the wall of the small intestine and stomach a few large hæmorrhages may be seen—in the stomach they are chiefly located towards its inferior and posterior aspects, and in the small intestine to the free border of the gut, opposite to the attachment of the mesentery ; and they do not extend to the muscular coat. The omentum also presents several large sub-serous hæmorrhagic extravasations.

The lungs present a few small hæmorrhagic points, chiefly towards the margins of the lobes. In the rest of their extent they are of normal appearance.

The lesions found in liver are generally similar to those recorded by M. Cornil as given below, but without the presence of bacteria.

The spleen may be slightly enlarged, and present a faintly mottled appearance like that of liver, but it is of firm consistency, and shows no bacteria unless death has occurred slowly.

In the *post-mortem* appearances described by M. Cornil, the essential lesions of abrus-poisoning are evidently complicated by the presence of the accidental bacilli derived from the wound, for in his cases death did not usually take place until a period of two days had elapsed—an interval of time which easily allowed of the absorption of bacteria from the wound.

In addition to œdema of the skin near the seat of injection, he speaks of a slight form of peritonitis with micro-organisms in the inflammatory products, ecchymosis in the gastric mucous membrane, swelling of Peyer's patches, often with hæmorrhage

into them. In the greater number of the cases he found isolated yellowish-grey areas on the surface of the liver. These islets were about 5 mm. in diameter, and disseminated in greater or less numbers on the inferior and superior surfaces of the organ. Scrapings from the surface of sections always exhibited under the microscope the bacterial rods of jequirity. Sections of these islets after being hardened in alcohol and coloured with methyl violet showed at the periphery of certain hepatic lobules an interlobular branch of the portal vein, sometimes filled with a clot containing in its meshes a quantity of the characteristic bacilli. In the same isolated foci of disease, whilst the capillaries were filled with the débris of blood corpuscles, the hepatic cells were also greatly changed ; they did not stain, and their nuclei were hardly visible, or they were replaced by vacuoles, and yellowish pigment granules were seen in the atrophied and mortified cells. *In certain of the opaque diseased areas bacteria were not found* (1).

These appearances narrated by M. Cornil, so far as they go, represent more or less correctly several of the conditions observable in cases of sub-acute abrus-poisoning; but that he overstates the extent to which bacteria are found, and misinterprets their real significance, will be appearent from the subsequent chapters.

CHAPTER IV.

The Bacilli at the Seat of Injection and its neighbourhood. Their numbers, variety, and significance. Description of the so-called "specific jequirity-bacillus" of Sattler. Evidence of the accidental nature of the bacilli.

The numbers of bacilli found at the seat of injection after the introduction of a fairly large quantity of infusion are proportionate to the time which the animal may survive. When it dies quickly, comparatively few are found ; but as the time advances, should the dose have been insufficient to kill the animal, they are found in increasing numbers, till the local inflammatory process ends in resolution or sloughing.

The bacillus which Sattler calls the specific jequirity-bacillus is described as being of about the same size as the bacillus of

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(1) The italics are ours.

tubercle, but considerably broader and thicker, and with square ends. These bacilli form a membrane on the top of the nutrient fluid, in which they grow, which after a time sinks to the bottom. They are motile, form end spores, and grow rapidly.

In the experiments about to be detailed, the bacilli were usually of different kinds. It was seldom that only one kind was found in the wound; and the form which was most abundant in any one case was frequently altogether absent in other cases, and no spore-forming bacillus like that described by Sattler was discovered. The extent of this variation in the form of the bacilli seems to be more or less related to the duration of the localized inflammation. In Exp. No. XXI only one form was present. They were large, with a length about $1\frac{1}{8}$th the diameter of a red blood-corpuscle, and with a breadth about $\frac{1}{5}$th of their length, and sharply cut across at ends. In Exp. No. XXII three kinds of bacilli were found, but none of them resembled the bacillus found in the previous experiment. The most numerous variety was one whose length was a little less than the diameter of a red blood-corpuscle, and a breadth of about one-seventh its length. The next most numerous variety was a very slender and delicate one, like the septicæmic bacillus of mice. The least abundant kind was a somewhat short bacillus, tending to form filaments of two, their length being slightly less than half the diameter of a red blood-corpuscle, and their breadth being about one-fourth their length. This variety was found in great abundance as the surface of the skin was approached. In Exp. No. XXIII two different kinds of bacilli were found. The most numerous was a slender bacillus with a length slightly less than the diameter of a red blood-corpuscle, and a breadth of about one-sixth the length, the extremity of rodlet being slightly rounded. The other was a large filament-forming bacillus, like that which is usually found in the soil: the ends of the rodlets were straight, and their breadth about one-third of their length.

The Significance of the Bacteria in Wound.

Evidence has already been adduced to show that the seeds themselves contain no bacilli. What, then, are the sources of the bacilli found in the neighbourhood of the site of injection?

1. In an unboiled, and therefore unsterilised infusion, such as that used by M. Cornil, and also for the foregoing experiments, it is impossible to exclude the possibility of entry of germs from the air, for they cling to the surface of the seed, or may fall into the liquid during its preparation.

2. A syringe, even when its needle and body are heated as strongly as they can bear, cannot be regarded as being altogether free from micro-organisms. The development of micro-organisms which Dr. Burdon Sanderson some years ago found to attend the inflammatory process following the subcutaneous injection of a solution of ammonia was attributed by him at the time to spontaneous generation. But Dr. Koch showed that in such injections, even when conducted with the greatest care, the nozzle of the syringe may carry organisms or their spores into the subcutaneous tissue. He made sections of the needle-tract, and demonstrated the organisms in the walls of this passage.

3. Hypodermic injection, apart from the difficulty of effectually sterilising the syringe and its contents, has another serious objection: unlike inoculation, hypodermic injection is not a pure experiment. The tissues may become so injured by the tension and chemical action of the injected fluid that their vitality is reduced, and this physico-chemical alteration in the tissues predisposes to the development of bacteria by rendering the tissue less able to resist the attack of micro-organisms (1).

The condition of the subcutaneous wound caused by the abrus-seed injection affords an example of such a case. And it would indeed be a matter for surprise were bacteria not found in such a wound or its immediate neighbourhood, for the superjacent tissue, even to the unaided senses, has its vitality after 24 hours so markedly reduced that the hairs over the seat of injection can be dragged out on the slightest traction, and the skin is obviously swollen and infiltrated, and its surface in part

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(1) It has been established by the observations of Messrs. KOCH, OGSTON, CHIENE, AND EWART, WATSON-CHEYNE, &c., that in the healthy state of the animal body there are no living micro-organisms present amongst the tissues. The healthy blood and tissues have the power of killing off ordinary bacteria even when the latter have been injected into the circulation (TRAUBE AND GSCHEIDLER, *Berlin Klin. Wochenschrift* No. 37). But when a particular tissue has its vigour reduced by inflammatory processes or otherwise, any bacteria which may reach it may rapidly multiply there, meeting no longer with effectual opposition to their development. M. CHAUVEAU'S '*bistournage*' experiments, described in JEANEL'S *De l' Infection Purulente*, offer examples of this kind of bacterial invasion.

denuded of epithelium, so that not only have bacteria which may have been introduced with the infusion or syringe got conditions favourable to their growth, but bacteria from the outer air can easily penetrate through the skin, the resisting power of which is diminished or lost. And that this may be one of the sources of the bacilli found in the blood in cases of abrus-poisoning is evident from the attached sketch (Plate II) of a section through the skin of the cat which was used in Exp. No. XXII. It represents the microscopical appearance of a vertical section through the skin over the seat of the hypodermic injection. The different parts of the preparation are sufficiently indicated in the description facing the illustration. The bacilli are seen at different stages of their passage from without inwards into the subcutaneous tissue. They were all of one kind, and differed in appearance from the majority of those which occupied the immediate seat of the injection. There were in all three different kinds found in the latter locality, and the variety which was most abundant towards the surface of the skin had here fewest representatives.

Thus we see that bacteria may gain an entrance to the wound in several ways, either during the process of hypodermic injection, or afterwards; and the fact that the bacilli found are not of one kind, but of a variety of forms, bears out the idea that the presence of bacilli at the seat of injection is purely accidental.

CHAPTER V.

The Bacilli in the Blood. Their numbers, variety, and significance. Evidence of their non-pathogenous nature.

In cases where death has occurred rapidly, no bacilli at all are found in the blood. Thus with the chickens in Exps. IX, X, XI, XII, and XVIII—XX, and with the cat in Exp. XXI, no bacilli were found either in the cardiac or portal blood. When the animal survives for about 24 hours, then a few bacilli may be detected in the blood; and in proportion to the time which elapses between the giving of the injection and the animal's death, bacilli are found in the blood in increasing numbers.

But when bacilli were actually present in the blood, in no case were they found in such numbers as to possibly account

PLATE II.

Vertical section through skin of a cat over seat of hypodermic injection. Only bacilli and cell-nuclei are stained. × 600 *circa*.

a. Remains of epidermis, separated up from *cutis vera*, with a few bacilli in its substance and adhering to its surface.

b. Inflammatory exudation between horny layer and *rete* of epidermis crowded with bacilli.

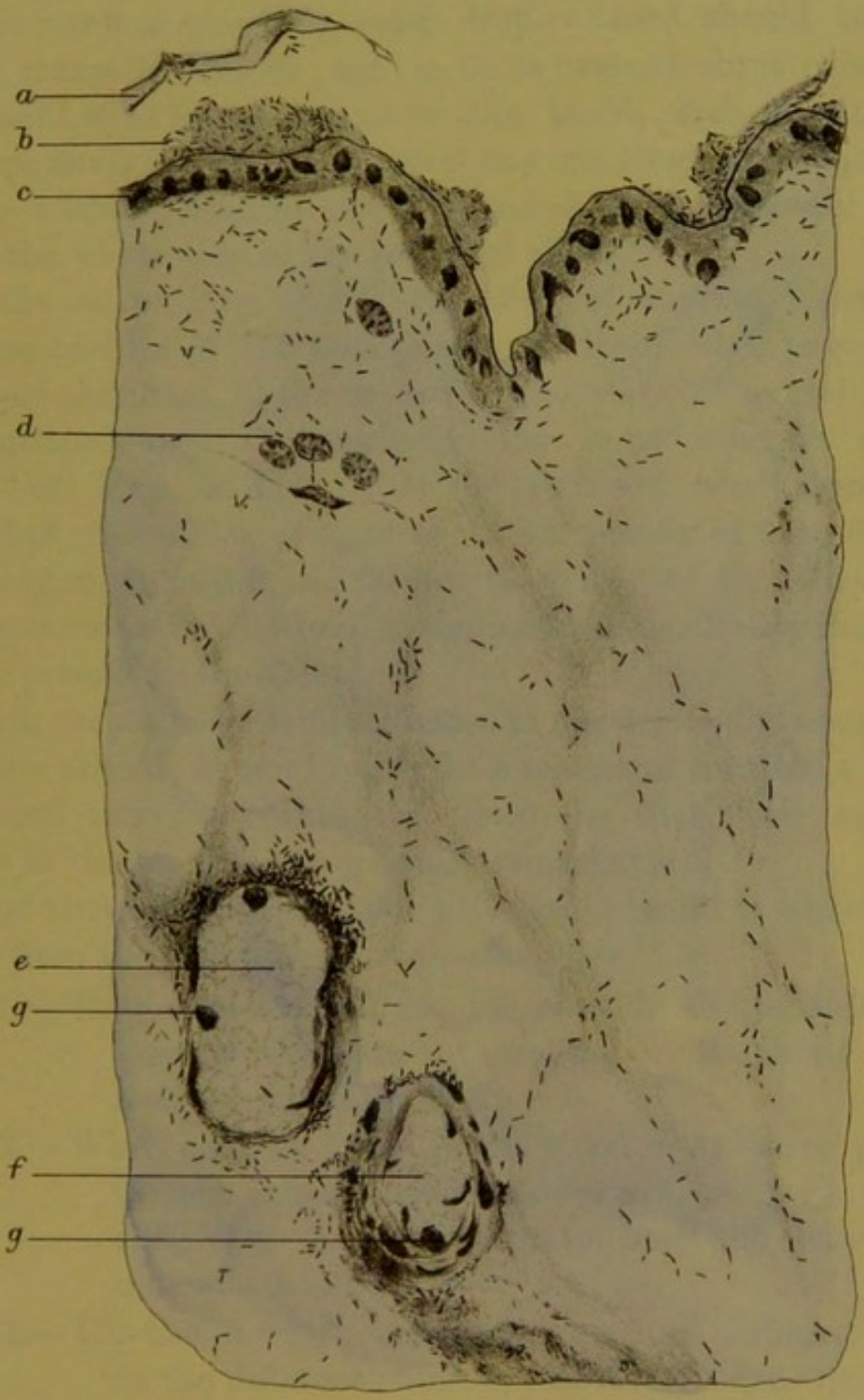
c. Nuclei of cells of rete mucosum. The bacilli can be seen in the act of passing through Malpighian layer.

d. Plasma cells.

e. Section of a small vein, the walls of which are thickly beset by bacilli. Its endothelium is turning inwards, evidencing loss of vitality. One solitary bacillus has penetrated the vessel, and is seen lying within.

f. Section through a small artery. Its endothelium is also turning inwards, but no bacilli have actually entered the vessel.

g. White blood-corpuscles.



L. A. WADDELL, DEL.

for the animal's death. A fatal issue as a consequence of bacterial invasion occurs only when the bacteria, having "multiplied within the circulating blood, interfere to such an extent with the functions of cells, so numerous or essential to life, that life becomes impossible (1)." The number of bacteria required to effect this result is enormous—each drop of blood should contain at least many thousands; but in those cases of abrus-poisoning where bacilli were found present in the blood, each field of the microscope never showed above two at any one time, and frequently only one solitary bacillus could be detected after closely scrutinizing the whole area of the prepared slide.

In the cat of Exp. XXII the slide of cardiac blood contained one bacillus of the variety already described at page 21 as being most abundant in the wound. The slide of portal blood also contained two of apparently the same kind as above. In cat of Exp. XXIII the portal blood was devoid of bacilli, but the slide of cardiac blood presented six, one of these being much larger and thicker than any of the other five. These latter were slender bacilli, similar to those already described as being present in the wound.

With such a large local collection of bacteria in the wound and its neighbourhood, it would only be a matter of time till a few of them found their way into the blood, so that their eventual presence in the blood is not specially remarkable.

That they are not specific or pathogenic bacilli is abundantly evident from the following considerations:—

1.—They were not found in the blood in all the fatal cases; therefore they are not essential to the toxic manifestations of abrus-seed.

2.—When actually found in the blood they were present in such infinitesimal numbers as to render it impossible that they could have been the cause of the animal's death.

3.—The bacilli which were found were of different forms in the different animals, and more than one form co-existed in the blood of same animal.

4.—The interval which elapsed between the time of injecting a large dose and the death of the animal was

(1) ZIEGLER'S *Pathological Anatomy*, Eng. Trans., Vol. I, p. 288, 1883.

altogether too short to admit of the possibility of death being due to bacterial invasion; and the same argument also holds good against the possibility of death by absorption of any poisonous product set free during the bacterial growth.

5.—If any further evidence be required to disprove the pathogenic character of these bacilli(1), it is had in the fact that *inoculation* with the blood containing these bacilli was in every instance unattended by any positive result. The inoculation experiments were as follows:—

A.—Inoculation with the Blood itself.

Exp. XXIV.—The blood from right auricle of a cat (Exp. XXII) which had just died of abrus-poisoning was inoculated into the inner aspect of right thigh of a healthy cat. A considerable pocket was made in the subcutaneous tissue, and about three large drops of blood inserted. No effect followed.

Exp. XXV.—At the same time as above experiment, and with the same blood, a healthy chicken was inoculated in the same matter. No result.

Exp. XXVI.—With the cardiac blood of cat used in Exp. XXI a healthy chicken was inoculated. No result.

Exp. XXVII.—Another chicken was at the same time inoculated with the portal blood of the same cat. No result.

B.—Inoculation with Pure Cultivations.

A cultivation was made of the cardiac blood of the cat used in Exp. XXIII. It gave after 48 hours several colonies of the two kinds of bacilli already described at page 25 as existing in the blood of that cat. The smaller variety existed in greatest numbers, and formed colonies with a sharply defined border. They were not chain-forming. The other larger variety was like the non-pathogenous bacillus which is found in soil. It liquefied the gelatine, and formed large filaments. A pure cultivation of each of these two forms was made.

Exp. XXVIII.—A large quantity of the pure cultivation of the smaller bacillus was inoculated into the leg of a chicken. No result.

Exp. XXIX.—A similar quantity was at the same time inoculated into the back of a house-mouse. No result.

Exp. XXX.—A large quantity was smeared over the eye of a cat. No result.

(1) Pathogenic for cats, fowls, and house-mice.

Exp. XXXI.—A portion of the pure cultivation of the larger bacillus was inoculated into a chicken. No result.

Exp. XXXII.—A portion of the same cultivation was freely applied to a cat's eye. No result.

CHAPTER VI.

The alleged Immunity against Further Attack which attends the injection of a single small dose is disproved. On the contrary, a preliminary small dose predisposes to fatal issue. CONCLUSION—That the local action and toxic manifestations are due neither to the presence of bacteria nor to the products resulting from their growth.

M. Cornil, in the zealous endeavour to explain the phenomena of abrus-poisoning as the workings of a specific infective disease, has crowned his observations with the statement that the subcutaneous injection of a small dose of the abrus-poison confers immunity from subsequent inoculations, in somewhat the same manner as the inoculation of the 'attenuated' virus of the infective diseases is alleged by Pasteur to secure the individual against further attack.

Amongst the specific infective fevers one attack usually exhausts the susceptibility of the patient to the disease. But when M. Cornil attributes even this property also to abrus-poisoning,—which is so obviously a condition brought about by a chemical poison, such a statement detracts still further from the reliability of his observations when it is found that not only is this alleged result incapable of demonstration, but that quite an opposite result follows under the circumstances indicated.

He reported that "the subcutaneous injection of small doses gives rise to the phenomena of local inflammation and gangrene, and confers immunity to that animal from subsequent inoculations." The following experiments disprove this statement:—

Exp. XXXIII.—The chicken used in Exp. XIII, which had received a subcutaneous dose of $\frac{1}{100}$th grain of seed, was given 20 days afterwards an additional $\frac{1}{2}$ grain subcutaneously. Death resulted in 16 hours.

Exp. XXXIV.—The chicken used in experiment, which had 18 days previously received $\frac{1}{100}$th grain of the seed, was given an additional $\frac{1}{2}$ grain. Death resulted in 15$\frac{1}{2}$ hours.

Expt. XXXV.—A chicken was given $\frac{1}{100}$th grain, and four days afterwards an extra $\frac{1}{2}$ grain of the seed. Death resulted in 14 hours.

These experiments indeed seem to indicate that a relatively small dose of abrus-poison, so far from protecting against a fatal dose, actually renders the animal more susceptible to the influence of poisonous doses. Abrus thus behaves like ordinary chemical poisons. It is well known that a certain amount of tolerance may be acquired with chemical poisons. When a poison like opium or nicotine is daily ingested in small doses, the quantity can after a time be so increased as to reach an amount that would be poisonous to a person who has not contracted the habit, or even to the same individual at a future time, should he after breaking off the habit at once proceed to take this poisonous dose. But the acquiring of this power of tolerance necessitates the daily ingestion of the poison for weeks and months; and even when acquired, it is a condition altogether different from the protection against further attack which one inoculation with the virus of a specific fever affords.

The chief facts established by the foregoing experiments are—

1. The absence of bacilli or their spores in the seeds. In one culture experiment, where an imperfectly sterilised seed was used, bacilli were found, but these proved to be non-pathogenous to cats, fowls, and mice—the animals used throughout these experiments.

2. Unsterilised abrus-seed infusion (and the infusion used by M.M. Cornil and Sattler was unsterilised) strongly favours the growth of bacteria, partly perhaps on account of its highly albuminous composition. But no special form of bacillus was found constantly in all the specimens; and all the bacilli and cocci found were innocent.

3. The local action of unsterilised infusion is usually accompanied by bacterial formation; but the bacteria found are of various kinds, and non-pathogenous. They enter the wound (1) in the injected fluid, or (2) from the syringe during the process of injection, or (3) afterwards, when the reduced vitality of the part allows the degenerated tissue to become invaded by bacteria from the air.

4. The intensity of the topical action of abrus-seed infusion, like that of other chemical irritants, depends upon the concentration and number of applications.

5. The toxic action of unsterilised abrus infusion is not necessarily associated with a generalised bacillar formation. The characteristic anatomical lesions are a profound alteration in the organized elements of the blood and the occurrence of generalised minute hæmorrhages into the substance of most of the highly vascular tissues and viscera. The hæmorrhages appear to occur by diapedesis without rupture of the capillary walls. These grave disturbances in the circulation, by lowering the resisting power of the tissues, favour the local development of any bacilli which may be carried to those remote parts with the circulating blood.

6. With large doses of the poison death quickly occurs, accompanied by all the characteristic lesions, but too rapidly to be attributable to bacterial invasion. And direct examination shows the complete absence of bacteria both in the blood and at the seat of the hæmorrhagic extravasations.

7. When bacilli are found in the blood, their presence is purely accidental; and they are non-pathogenous and non-specific.

8. The blood of an animal killed by abrus-poison is not infective.

9. Varying doses produce definite effects proportionate to the largeness of the dose, in the same manner as any other chemical poison.

10. From experiments afterwards to be detailed, it will be seen that a short exposure to a temperature of 60°C. is sufficient to destroy completely the activity of the poison; and this temperature is much too low to effect the destruction of bacteria.

11. M. Cornil's statement that, like the specific fevers, one small dose, when recovered from, confers immunity against further inoculation, is disproved. A preliminary dose, on the contrary, appears to precipitate the fatal result.

Each of these several points, taken individually, offers a sufficiently conclusive argument against the belief that the toxic effects of the abrus-seeds are due to bacilli; but when taken collectively, they present an array of adverse evidence which is altogether overwhelming.

It is difficult to conceive in what manner the distinguished authors of the bacterial theory of abrus-poison could have been so far misled in their observations as to seize upon phenomena which are purely accidental, and magnify them into the first importance as factors in the production of the poisoning symptoms in question.

PART II.

The Chemical Nature of Abrus-poison.

THE CHEMICAL NATURE OF ABRUS-POISON.

CHAPTER I.

Abrus seeds owe their activity to a chemical poison of a proteid nature. Manner in which this poison was detected. Form in which it exists in the seeds. Effect of heat in destroying the activity of this poison not due to coagulation. The physico-chemical properties and composition of the active principle—*abrin*. The place of abrin amongst the proteids. Abrin compared with vegetable albumins. The albumin of the Roots and Stems of *Abrus precatorius* is also poisonous.

FINDING that the poisonous properties of abrus-seeds are due neither to bacteria nor to decomposition products set free during bacterial growth, we then turned to chemistry, in the endeavour to isolate the poisonous principle, which from the preceding observations was evidently of a chemical nature.

We have already seen that the seeds contain no volatile or fixed alkaloid or glucoside, and that the crystalline acid—*abric acid*, is inert, so that we are forced to conclude that the active principle of abrus-seeds must belong to an altogether different category from that which includes ordinary vegetable poisons, and that unusual means must therefore be resorted to for its detection and isolation.

Whilst filtering the watery infusion of the seeds, we observed that an opalescent haze speedily formed in the clear filtrate on exposure for a few minutes to the air; and removing this hazy precipitate by re-filtration, a fresh precipitate, slightly less dense, formed again; and it was only after filtration and re-filtration through 12 to 14 filter-papers that a permanently clear filtrate was obtained. The original filtrate gave with picric and nitric acids a copious white, flaky precipitate, showing it to be loaded with albumin, while this permanently clear filtrate gave no definite precipitate with these reagents.

Here, then, was some substance of an albuminous nature which had been removed from the infusion by the repeated filtrations, and a question arose as to whether or not the resulting liquid still retained its toxic power undiminished. The three following experiments were made to elicit this point:—

Exp. XXXVI.—Ten minims of the fresh infusion, which had been passed through two folds of filter-paper, were injected into a chicken. Death resulted in 18 hours.

Exp. XXXVII.—Of the same infusion, after passing it through 14 folds of filter-paper, 15 minims were injected into a chicken. No apparent effect for four days. Then it refused food, pined, and died on the 7th day.

Exp. XXXVIII.—A similar experiment to the last was made at the same time on another chicken. Death occurred on the 10th day.

From these experiments it was therefore evident that the activity of the seeds was associated with this proteid material, which had been in great part removed by the repeated filtrations (1).

To isolate this proteid material so as to enable us to test directly its physiological action, we precipitated it by absolute alcohol from the clear filtrate obtained from a concentrated watery infusion. It fell as a fine white, flocculent precipitate, which, collected on a filter, became of a light slaty hue on exposure to air. About 1½ grains of this *moist* precipitate mixed with 15 minims of distilled water and injected into a chicken caused death in 20 hours. While a similar quantity, to which a few drops of sodic carbonate solution were added with the effect of thoroughly dissolving the precipitate, on injection into another chicken, caused death in 11 hours, with the characteristic *post-mortem* appearances of abrus-poisoning. The details of these two experiments are given below:—

Exp. XXXIX.—A freshly-prepared concentrated watery infusion was filtered through two folds of Swedish filter-paper, and the clear filtrate treated with absolute alcohol in excess. A copious fine, white, flaky precipitate immediately appeared, and was collected by filtration. The

(1) Schmidt showed that on filtering an albuminous liquid the filtrate contains less albumin, but no qualitative change occurs—*Poggendorf's Annalen* for 1865.

filtrate, which was clear and of a light straw colour, gave no precipitate with picric or nitric acids. Of the *moist* albuminous residue on the filter, about 3 grains were taken and mixed with 30 minims of distilled water, in which the albumin appeared to dissolve sparingly. Half this quantity of liquid, *i.e.*, 15 minims, were injected into a chicken. It died in 20 hours with all the congestive and minute hæmorrhagic extravasations characteristic of abrus-poisoning.

Exp. XL.—The remaining portion of the mixture of water and the alcoholic precipitate had 2 minims of concentrated sodic carbonate added to it. A clear solution was at once obtained, the liquid becoming of a faintly yellowish tinge. This on injection into a chicken caused death in 11 hours.

The *post-mortem* examination showed slight tendency to sub-serous extravasations over walls of stomach and bases of lungs towards their attachment to chest wall. The intestines were not very markedly injected.

The serum from the seat of wound showed a few bacilli of two different kinds, one variety being small, thick-set, with a length less than the diameter of the nucleus of a red blood-cell, and its breadth $\frac{1}{3}$ of its length, ends abruptly rounded off. The majority of these formed small chains of two and three. The other form was about $\frac{1}{2}$ the diameter of the nucleus of a red blood-corpuscle, with a slender body and square ends, not chain-forming.

This proteid body was therefore without doubt the active principle of the seeds, and it seemed to act with greater rapidity in proportion to the completeness of its solution at the time of administration.

Form in which it Exists in the Seeds.

It exists in the seeds in a form which is soluble in water, from which solution it is not precipitated by strong acids, by alkaline carbonates or by chloride of sodium. It thus behaves like a native animal albumin. It is, however, precipitated, like globulin, from its watery solution by a current of carbonic anhydride, but re-dissolves as the carbonic acid evaporates. The precipitate obtained in this way is readily soluble in distilled water. The hazy precipitate which forms in the infusion on exposure to air is apparently due to the carbonic acid contained in the air, for when the filtrate is collected *in vacuo* it remains permanently clear. The watery solution is highly acid on account of the abric acid present; but the proteid does not exist in the seed in the form

of an acid albuminate, for a large proportion of it is precipitated on boiling the infusion, and on neutralising its aqueous solution it is not thrown down.

Effect of Temperature on the Activity of the Poison.

The effect of temperature upon the activity of the poison is very marked. Boiling the watery infusion for an instant renders the poison permanently inert. And a short exposure of the watery infusion to a temperature of about 70°C. is sufficient to bring about permanent loss of its physiological properties. That a temperature of much less than 100°C. will destroy the activity of the poison was found out while evaporating some of the watery extract at a considerable distance above the water-bath, where the temperature ranged from 65° to 75°.

A temperature considerably below that necessary to coagulate albumin is sufficient to lower the activity of this poison. Thus, exposure for three or four days to so low a temperature as 32°C. was found to reduce in a very marked degree the activity of the alcoholic precipitate kept submerged in alcohol,—to prevent the development of bacteria; and, after exposure for two weeks, the precipitate had become completely inert. That the loss of activity is due to the heat, and not to coagulation of the proteid by the alcohol, seems evident from the fact that the precipitate, even after two weeks' contact with alcohol, was readily soluble in great part in distilled water with the aid of sodic carbonate and weak caustic soda solutions—reagents which do not destroy, but on the contrary increase, the activity of the fresh poison. The powdered seed also, on exposure to a similar temperature in the air, has its activity similarly reduced.

The following experiments also show that the effect of heat in destroying the activity of the watery infusion is not due to simple coagulation of the proteid, for it also occurs when coagulation is prevented by solution in an alkali or an acid. Thus, in the case of the sodic and acetic acid solutions no precipitation occurs even on boiling; but the activity of the poison is lost. And the precipitate obtained by heating the watery infusion from 70° to 100°C. may be re-dissolved by the aid of a small quantity of

sodic carbonate and caustic soda; but this solution when injected is inactive.

Exp. XLI.—Three grains of the powdered seeds were rubbed up with a small quantity of water and boiled for an instant. Half this quantity was injected into a chicken. No effect whatever.

Exp. XLII.—Two grains of the freshly-prepared moist alcoholic precipitate were dissolved in a small quantity of water, to which a few drops of sodic carbonate solution had been added. This solution was boiled for two minutes without any precipitate forming. The boiled liquid after being cooled was injected into a chicken. No effect.

Exp. XLIII.—The acetic acid solution of the alcoholic precipitate was boiled for two minutes and evaporated to the consistency of an extract. It was then dissolved in water and injected. No effect.

A further illustration of this point is had in the behaviour of the peptone formed by the action of pepsin on abrin. We shall afterwards see (Exp. LXVII) that the peptone thus formed possesses considerable activity. But on boiling for an instant it is rendered wholly inert, although no precipitation occurs.

The watery infusion kept at a temperature of 10°C. for several hours retained its activity undiminished.

Effect of Dry Heat.

Moisture plays a very important part in facilitating this decomposition, which occurs through heat.

Although the exposure of the watery infusion for an instant to a temperature of 100°C. suffices to destroy altogether the activity of the poison, the *dried* seeds may be exposed to a temperature of 100° for several hours without having their activity seriously deteriorated. But prolonged exposure to 100°, even in the absence of air and moisture, serves also to destroys the activity.

In the following experiments the seeds were reduced to a very fine powder and placed in Bohemian glass tubes, which were attached to a Sprengel pump and the air exhausted. These tubes, after their contents were thoroughly dried, were then sealed off *in situ* and put into a water-bath for the different periods as noted in the experiments, and the activity then tested by hypodermic injection.

Exp. XLIV.—About 15 grains of the finely-powdered seed was introduced into a piece of Bohemian glass tubing closed at one end. The

open extremity was attached to a Sprengel pump and retained for about 20 minutes after a complete vacuum had been made. It was then sealed off *in situ* and introduced into a water-bath at a temperature of 100°C. for *one* hour. The tube was then broken, the inrush of air testifying to the completeness of the vacuum. Half a grain of this crisp powder was rubbed up with a little water and injected hypodermically into a chicken. The animal manifested the usual signs of abrus-poisoning and died in 26 hours.

Exp. XLV.—One grain of the above dried powder was injected into another chicken. Death occurred in 20 hours.

Exp. XLVI.—Another quantity of the freshly-pounded seeds was dried *in vacuo* in a similar manner and then exposed to a temperature of 100°C. for *three hours*. Of this $\frac{1}{2}$ grain was injected in the usual way into a chicken, and death resulted in 30 hours.

Exp. XLVII.—$1\frac{1}{2}$ grains of the same dried and heated powder were injected into another chicken. Death occurred in 20 hours.

Exp. XLVIII.—Another quantity of the powder, dried *in vacuo* as before, was heated to a temperature of 100° for 80 hours. Its colour had become slightly darker, and it gave off a faint burnt smell. Of this $4\frac{1}{2}$ grains were injected into a healthy chicken. On the day following it was manifestly affected, refused food, and drooped. After three days it had improved considerably. In about eight days it had almost recovered, with the exception of extensive swelling of the injected leg, which rendered it lame for about three weeks.

Exp. XLIX.—Another quantity of the powder was simply sealed up hermetically, without having been dried and exhausted of air. This was subjected to the same degree of heat and for a similiar period of time (*viz.* 80 hours) as in last experiment. Its colour was then of a light coffee colour, and it gave off a strongly burnt smell. Of this 3 grains were injected into a chicken, and no effect whatever ensued.

This last experiment appears to show that the moisture contained within the seed is in itself sufficient to effect rapid decomposition.

In the preparation of "*suis*" (1) the poison is exposed to the direct rays of the tropical sun to dry. Lard or other greasy matter, however, is always previously mixed with the poison, and apparently tends to hinder this decomposition which occurs by heat. But "suis" are very much less active than the freshly-powdered seeds. One "sui" weighing 2 grains, on being rubbed up with water and injected into a chicken, does not usually

(1) *Vide* Appendix II.

produce a fatal result till after the lapse of about 36 hours; whilst ½ grain of the fresh seed produces death in about 18 hours (1).

The Mode of Extracting the Active Principle—Abrin.

Considerable difficulty was experienced in obtaining the active principle in a pure form, chiefly through its great susceptibility to heat and its association with abric acid and extractives, which cause the crude product to become of a dark, slaty hue on exposure to the air. Of the two following methods of extraction, the second is that which appeared to yield a product less contaminated with extractives.

The first method was as follows :—The seeds were reduced to a coarse powder by pounding in an iron mortar, the testæ being removed to a considerable extent by winnowing. The powder was packed in a percolator plugged with cotton wool and a layer of sand, and percolated with cold distilled water, the process being hastened by connecting the receiver to an exhausting pump. The first portions of the percolate were turbid, but after exhaustion the liquid that passed through was bright. The dark sherry-coloured and strongly acid percolate was now mixed with a large excess of 60 per cent. alcohol, and the precipitate allowed to settle. The supernatant liquid was then siphoned off, and the precipitate collected on a paper-filter. After exposure to air for a few hours to vaporise the alcohol, the precipitate was scraped off the filter and mixed with cold distilled water, the resulting mixture being of a slate-grey colour and very turbid. Alcohol was again added, the precipitate allowed to settle, collected on a filter, and again treated with water and alcohol. The principle obtained by this process while moist was of a dark-slate colour which rapidly deepened on exposure to air. It was

(1) The effect of heat in destroying the inflammation-exciting power of the seeds was determined as follows by M. Salomonsen (*vide* footnote, p. 7). He exposed small quantities of the watery infusion in sealed tubes to temperatures varying from 60° to 100°C. in a water bath from ½ an hour to 1 hour, and then tested their inflammation-exciting power after rapid cooling. After ¾ hour's exposure to 64° their activity was considerably weakened, although not completely annulled. A freshly-prepared, very active infusion was warmed at 65° for one hour, and when afterwards dropped into the eye produced an evanescent hyperæmia without any swelling or pus-formation. Exposure to 70° for one hour completely destroyed this power.

dried under the receiver of an air-pump with sulphuric acid, powdered and percolated with chloroform (1), which removed some fatty matter and traces of abric acid; the chloroform being succeeded by absolute alcohol, which dissolved traces of extractive. The principle thus purified was when pulverised of a dark fawn colour and somewhat hygroscopic.

The second method of separation was conducted as follows:— The pulverised seeds were first percolated with chloroform, which removed fatty matter, some abric acid, and a yellow colouring principle. The powder was then exposed to air to evaporate the chloroform, and re-percolated with 40 per cent. alcohol (to remove extractives, until the percolate was nearly colourless. The powder was again exposed to air, and, when free from alcohol, percolated with cold distilled water. The resulting percolate had only a slight yellow tinge, and was very faintly acid in reaction. The active principle was obtained from this percolate by precipitation with alcohol, and purified by repeated precipitation and solution in water, as already described, and subsequently dried over sulphuric acid. The precipitate, whilst contained in the liquid from which it had been precipitated, is perfectly white, but on exposure to air it becomes, whilst drying, of a very light slate colour.

To this proteid so obtained we have applied the name *abrin* It is much more active than an equal weight of the powdered seed, as will be seen from the experiments which are detailed further on.

The Physical Properties of Abrin.

When obtained in this purified form, abrin is an amorphous solid of a pale grey colour, and tasteless. In thin layers, it is of a gummy translucent appearance and yellowish colour, like dried white of egg. Cold water readily dissolves it, with the exception of a few flocks, and the solution, which is of a faintly yellow colour, froths on agitation. In glycerine it is also soluble. And it is precipitated from its aqueous and glycerine solutions by alcohol in white, curdy flakes, which become of a light slaty hue on exposure to air.

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(1) Chloroform was used as being a better solvent of abric acid than ether, as noted in Appendix III.

On boiling the watery solution of abrin it becomes opalescent, and a whitish flocculent deposit falls, and the supernatant fluid becomes of a light brown colour. This precipitate collected by filtration is partly soluble in caustic soda, from which solution on neutralization it is precipitated by picric and nitric acids and alcohol, and the alcoholic precipitate is sparingly soluble in distilled water. The filtrate, which is of a light amber colour and of acid reaction, gives a slight cloudiness with distilled water; and weak solutions of acetic acid throw down a flocky precipitate, which dissolves in excess of the acid. A copious white precipitate is thrown down by tannin, alcohol, and ether; and the alkaline carbonates give a slight precipitate. On neutralizing this amber-coloured filtrate no precipitate is thrown down, showing that the proteid is not an acid albuminate.

With a dry heat, as has been already seen, decomposition takes place much more slowly.

Its Chemical Reactions.

The concentrated aqueous solution of abrin has a decidedly acid reaction. It gives the following reactions. *Absolute alcohol* readily precipitates abrin from its aqueous or glycerine solutions. If the solution is a dilute one, a very large excess of alcohol requires to be added to effect precipitation, as abrin is slightly soluble in dilute alcohol.

Ether agitated with a watery solution of abrin throws down no precipitate but the addition of ether or chloroform appears to hasten the subsidence of a precipitate with alcohol.

Very dilute *hydrochloric* or *nitric acid* produces a precipitate which is extremely soluble in excess of the acid.

Glacial phosphoric acid and metaphosphate of soda give a white precipitate which is soluble in large excess.

Dilute *acetic acid* gives a white precipitate soluble in large excess of acid.

Tannic acid gives a copious white curdy precipitate.

Basic acetate of lead, *mercuric chloride*, and *silver nitrate*, give a white precipitate insoluble in excess.

Potasssium ferrocyanide and *perchloride of iron* do not precipitate abrin from its watery solutions.

Millon's reagent gives the usual purple-red proteid reaction.

Strong *caustic potash* gives rise to no precipitate. On boiling this solution ammonia is evolved, and the liquid becomes of a somewhat darker hue (1).

The Ultimate Composition of Abrin.

The abrin which was obtained by the first described method, after having been dried over sulphuric acid for 48 hours yielded the following results on combustion with cupric oxide and oxygen in an open tube, the usual precautions being adopted for nitrogenous compounds:—

(I) ·1790 gram. gave ·2868 CO_2 and ·1258 gram. H_2O.
(II) ·2142 „ „ ·3442 „ „ ·1508 „ „

These results expressed in parts per 100 give—

	(I)	(II)
Carbon	43·5754	43·8235
Hydrogen	7·7652	7·7964

Two nitrogen determinations by the soda-lime process, the bulbs being filled with dilute hydrochloric acid, and the ammonium chloride converted into the double platinum-ammonium salt, yielded on ignition of the double salt the following amounts of spongy platinum:—

(I) 1·3492 gram. abrin gave ·9640 gram. spongy platinum,
(II) ·7684 „ „ „ ·5622 „ „ „

which is equivalent to—

(I) 10·2801 per cent. Nitrogen.
(II) 10·5283 „ „ „

Two ash determinations gave the following percentages:—

(I) 9·1620 per cent. of ash.
(II) 9·3370 „ „ „ „

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(1) Salomonsen (*vide* foot-note p. 7) also being led to conclude that the local action of the seeds on the conjuctiva was not due to bacteria, endeavoured to isolate the poison by chemical means, and adopted the ordinary method for extracting a proteid—somewhat similar to that made use of by us; and he found that the dried alcoholic precipitate was "soluble in water or glycerine, and a few drops of this watery or glycerine solution brought into the conjunctival sac of a rabbit calls forth an inflammation with all the clinical and anatomical characters of abrus-ophthalmia."

One sulphur determination, with fusion mixture of 1·3550 gram. abrin dried at 140°C., yielded ·0376 grams Ba SO_4, equivalent to ·3763 per cent. sulphur.

The ultimate percentage composition of abrin prepared by the first method may therefore be stated as follows:—

	(I)	(II)	Mean.
C.	43·5754	43·8235	43·6994
H.	7·7652	7·7964	7·7808
N.	10·2801	10·5283	10·4024
O.	28·8599	28·1574	28·5105
S.	·3574	.....	·3574
Ash ...	9·1620	9·3370	9·2495
	100·0000	99·6426	100·0000

On drying abrin in the hot-air bath at 140°C. it lost 5·2540 per cent H_2O. Deducting ash and water, the mean percentage would be as follows:—

C.	50·8241
H.	8·0422
N.	12·0878
O.	28·6313
S.	·4146
	100·0000

The abrin prepared by the second method was first dried over sulphuric acid and then in a hot-air bath at 140°C. On combustion with oxide of copper the following results were obtained:—

(I) ·1862 gram. gave ·2872 CO_2 and ·1174 gram. H_2O.
(II) ·1751 „ „ ·2687 „ „ ·1105 „ „

These results give the following percentages:—

	(I)	(II)
C.	42·3300	41·3503
H.	7·0032	6·9674

One nitrogen determination with soda-lime gave—

·5458 gram. abrin gave ·3276 gram. spongy platinum,

which is equivalent to—

8·6502 per cent of Nitrogen.

Two ash determinations gave—

(I) 11·9359 per cent of ash.
(II) 12·2449 „ „

The ultimate percentage composition of abrin prepared by the second method may therefore be stated as follows:—

	(I)	(II)	Mean.
C.	42·3300	41·8503	42·0901
H.	6·9674	7·0032	6·9853
N.	8·6502	.....	8·6502
O. and S.	29·8075	.....	30·1840
Ash	12·2449	11·9359	12·0904
	100·0000	.....	100·0000

Deducting ash, the mean percentage composition would be as follows:—

C.	47·8674
H.	7·9460
N.	9·8273
O. and S.	34·3593
	100·0000

The ash was found to contain a large amount of phosphoric acid. It was very faintly alkaline in reaction, and contained a decided trace of iron.

The Place of Abrin amongst the Proteids.

The classification of vegetable proteids at present in use is that of Liebig (1). He distinguishes:—

1. As *plant-albumin* the proteid held in solution in aqueous plant juices or extracts, which is not precipitated by acetic acid, but which coagulates when heated.
2. As *plant-fibrin* the constituent of seeds which is insoluble in water and aqueous ammonia.
3. As *plant-casein* the constituent which dissolves in cold water and is not precipitated from its aqueous solution by heat, but is precipitated by acetic acid.
4. The last class is *plant-gelatin*, which is generally similar to animal-gelatin.

According to this classification abrin cannot belong to either the 2nd or 4th category, and its being precipitable by acetic acid prevents its being regarded as "plant-albumin," whilst its being precipitated from its aqueous solution on boiling prevents its being

(1) On the Nitrogenous Food-stuffs of the Vegetable Kingdom.—*Ann. Pharm.*, *XXXIX*, 129.

classed as plant-casein. So that abrin is altogether excluded from a place in this unduly restricted classification. If, instead of "not precipitated by acetic acid," we read "soluble in excess of acetic acid," then abrin would obtain a place amongst the "plant-albumins," to which class it seems naturally to belong.

Abrin cannot certainly be considered as being a form of plant-casein, for casein, which is now believed to be identical with alkali-albuminates (1), is not precipitated from its aqueous solutions on boiling, and is insoluble in distilled water. Abrin has the properties, not of a *derived-albumin*, but of a *native-albumin* (animal) such as that described by Foster (2), being "soluble in water and not precipitated by very dilute acids, by carbonates of the alkalis, or by sodium chloride, coagulated by heating in solution to a temperature of about 70°C. If dried at 40°C., the resulting mass is of a pale yellow colour, easily friable, tasteless, inodorous, and soluble."

The typical native albumin is egg-albumin. In the following table is given the percentage composition of egg-albumin, together with that of pea-albumin, and a few other vegetable albumins for comparison with the percentage composition of abrin, which is also appended :—

Table showing Percentage Composition of certain Vegetable-albumins with Egg-albumin and Abrin.

	C.	H.	N.	O.	S.	Ash.
Egg-albumin (3)	53·98	7·51	14·24	22·34	1·93	2·3
Pea-albumin (4)	52·45	6·81	...	.....	0·80	0·89
Gourd-seed vitellin (5)	51·36	7·58	17·86	22·66	0·54	1·12
Para-nut vitellin (6)	52·43	7·12	18·10	21·80	0·55	.....
Wheat albumin (7)	53·74	7·11	15·65	23·46	1·04	8·5
Rye ,, (8)	53·71	7·77	15·85	22·67	0·77	.....
Almond ,, (9)	55·96	7·53	13·75	22·76	.....	.....
Potato ,, (10)	53·81	7·32	.....	.....	0·98	1·4
Abrin	50·82	8·04	12·08	28·63	0·41	Deducted.

(1) FOSTER'S *Physiology*, p. 708, 4th edn.
(2) *Ibid.*, p. 702.
(3) THEILE, *Kopp's Jahresb.*, 1867, 774.
(4) RÜLING. *Ann. Pharm.*, 58., 306.
(5) J. BARBIERI, *Jour. Prakt. Chem.* [2] 18., 102-16.
(6) WEYL, *Pfluger's Archiv.* Bd. 12.
(7) DUMAS & CAHOURS, *N. Ann. Chim. Phys.* 6, 409.
(8) JONES, *Ann. Pharm.*, 40, 66.
(9) GMELIN, *Handbk. Org. Chem.*, Vol. XII, p. 427.
(10) RÜLING, *loc cit.*

It will be seen that the composition of abrin approximates somewhat closely to that of egg-albumin and the vegetable albumins. It is to be noted that in the foregoing tabulated analysis of these latter the albumin was obtained by coagulation of the cold aqueous extract by boiling.

The best proof that abrin is nothing more nor less than the albumin of *Abrus precatorius* is had in the fact that the albumin of the roots and stems of that plant is possessed of the identical poisonous properties which characterize the albumin of the seeds.

The Albumin of the Roots and Stems of Abrus Precatorius is also poisonous.

The roots and stems of *Abrus precatorius* contain the same active principle—abrin which exists in the seeds.

The fresh roots and stems, gathered in the month of February were reduced to a coarse powder, and a concentrated, cold, watery infusion made after the same manner as when operating with the seeds. This infusion on being filtered was of a pale straw colour and slightly acid reaction. It yielded with nitric and picric acids in the cold a fairly copious white precipitate, and also on boiling. With alcohol a white precipitate was thrown down, which was slightly soluble in distilled water, and more readily in caustic soda or sodic carbonate. Both the infusion and the alcoholic precipitate on injection subcutaneously produced death with the usual appearances of abrus-poisoning. The infusion also, when applied to the ocular conjunctiva of a rabbit, induced acute abrus-ophthalmia, going on to partial sloughing of the cornea.

Exp. L.—Of the concentrated infusion of pounded abrus root and stems, 25 minims were subcutaneously injected into a chicken. Death occurred in 50 hours with the usual symptoms and *post-mortem* appearances of abrus-poisoning.

Exp. LI.—Two grains of the moist alcoholic precipitate dissolved in 20 minims of water and injected hypodermically produced death in 18 hours.

Exp. LII.—A small quantity of the filtered watery infusion applied to the eye of a rabbit produced on the following day intensely acute inflammation of conjunctiva, with hæmorrhagic extravasations and iritis, and ultimately the formation of a large corneal ulcer.

The following experiments show that the active principle—abrin is more abundant in the rind than in the duramen of the stems and roots :—

Exp. LIII.—¼ oz. of the mixed rind of the roots and stem was reduced to a coarse powder and mixed with water and macerated with occasional trituration in a mortar for three hours. The resulting infusion was filtered, and of the clear filtrate 30 minims were injected subcutaneously into a chicken. Death occurred in 17 hours.

Exp. LIV.—A similar quantity of the clear filtrate was injected into another chicken. Death occurred in 18½.

Exp. LV.—¼ oz. of the mixed heart-wood of the roots and stems was cut into small, thin slices and pounded in a mortar, then macerated with occasional trituration for three hours and filtered. Of this clear filtrate 30 minims were injected into a chicken. Death occurred in 43 hours, with the usual appearances of abrus-poisoning.

Exp. LVI.—The foregoing experiment was repeated on another chicken, and death took place in 47 hours.

This discovery that the roots and stems contain large quantities of the deadly principle—abrin, is of very great practical importance, and should serve to banish from the Indian Pharmacopœia the roots of this plant, which are recommended as a substitute for those of *Glycyrrhiza glabra*, as a demulcent. And the dangerous practice, so common amongst the natives of this country, of chewing the roots of this plant for the sake of the faintly sweetish principle (1) contained therein, is to be seriously discountenanced, for should any excoriations exist in the person's mouth there is nothing to prevent the poison from being absorbed into the system with fatal results.

This remarkable property of being harmful only when introduced directly into the circulation is very suggestive of the possibility of morbid states being occasionally produced autogenetically by the absorption of certain animal excretions and secretions which are harmless only so long as they pass off by the healthy and unbroken alimentary or other mucous tract.

In Appendix VI are given the chief points of contrast between the roots of *Abrus precatorius* and those of *Glycyrrhiza*

(1) Isolated by Berzelius in 1827, and apparently similar to the sweet principle contained in true liquorice-root.

glabra so as to facilitate the detection of cases of false substitution of the former root for the latter. The differences between these two roots can be readily and certainly determined by microscopical examination.

CHAPTER II.

The Mode of Action of Abrin. The probability of its being a Ferment considered—its chemical constitution is somewhat similar to vegetable "enzymes," but it is incapable of rendering poisonous the bland leguminous matter of the common pea. It has no amylolytic power or peptonising action on egg-albumin. Alleged toxic action of digestive ferments when administered subcutaneously. Papayatin contrasted with abrin, and found to have no similarity. Effects of ptyalin and pepsin when administered hypodermically. Destructibility of active properties by heat not peculiar to ferments. The relatively slow onset of symptoms, even after what ought to be overwhelming doses, not apparently due to leavening action, but to abrin being a colloid and slow of absorption. Undesirability of terming abrin a "ferment." Abrin compared with Snake-poison. Action of Pepsin upon abrin.

In seeking to ascertain the manner in which this active principle—abrin, exercises its toxic action on the animal economy, we are at once led to consider whether or not it may behave as a chemical ferment. Its proteid nature, as well as the destruction of its toxic power by exposure of its aqueous solution for an instant to a temperature of 100°C.; the considerable interval which elapses between the administration of what ought to be an overwhelming dose and the development of symptoms; its harmlessness when given by the mouth or injected *per rectum*, all suggest the probability of its acting in this way.

The term *ferment* has hitherto been applied to "two groups of agents, which, although nearly allied in origin and mode of action, nevertheless belong to essentially different categories. The *organised* or *formed ferments* of which yeast is the type are independent organisms, with powers of growth and reproduction, and the transformations which constitute their special characteristics as ferments are inseparably associated with the nutritive operations of these organisms. The ferment power cannot be separated from the ferment organism by any method or by any solvent. The *soluble ferments*, on the other hand, pass freely into

solution in water; their action is dissociated from the life of the gland-cells which produced them, and they are wholly devoid of the power of growth and reproduction. Kühne designates these soluble ferments *enzymes* (1)." Examples of chemical or soluble ferments are emulsin, papayatin, diastase of malt, myrosin, ptyalin, trypsin, &c.

It is to this latter class—the so-called "enzymes" (ἐν, in, and ζύμη, ferment)—that abrin would belong if it proved to be a ferment. The mode of extracting chemical ferments from vegetables is identical with that which we have employed for the isolation of abrin. But it is a similar process also which serves to extract albumin from seeds or other vegetable tissues:—emulsin may, in fact, be called sweet-almond albumin; papayatin, papaya albumin; diastase, wheat or barley albumin; and abrin, abrus albumin; and so on.

The chemical composition of the known vegetable enzymes has not yet been completely worked out. In the following table the published composition of three of these ferments—the only ones which appear to have been analysed—is contrasted with that of abrin:—

Table showing the Percentage Composition of Vegetable Enzymes as compared with that of Abrin.

	C.	N.	O.	H.	S.	Ash deducted.	Remarks.
Emulsin, or Synaptase (2).	43·59	11·64	36·56	6·96	1·25	22·0	
Diastase (3) ...	48·63	4·8	39·16	7·34	A trace.	7·34	
Papayatin (4) ...	46	14	.....	... ..	2·2	4	Composition varied according to whether got from tree-sap or fruit.
Abrin by first method.	50·82	12·08	28·63	8·04	·41	9·24	Dried at 140°.
Abrin by second method.	47·86	9·82	34·35	7·94	.....	12·09	Ditto

But the term "ferment" implies the possession of a special set of qualities—ferments being "substances which possess the property of exciting chemical changes in matters with which they

(1) W. Roberts, *Proc. Roy. Soc.*, 32, p 145.
(2) Bull, *Ann. Ch. Pharmac.*, LXIX, 145.
(3) C. Kranch, *Bied. Centr.*, 1879, p. 122.
(4) A. Wurtz, *Compt. Rendus*, 90, 1379 (1881).

come into contact" (1). And in the exercise of this action, the ferment itself appears to be undestroyed, it being "asserted that in the fermentive process excited by soluble ferments, the amount of ferment at the end of the process is the same as at the beginning" (2).

To ascertain whether or not abrin might possibly consist of ordinary pea-albumin *plus* some soluble ferment which so reacted upon pea-albumin as to render it poisonous, the following experiments were undertaken. First of all the bland leguminous matter of the common pea (*pisum*) was injected without any poisoning symptoms developing :—

Exp. LVII.—The solid matter of one pea deprived of its cuticle was, rubbed up with 20 minims distilled water and injected hypodermically into thigh of chicken. No effect.

Exp. LVIII.—The above experiment was repeated on another chicken with no effect.

Then a very small quantity of a weak infusion of abrus-seed was rubbed up with the bland leguminous matter of the common pea, and injected, but death did not occur sooner under these circumstances than in the control experiments, where a similar quantity of the weak abrus infusion had been given by itself, as the following experiments show :—

Exp. LIX.—One-eighth grain of abrus-seed was rubbed up with about 20 minims of distilled water and injected into a chicken. Death occurred after 6 days.

Exp. LX.—The foregoing experiment was repeated in another chicken. Death occurred in 5½ days.

Exp. LXI.—With an ⅛th of a grain of abrus-seed, 1½ grains of bland pea-albumin were rubbed up along with 20 minims of distilled water and injected. Death took place in 6 days.

Exp. LXII.—The foregoing experiment was repeated on another chicken. Death occurred in 7 days.

The most common property of ferments is the power of decomposing proteids or starch. Direct experiment showed that abrin possesses no amylolytic power, or peptonising action on egg-albumin.

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(1) McKendrick's *Physiology*, p. 49.
(2) *Ibid.*, p. 54.

It has been asserted that certain ferments, although harmless when taken by the mouth, become fatally active when injected subcutaneously. Thus Rossbach is reported (1) to state that after the intravenous injection of a solution of papayatin the blood contains in a few hours enormous quantities of micrococci and biscuit-shaped bacteria in lively movement, and death speedily results with all the symptoms of septicæmia. This property attributed to papayatin rendered a comparison of papayatin with abrin highly desirable.

Papayatin contrasted with Abrin.

Papayatin is a ferment obtained from the juice of the fruit and trunk of *Carica papaya*, an exceedingly common fruit-tree in India, by precipitation with alcohol. It presents all the characters of a strong digestive ferment, resembling pepsin and that secreted by carnivorous plants. Placed in contact with *moist* fibrin in slightly acid, neutral, or slightly alkaline solutions, it dissolves large quantities of that substance—the fibrin, first softening, then disintegrating without swelling, and, becoming dissolved, leaves a residue of dys-peptone (2). Indian cooks are aware of this property of papaya juice, and use it for rendering tough meat tender.

The following experiments were made with the fresh papaya juice.

Exp. LXIII.—An eighth of an ounce of the fresh juice was mixed with an equal quantity of water, well rubbed up in a mortar and filtered. The clear filtrate gave a copious precipitate with alcohol and nitric and picric acids. Of this clear filtrate 20 minims were injected hypodermically into the thigh of a chicken. No result whatever.

Exp. LXIV.—A similar amount was injected subcutaneously into another chicken. No result.

Exp. LXV.—A large amount of the fresh juice was freely smeared over the ocular conjunctiva of a rabbit. No result.

From the above experiments we must conclude that, however true Rossbach's statement may be as regards intravenous injection, the *subcutaneous* injection of tolerably large quantities is unattended by toxic results.

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(1) *Lancet*, Vol. I, 1882, p. 280.

(2) Wurtz and Bouchet, *Compt. rendus*, 89, p. 425 (1879).

SALIVA is asserted by M.M. Pasteur and Vulpian to possess toxic power when injected under the skin. M. Griffini has lately repeated their experiments, and finds that ordinary mixed saliva, when filtered through porous plates, so as to exclude bacteria, and injected beneath the skin of rabbits, does not produce any local gangrenous changes, but a general infection of the blood, resembling in all essential respects septicæmia. The unfiltered saliva produces gangrene of the part where injected(1). But, as he found pure parotid saliva was innocuous, it would appear likely that the toxic properties of mixed saliva were due to some poison generated during the growth of the non-specific bacteria which infest the saliva once it has entered the buccal cavity.

The subcutaneous injection of small quantities of *PEPSIN* also seems (Exp. LXIX) to be unattended by any marked constitutional effects, so that it cannot be regarded as a property of soluble ferments that they necessarily produce poisoning symptoms when introduced hypodermically.

Destructibility of the active properties by exposure to a temperature of 100°C. is a quality common to almost all forms of albuminous matter possessed of special properties, and does not necessarily imply that the substance is a ferment.

The relatively slow onset of the symptoms even after the subcutaneous injection of what ought to be an overwhelming dose is not apparently the result of any fermentative change or leavening action, but seems due to the fact that abrin is a colloid body and not readily absorbed. It has been already seen (Exp. XL) that when the proteid is rendered more soluble by the addition of sodic carbonate or caustic soda, death occurs more rapidly. And in intravenous injection, where the poison gains speedy access to the circulation, death occurs with much greater rapidity than under any other conditions.

Exp. LXVI.—Two grains of the moist alcoholic precipitate were dissolved in about 20 minims distilled water, and the solution which was faintly acid neutralised with sodic carbonate solution. A small quantity of one per cent. solution of common salt was added, and the whole injected into the pectoral vein of a chicken. Death took place in 10 hours.

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(1) *Archiv. per le Scienze Mediche.* t. v. 1882.

We thus find no direct proof that abrin possesses any of the properties which specially characterize the soluble ferments—papayatin, ptyalin, and pepsin; and as the use of the term 'ferment,' when applied to an unorganized poison, such as abrin, is calculated to convey an altogether erroneous impression as to its true nature, it seems highly undesirable to make use of this term with regard to abrin. We therefore prefer to designate abrin simply as *a chemical poison of a proteid nature.*

Abrin compared with Snake-poison.

Abrin bears in many ways a strong analogy to snake-poison. Like snake-poison, it may be taken by the mouth with impunity; it is only when introduced into the subcutaneous tissues, or directly into the circulation, that toxic symptoms develop. Heat lessens the activity of both poisons, but affects abrin much more powerfully. The toxic symptoms of these two poisons also exhibit a certain amount of similarity—general depression, drowsiness, fall of temperature, and hæmorrhagic lesions being more or less common to both. The marked differences, especially the convulsive phenomena, can be accounted for by the more complex constitution of snake-virus.

Snake-venom appears to consist of a mixture of several toxic agents. Dr. S. Weir Mitchell has published in the *Lancet* (1) the results of his latest observations, which show that "snake-poison can be separated out by dialysis into at least three proteid constituents: *one*, dialysable and resembling a peptone—'venom-peptone,' and apparently a hastener of putrefactive change, and a convulsive agent, but with little power to prevent coagulation of the blood, and varying greatly in power in different snakes. A *second*—'venom-globulin,' a more deadly poison, acting powerfully on the blood and capillaries, so as to cause enormous local hæmorrhages at the point where the poison is injected. It was destroyed at 100°C. in all the venoms studied. The *third* proteid, 'venom-albumin,' resembles serum albumin. It is also an active poison resembling globulin in its mode of action." His observations make it probable that "the differences between the most distant genera of thanatophidiæ will be found rather in the

(1) Vol. II, 1883, p. 94.

relative amount and energy of these various elements than in any distinct qualitative peculiarities."

But in addition to these three proteids, snake-poison contains a crystallizable and very active non-albuminous constituent. Blyth(1) found that after the proteids had been removed by precipitation with alcohol and filtration, the resulting alcoholic extract yielded crystals having a markedly acid reaction and toxic properties. To this substance he applied the name *cobric acid* provisionally. Mr. A. Pedler also states (2) that he found the alcoholic extract very active. Alcohol precipitated about 60 per cent. of albuminous matter from the fresh poison, and the remaining 40 per cent. was soluble in alcohol. The alcoholic extract was 50 to 100 times more active than the albuminous precipitate (3).

The very great rapidity with which snake-poison acts, and which so strongly contrasts with the slower action of abrin, would thus appear to be due to the fact that one of its constituents is crystalline and readily absorbed. And amongst its proteid constituents venom-peptone would also be readily dialysable, and so would rapidly induce poisoning symptoms.

Putting aside, then, from the phenomena of snake-poisoning those sudden effects which may be reasonably attributed to this crystalline principle and to the readily dialysable peptone, we have left two proteid constituents which are more or less comparable to abrin as regards their rate of absorption. And it is doubtless to one or other of these two latter constituents that snake-poison owes whatever resemblance it bears to abrus-poison.

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(1) *Analyst* for 28th February 1877.

(2) *Trans. Roy. Soc.*, p. 19, 1878.

(3) Dr. Weir Mitchell, the latest exponent of snake-poison, is apparently unaware of this fact, that at least one variety of snake-poison, viz., cobra venom, has been shown to contain an intensely active crystalline principle which is not of an albuminous nature. When this fact is recognized, it will be evident that the method adopted by Weir Mitchell is insufficient to remove all this poison from the dialyser, so that his 'venom-globulin' and albumin as well as the 'venom-peptone' must have been contaminated with this poison. The first thing to do is to separate out this active non-albuminous constituent; and as it is said to be crystalline, there ought to be comparatively little difficulty in isolating it and testing its physiological action. The proteids which are left might then be obtained in a more or less pure state by dialysis or otherwise, and their individual properties tested. We are undertaking an analysis of cobra-poison on the lines just now indicated, and will publish the results in due course.

Of these two constituents of snake-poison, viz., 'venom globulin' and 'venom-albumin,' abrin is physically more nearly allied to 'venom-albumin;' for we have already seen that abrin does not exhibit the characteristic properties of animal globulin, with the exception that it is precipitated by carbonic anhydride. But Weir Mitchell asserts that 'venom-albumin' possesses toxic properties generally similar to those of 'venom-globulin.'

Like abrin, 'venom-globulin' (and therefore also 'venom-albumin') is said to exert a special action on the blood. "One-twentieth of a grain kills a strong pigeon in a little over two hours, and gives rise within a few minutes (1) after injection to the production of enormous infiltration of blood into the neighbouring tissues." It is also reported to destroy the power of blood to clot, and is believed to attack the respiratory centres. The hæmorrhagic lesions appear to be most pronounced in cases where the animal survives for a time, *i. e.*, to say in cases where the quantity of the crystalline principle and peptone are evidently in such small amount as to allow of the animal surviving till the effects of the globulin are developed. The blood changes are most marked in cases of viper-poisoning. The *post-mortem* appearances in viper-poisoning as recorded by Dr. Badaloni (2) are strikingly similar to those of poisoning by abrin. He notes intense hyperæmia of the mucous membrane of the stomach and intestines, with numerous hæmorrhagic points of extravasation, especially into mucous membrane of small intestine. The blood was dark and fluid, and slow to coagulate.

It would thus appear that there is a considerable analogy between abrin and snake-poison.

Action of Pepsin on Abrin.

As bearing on the comparative harmlessness of abrin when taken by the mouth, it is interesting to note the results of the following experiments, in which abrin was digested with pepsin outside the body, and the resulting product, apparently a peptone,

(1) Globulin is readily soluble in neutral solutions, so that 'venom-globulin' should be readily absorbed when injected subcutaneously. But it has been already shown that this so-called 'venom-globulin' is in all probability a mixture of two distinct substances.

(2) *Lancet*, I, 1883, p. 768.

then injected into chickens. The pepsin used in these experiments was found to be fairly well up to the British Pharmacopœia standard of activity, where two grains of pepsin are stated to dissolve 100 grains of coagulated egg-albumin.

Exp. LXVII.—Six grains of the freshly-prepared moist abrin from which the alcohol had been entirely driven off were dissolved in about ¼ oz. of distilled water. To this were added three grains of pepsin with 6 minims of dilute hydrochloric acid, and the whole digested for six hours at a temperature of 38° Cent. This solution was then filtered, the filtrate being a clear, limpid, and almost colourless fluid, which gave a scanty white precipitate with absolute alcohol, and on boiling deposited no precipitate, showing that the proteid had apparently become converted into a peptone. Of this peptone solution 25 minims, representing about 1½ grains of moist abrin, were injected into a healthy chicken. The chicken presented no symptoms till the following day. It died 53 hours from the time of administration of the injection with all the usual symptoms of abrus-poisoning.

Exp. LXVIII.—The previous experiment was repeated on another chicken, which died 60 hours after the administration of the injection.

As the abrin-peptone proved fatal in both these experiments, it became necessary to ascertain what the effect of a hypodermic injection of pepsin by itself might be. In the following experiment twice the amount of pepsin which had been used in the two foregoing experiments was injected subcutaneously into a chicken without any positive result.

Exp. LXIX.—Three grains of pepsin dissolved in 25 minims of distilled water to which three minims of dilute hydrochloric acid had been added were injected into a chicken. No result.

From these experiments it would appear that the peptone of abrus-albumin is poisonous, although very much less active than abrin itself. It becomes therefore difficult to reconcile these results with the acknowledged innocuousness of the seeds when taken by the mouth. For on introduction into the stomach a peptone will be formed, and this readily becoming absorbed ought to prove poisonous according to the foregoing experiments. But it is just possible that in these experiments a true peptone was not really formed, as the albumin was not presented to the action of the pepsine in a coagulated form—the failure of the resulting filtrate to give a precipitate on boiling being probably due to the conversion of the abrin into an acid albuminate by the action of the hydrochloric acid. And the acid albuminate of abrin, as we have seen, is poisonous.

The intestinal juices appear to have the property of rendering the poison inert, for a large quantity of abrin may be given *per rectum* with no other effect than the production of acute colitis.

CHAPTER III.

The Physiological Effcts of Abrin.

The following account of the action of abrus-poison on several of the systems and tissues of the animal body is somewhat fragmentary, but such as it is, it affords considerable insight into the manner in which this poison exerts its action. We propose continuing this series of observations, and hope in a future paper to give a more detailed account of the physiological action of abrus-poison.

I.—Action on the Blood.

The alterations in the blood produced by abrin have already been noted in some detail. The most striking changes are slightly undue fluidity, with the presence of enormous numbers of the so-called "blood-plates" and of those larger, dark, granular masses which are usually believed to be the broken-up nuclei of white corpuscles.

This alteration in the constitution of the blood allows of passive hæmorrhages by diapedesis, without apparent rupture of the vessel wall. These minute hæmorrhagic lesions are found most abundant in the capillary areas of the most highly vascular tissues and viscera, viz., the lymphatic glands, voluntary muscles, mucous membrane of stomach and intestines, lungs, liver, and spleen.

The exact significance of an enormous presence of "blood-plates" is not yet well ascertained. In small numbers they are sometimes found in the blood of persons apparently in good health; in large numbers they are found in certain febrile diseases, pneumonia, typhus fever, and cholera (1). They evidently indicate grave interference with nutritive processes.

(1.) Dr. D. D. Cunningham's Microscopical and Physiological Researches into Nature of Agents producing Cholera, 1872.

On the white blood-corpuscles abrin when directly applied was found to exercise no very marked action.

As the tissue at the seat of the hypodermic injection was found to undergo rapid degeneration and death, it became desirable to ascertain whether or not abrin acted as a protoplasm poison. The fact that the aqueous solutions of abrin favoured the growth of bacteria rendered it *à priori* somewhat unlikely that abrin did act in this way, but its marked local action on the tissues rendered this point deserving of special elucidation. The white blood-corpuscles offered a ready means of testing this point. The following was the method adopted(1). A ·75 per cent. solution of common salt was made, and a large drop of this salt solution placed on a glass slide The cut surface of a frog's toe was touched with a clean cover-glass 1 inch in diameter, and a few seconds having been permitted to elapse, to allow of coagulation beginning, the cover-glass was carefully inverted on the drop. The excess of fluid was then drained from the edges of the preparation with bibulous paper, and a ring of oil painted round it to prevent evaporation. Two slides were prepared in this way and kept as control experiments. A solution of abrin in salt solution of a similar strength had previously been made; and at the same time that the two slides were prepared with simple saline solution, two other slides were prepared with the abrin solution.

Although the amæbic movements of the leucocytes were slightly more restricted in the specimens treated with the abrin solution, the difference was not sufficient to warrant us in concluding that abrin acted as a 'protoplasm-poison' like quinine. We shall also see under the next heading that the direct application of abrin to the frog's heart was not attended by marked paralysis of the cardiac muscle.

II.—On the Circulatory System.

Circulatory depression is a prominent symptom from an early stage in the progress of the case. The blood-pressure was not tested.

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(1) The scheme followed was generally similar to that used by Dr. Buchanan Baxter in his research on the action of quinine.—*Vide Pract.*, November 1873.

The heart is arrested in diastole,—the immediate cause of death apparently being cardiac palsy.

The direct action of abrin on the frog's heart was tested as follows. The hearts of two decapitated frogs were removed from the body, after tying the great vessels, and one was immersed in ·75 per cent. saline solution, and the other in saline solution to which abrin had been added in considerable quantity. The automatic movements were visible quite as long in the heart which was bathed in the abrin mixture as in the heart which was kept in the normal saline solution, and the irritability of the cardiac muscle to mechanical stimuli persisted for a nearly similar time in both hearts.

III.—On the Body-Temperature.

Coincident with the circulatory depression, there is in acute cases a marked lowering of the temperature, which is probably due to a general interference with the oxidation processes throughout the body.

In a cat the rectal temperature of which, at the time of injection of $\frac{1}{5}$ grain of the seed, was 103·6° Fah., the temperature had fallen on the second day to 92·67° Fah. In another cat, whose rectal temperature was 103·8° Fah. at the time of giving the hypodermic injection, 6 hours afterwards the thermometer registered 103·° Fah., and after 12 hours the temperature had fallen to 98·6°. The cat died 28 hours after the administration of the injection, and the rectal temperature 4 hours before death was 96° Fah.

In sub-acute cases, where the animal lives for over 48 hours, should there be much tendency to local inflammation at the seat of injection, febrile symptoms may develop, but this must be considered as an accidental occurrence.

IV.—On the Nervous System.

No convulsive effects are produced, and the animal retains consciousness up till the time of death. There is no definite paralysis of the limbs, but only languor and debility—the result of extreme exhaustion.

Muscular irritability persisted for some time after systemic death.

V.—On Respiratory System.

The frequency of the respirations was evidently lessened, whilst at the same time the respiratory act became more laborious.

VI.—On Glandular System.

The lymphatic glands, both superficial and deep, are in a state of acute congestion, presenting an appearance not unlike that of septicæmia, except that whilst they are enlarged they are not softened. The salivary glands in cats appeared to be stimulated to excessive secretion. The numerous opaque areas throughout the liver appear to show that the poison kills the hepatic cells, with which it comes into contact, in a manner similar to that in which it acts upon the tissues at the seat of injection. The amount of bile did not appear to be increased. The urine was not found to contain albumin, and its amount was not apparently increased.

VII.—On Nutrition.

Loss of appetite is a very marked symptom even with small quantities of the poison, much short of lethal doses.

In acute cases death occurred too rapidly to admit of emaciation taking place, but this symptom was present in all the animals which lived for over three days, and in those which ultimately recovered from poisonous doses.

VIII.—On Digestive System.

Slight thirst usually attends the loss of appetite. No vomiting was remarked. After about 20 hours muco-sanguineous stools are usually passed, and this when the poison has been injected subcutaneously. The poison appears to have a special determination to the alimentary canal, and being eliminated there exerts its peculiar action on the intestinal mucous membrane, lowering the activity of the cells and so favouring the free development of those bacteria which are always to be found in the intestinal tract.

A large quantity of the powdered abrus-seed (about ¼ oz.) was rubbed up with water and injected *per rectum* into a cat. No

general poisoning symptoms followed, but a severe attack of colitis with bloody stools resulted and lasted for several days.

CHAPTER IV.

The management of cases of Abrus-poisoning. Practical application of our physiological knowledge of abrin to the treatment of cases of poisoning. Indications for treatment locally and generally. Beneficial effect of Iron.

A THOROUGH knowledge of the manner in which a poison exercises its toxic power on the animal body is, of course, a very desirable, and almost necessary, preliminary to the successful treatment of cases of poisoning occurring through its agency. But such intimate physiological knowledge is not easily attainable. Even with the most common poisons, the toxic properties of which were well known to the ancients, our accumulated experience at the present day affords in only a few instances any satisfactory information as to the actual manner in wnich the poison induces a fatal result. With a newly-discovered poison, therefore, like that now under consideration, it was not to be expected that this preliminary series of observations could have afforded a sufficiently profound acquaintance with its physiological action as to indicate clearly a suitable physiological antidote—if indeed any such actually exists amongst our known drugs.

But although we have not yet attained to this profound physiological knowledge of abrus-poison, which is so desirable, still we already have acquired in certain directions an amount of physiological information which admits of practical application to the treatment of cases of abrus-poisoning. We have seen the considerable analogy which exists between abrus-poison and snake-venom. To say that the local treatment in cases of abrus-poisoning should be generally conducted on the same lines as those recommended in snake bite, does not seem at first sight to afford much promise of success, seeing that all the so-called remedies for snake-bite are usually of no avail whatever. In abrus-poisoning, however, there is a very much greater prospect of success in saving life, on account of the slow rate of absorption of the poison and the greater interval of time over which the symptoms are

distributed—death never apparently taking place in criminal cases till after the lapse of about 48 hours.

Any indications for the treatment of cases of abrus-poisoning must take cognizance of (1) *the wound* by which the poison was introduced, as well as (2) *the general constitutional affection.*

I.—The Local Treatment.

In the reported cases of abrus-poisoning occurring in man, but more specially in cattle, the fact of poisoning has only been discovered a considerable time after the introduction of the abrus-spike—a sufficient quantity of the abrin having been absorbed to produce poisoning symptoms before the individual was brought for treatment. With cattle, indeed, the fact of poisoning may not be suspected until the animal is *in articulo mortis.*

Until we become aware of a true physiological antidote, the first indication in the treatment will be to prevent the absorption of any more of the poison taking place where absorption is still going on. For this end, as in snake-bite, we ought to—

Endeavour to cut off from the general circulation the lymphatic and blood-supply coming from the wound. If the site of insertion of the abrus-spike be a limb, this indication could be readily carried out; but when, as is usually the case, it is on the trunk or on the posterior aspect of the neck, then this operation is less easy of practice.

Extraction of the spike or its remains from the wound.—The abrus-spike takes a considerable time to undergo the softening and breaking down process which precedes its absorption. Every portion of the spike which can be removed must tend towards improving the chance of the animal's recovery. Where the spike has been discovered soon after its insertion, it ought to be at once carefully extracted, the utmost care being taken to avoid breaking it, so as leave any fragment behind in the wound.

Excision of the wound.—Even where the whole spike can be withdrawn, the wound ought to be deeply scarified and active pressure made from some distance around it towards its centre so as to make it bleed freely. Where the spike has undergone softening, the diffluent portion which still remains unabsorbed in the tissues must be at once removed by free excision of the part

and steady pressure made from the surrounding parts towards the bleeding wound.

Any poison which still remains in the tissue in the neighbourhood of the wound should be destroyed —A solution of potassium permanganate (strength at least 2 per cent.) should be freely applied to the wound. That potassium permanganate has the power of destroying abrin is seen from the following experiments:—

Exp. LXX.—Half grain of the fresh abrus-seed was rubbed up with 15 minims of distilled water and 10 minims of a one per cent. solution of potassium permanganate added. The whole was then injected into a chicken. No apparent effect.

Exp. LXXI.—The above experiment was repeated in another chicken. Also with negative results.

Permanganate of potassium has, however, no special selective affinity for abrin, so as to render it an antidote to the poison. It has merely the property of forming an insoluble compound with albuminous material. When applied to the wound in abrus-poisoning, it will destroy the proteids of the tissues, and along with these any abrin with which it may chance to come into contact.

Antiseptic treatment of resulting wound.—The wound in abrus-poisoning has been seen to present unusually favourable conditions for the development of bacteria, and these bacteria after a time gain an entry into the general circulation. As the general effect of abrin seems to be exercised in the direction of reducing the vital activity, the presence of these bacteria in the general circulation must further embarrass the already depraved nutrition, so that the local application of antiseptic agents, such as carbolic oil, &c., seems called for.

Painting the skin in the neighbourhood of the wound with the B. P. liquor ferri perchloridi, which has been of such ascertained benefit in erysipelatous and diphtheritic inflammation, might be tried.

When there is much œdematous swelling around the wound, free incisions ought to be made to allow of the escape of this fluid which swarms with bacteria and the decomposing septic products of their growth. Subcutaneous injections of quinine salts—especially

the non-irritating neutral hydrochlorate,—would assist the destruction of these micro-organisms.

II.—The General Treatment.

We have seen that abrin exerts a very special action upon the formed elements of the blood, apparently interfering with the development of the red blood-corpuscles. It also weakens the heart and lowers the temperature, and has a special determination to the small intestines, producing mucous diarrhœa with bloody stools.

In cases of poisoning, therefore, until we find a true physiological antidote, *i.e.*, an agent which will follow the poison through the economy and prevent those modifications in certain structures which would otherwise result in death—until we discover such an agent, our treatment must be directed against the above noted symptoms and ascertained morbid conditions.

First, then, concerning the blood-changes. These, both as regards the alteration in the formed elements, as well as the multiple minute hæmorrhages, bear a certain resemblance to the conditions observed in pernicious anæmia, for which iron and arsenic are the recognised remedies—although it must be acknowledged that even these so-called remedies are usually unavailing in that obscure disease. In purpura also, where the hæmorrhages are apparently of a passive character, iron is believed to be of benefit.

Iron, from its general tonic, restorative, and hæmatinic properties, seems specially indicated in abrus-poisoning. It ought to be a per-salt of iron which is used, for the per-salts, while they contract the capillaries in a manner analagous to digitalis, have no direct action on the heart, and certainly do not lessen its irritability as the proto-salts do(1) —a most important point where we are dealing with a heart already weakened.

When iron is mixed with a lethal dose of abrin outside the body and the mixture then injected, it proves to be practically inert. This result would almost appear to be due to the beneficial hæmatinic action of the iron counteracting the poisonous effects

(1) Blake, *Jour. Anat. and Phys.*, 1869.

of the abrin, for albuminates of iron have been proved to be soluble(1).

Exp. LXXII.—One-fifth grain of abrus-seed was rubbed up with 15 minims distilled water and six minims of the B. P. dilute liquor ferri perchloride added. This mixture was injected into a chicken. On the second day following it gave up taking its usual quantity of food, but a few days afterwards it seemed to have recovered, and was still alive after 15 days.

Exp. LXXIII.—A similar quantity was given to another chicken It also survived.

The internal administration of iron by the mouth to animals already suffering from abrus-poisoning was not attempted with chickens, but the following experiments show the results of *hypodermic* injection of "dialysed" iron—the non-irritant hydrated oxide—in animals already labouring under poisoning symptoms. To render the duration of the cases somewhat parallel to the criminal cases of abrus-poisoning, $\frac{1}{4}$ grain only of the seed was used—an amount ordinarily insufficient to kill a chicken till after an interval of 48 hours. Three chickens were each given this dose, and one of them kept as a control experiment.

Exp. LXXIV.—This chicken, which had received $\frac{1}{4}$ grain of the seed, was kept as a control experiment. It died in 46 hours.

Exp. LXXV.—To this chicken, which had also received $\frac{1}{4}$ grain of abrus seed, 20 minims of Wyeth's solution of dialysed iron was injected into the tract of the abrus injection 4 hours afterwards, and after 24 hours a similar quantity was injected into the right breast. Death occurred in 78 hours.

Exp. LXXVI.—This chicken, after the injection of $\frac{1}{4}$ grain abrus-seed, was allowed to remain for 24 hours without treatment; 20 minims of the "dialysed" iron solution were then injected into seat of the abrus injection. There was a very large amount of œdema surrounding the

(1) Iron when taken by the mouth combines with the albuminous material met with in the stomach to form an albuminate. The precipitate formed by per-salts with albumin are soluble under various conditions. Adding $1\frac{1}{2}$ parts of ferric chloride to an albuminous solution, H. Rose found the precipitate dissolve in an excess of the salt, and when quite fresh, even the "blood-alkalies" dissolve it. When albumin came into contact with weak iron preparations, a ew drops of weak acid or sometimes alkali were enough to help solution in the gastric juice. (Phillip's *Mat. Med.*, 1882.)

Dietl found that iron albuminate was soluble in soda solutions; that iron phospho-albuminate was soluble in contact with phosphate of soda; and that alkaline phosphates generally favoured the absorption of iron salts after they had become albuminates.—(Schmidt's Jahrb., Bd., CLXXIII, 1877.)

wound extending downwards and also upwards to trunk. Death occurred in 58 hours.

These experiments appear to show that the use of iron prolonged life. But it should be given in much more frequent doses, and be combined with local and other treatment. For administration by the mouth the iron tincture of the British Pharmacopœia (say 15 to 30 minims every 2 or 3 hours) might be given (1), or the liquor ferri pernitratis, which has been highly recommended by Neligan for mucous diarrhœa with bloody stools.

Turpentine is another drug which seems indicated not only on account of its stimulant properties, but also on account of its constringing the capillaries, its topical action on the intestinal mucous membrane, and its supposed oxidizing action. It should be given in small doses to avoid purgation or narcotic effects—say 30 minims in mucilage every 2 or 3 hours; and where there is much abdominal pain and bloody stools, it should be given by enema with starch mucilage and opium.

Quinine does not appear to be a suitable remedy for internal administration, as it seems to act to a certain extent in a manner similar to abrin, reducing the temperature very considerably. And *ergot* is contra-indicated on account of its depressant action on the heart.

For the acute inflammation of the intestines, milk and demulcent drinks, viz., eggs, flour, fat, &c., should be given, and the patient be well nourished with beef-tea, soup, &c, and the body kept warm, and diffusible stimulants given to counteract the general depression.

Tetanus was a complication in one of the reported cases of abrus-poisoning. The local irritation produced by the insertion of the spike may be expected to predispose at certain seasons to an attack of traumatic tetanus—a complication at all times grave, but especially so in abrus-poisoning, where the patient is already the subject of such extreme depression.

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(1) Dr. Russell Reynolds used the perchloride with success in intestinal hæmorrhage—*Med. Times and Gaz.*, I, 1867, p. 32.

APPENDICES.

APPENDIX I.

THE BOTANICAL CHARACTERS OF ABRUS PRECATORIUS (WILLD).

Abrus Precatorius (1) (Nat. Ord. Leguminosæ) is commonly known as the Indian liquorice plant. In Bangal it is called *kunch* or *gunj;* its Hindustani name is *rattī*. It is one of the most common plants in every part of India, and appears also to be indigenous to Brazil, where it is called *jequirity*. WALLACE (2) accounts for its extensive distribution by supposing that birds are specially attracted by the bright colour of the seeds; but the hardness of the envelope allows the seeds to pass through the alimentary canal undigested, and so they get deposited in a remote locality.

ROXBURGH (3) describes its botanical characters as follows:— "Flowering time at the close of the rains. *Root* ramous; *stem* ligneous, twining; *bark* smooth; *young shoots* with a few white depressed hairs. *Leaves* alternate, abruptly pinnate, from two to six inches long. *Leaflets* opposite, subsessile, from eight to fifteen pair, linear, oblong, smooth, entire, both ends obtuse, the lower pair smaller. *Petioles*, the common channelled on the upper side, and a little hairy. *Stipules* of the leaves lanceolate, of the leaflets minute. *Racemes*, axillary, solitary, long peduncled. The peduncle itself horizontal, thick, and strong; often leaf-bearing. The raceme, or flower-bearing part, erect, secund, with the apex projecting in a curve. *Flowers* numerous, short pedicelled, inserted on two rows of large, alternate, round, glandular tuberosities growing on the exterior side of the raceme, pretty large and of a pale pink colour. *Calyx* campanulate, mouth obscurely five-toothed. *Corolla; banner* ovate, sides deflected, apex ascending the length of the wings. *Wings* falcate, projecting horizontally. *Keel* cimbiform, the length of the other petals. *Filaments* nine,

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(1) *Abrus* is given by PROSPER ALPINUS (1592) as the name of the plant in Egypt, where the seeds were used for necklaces. THEIS derives it from αβρος, delicate. (BENTLEY and TRIMEN'S *Medicinal Plants*. No. 77.)

(2) *Tropical Nature.*

(3) *Flora Indica*, p. 544, ed. 1874.

conjoined into a cylinder, with a fissure on the upper side, the distinct portions erect, and alternately shorter. *Anthers* ovate, small. *Pistil* minute, hid in the base of the tube of the stamens *Germ* hairy. *Style* very short. *Stigma* headed. *Legume* of a long rhomboidal shape, protuberant at the seeds, divided by transverse membranes into as many cells as there are seeds. *Seeds* generally four or five, spherical, smooth, of a bright, shining red, or white, with a black mark at the eye, or more rarely black with a white eye.

Three varieties of the plant have been met with in India.

1*st*.—With rose-coloured flowers, red seed, and black eye.

2*nd*.—With dark-coloured flowers, black seed, and white eye.

3*rd*.—With white flowers, white seed, and black eye."

The following description of the microscopic structure has been kindly supplied by Dr. D. D. Cunningham, Professor of Physiology, Calcutta Medical College :—

"The integument of the seed consists of no less than nine distinct layers of cells, differing considerably from one another in their characters.

Proceeding from without inwards, we find :—1. A layer of considerable thickness, but containing only a single stratum of cells. They are thick-walled, columnar, contain the colouring matter to which the seed owes its bright scarlet hue, and are arranged in radiant fashion around the deeper portions of the integument. Each cell is dilated peripherally, and in many cases a slight basal bulbosity is also present. The peripheral dilated portion is cut up into a number of more or less cuneate portions, which are closely adapted to one another. In many cases, in the mature seed the central point, where the apices of the segments come into relation to one another, really consists of a narrow canal leading directly into the cell cavity. The surface of the seed coat, due to the close opposition of the cells, necessarily comes to present the appearance of being composed of a layer of cuneate facets arranged in rosetted fashion around central points—each rosette representing the extremity of one of the columnar cells, and the central points in many instances being openings leading directly into the cell cavities.

2. A thick stratum of small cells, with thick walls and irregular sinuous outlines.

3. A thick stratum of large thin-walled cells.
4. A thin stratum of small, also thin-walled, cells.
5. A stratum of elongated thin-walled cells.
6. A stratum of thickened cells, two or three layers deep.
7. A single row of minute thin-walled cells of more or less cubical contour.
8. A stratum of thick-walled cells with dense yellowish granular contents.
9. A stratum of thickened, more or less parenchymatous cells, with more traces of cavities or contents.

The entire thickness of this stratified coating may be broken up in various ways, but apparently the line which may be taken as representing the transition from testa to tegumen runs through the thin-walled cells of the 7th stratum. The cells, save in the 1st and 8th stratum, appear to be almost or quite devoid of contents.

The great mass of the nucleus of the seed naturally consists of the thick cotyledonary lobes. These are composed of a dense parenchyma built up of large cells, with extremely thick walls and granular protoplasm, including numerous oil globules. The most remarkable structural feature present in the tissue is due to the existence of numerous perforations penetrating the entire thickness of the cell walls and giving rise to a system of canals which are occupied by processes of the protoplasm of the cell contents. The entire mass of tissue is thus converted into a continuous system of channels and cavities occupied by a more or less continuous ramified mass of protoplasm."

In India the seeds are employed for various purposes—the red ones by goldsmiths and native druggists, on account of their uniform weight, or a standard *rattī* or *rettī* weight. The *rattī* is usually considered to be equal to 1·951 grains Troy. Flückiger* states it to be equivalent to $2\frac{3}{16}$ grains. A few specimens of each variety of the seeds were weighed with the following results:—

Red.	*Black.*	*White.*
·0980 grams.	·1130 grams.	·1222 grams.
·1350 ,,	·1190 ,,	·1340 ,,
·1100 ,,	·1140 ,,	——

* *Pharmacographia* by FLÜCKIGER AND HANBURY, page 164.

Giving a mean weight of 1·75, 1·77, and 1·97 grains respectively for the three varieties.

APPENDIX II

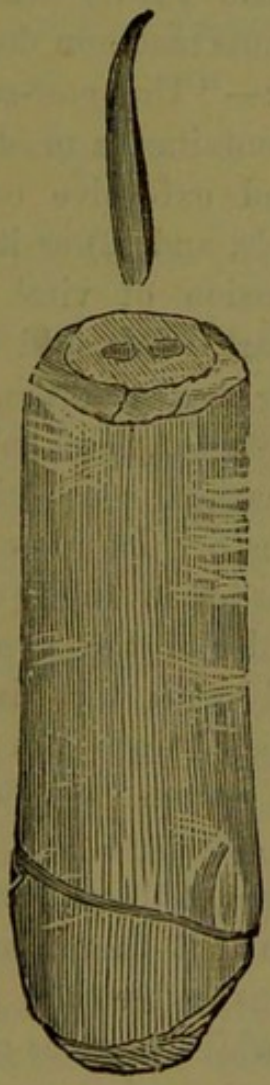
MODE OF USING THE SEEDS FOR POISONING CATTLE.

The Cattle Plague Commission, in their report dated 1870, remark that a large proportion of the criminal cases of cattle-poisoning were effected through the agency of these seeds. In 1873 Dr. Center, Chemical Examiner to the Government of the Punjab, drew special attention to this fact; and more extended inquiry showed that this practice was not confined to the Punjab, but was common throughout the greater part of India; and during the past few years it appears to be on the increase. The Chamār or 'Skinner' caste are the class who mostly practise this mode of poisoning; and although their object usually is to obtain a supply of hides, they have been known to use these seeds for the purpose of committing murder.

The mode of preparing the seed is as follows. The information was gained from a *chamār* prisoner in Patna Jail, who consented to prepare the spikes before a police-officer. A bullock was stabbed in the back of the neck with one of the prepared spikes, and died on the second day following.

The shell of each seed is carefully broken and removed, and the seeds softened by soaking in water, and pounded on a stone in order to form a paste. The lump of paste is then rolled with the palm of the hand on the stone, until it is of a cylindrical shape, with a sharp point. The point, about ¾ of an inch long, is then cut off, and forms the "sui," needle, or, as it is termed in some districts, "sutari," from its resemblance to the point of a cobbler's awl, as seen in the annexed figure. After half a dozen or more "sutaris" have been made, some straw is cut into lengths of about 2½ inches, and a "sutari" inserted in each end; the straws are then put in the sun to dry, care being taken that the "sutari" points are not injured. As soon as a "sutari" is thoroughly dry and hard, the point is "edged" on a brick, after which it is soaked in some animal fat for a night, and the instrument is ready. Occasionally the point is slightly curved. "Suis" weigh on an average 1½ to 2 grains, and vary in colour from dirty

white to dark brown, or nearly black. A handle of wood is then made, about 3 to 3½ inches long, and like the handle of a bradawl. At the end of the handle, which is about an inch in diameter, two holes are drilled, about ¼ to ⅜ of an inch in depth and about ¾ of an inch apart, and into each hole the thick end of a "sutari" is pressed, a piece of cloth being first spread over the holes in order to afford a firmer hold. Bamboo wood is frequently used for a handle, a small cane being selected, and a portion cut off so as to include two joints: one joint has the holes drilled for receipt of the spikes, while the other is sometimes removed, exposing the cavity of the bamboo, in which the spare spikes are kept wrapped in a rag. The form of handle shown in the accompanying illustration is perhaps the most common. The blow



'SUI' AND HANDLE (natural size).

given with this instrument is delivered with great force, so that the whole of the *sui* protruding from the end of the handle is driven into the flesh; any attempt to withdraw the spike by pulling at the piece sticking out invariably breaks it, a portion being left in the wound.

In some cases "suis" are made with the milky juice of the *Calotropis gigantea*—madār—instead of with water, and the effect is then supposed to be more rapid. Metallic mercury, dhatura, aconite, and arsenic are also occasionally incorporated with the paste from which spikes are prepared. When the subject of "sui" poisoning first engaged attention, there was a suspicion that dried snake-poison might possibly be the active principle: a number of spikes were therefore forwarded to Dr. Ewart, President of the Snake-poison Committee, who came to the conclusion that the snake-poison theory was untenable, basing this opinion on two experiments made on dogs, the results of which he summarizes as follows:—"The *post-mortem* examination shews that in these spikes is contained a most virulent irritant poison, producing (1) rapid and extensive cellulitis and inflammation of the lymphatic glands, and (2) as it gets slowly conveyed into the blood, great depression of vital power, ending in death, commencing at the heart. We did not note any of the nerve symptoms accompanying snake-poison, such as local paralysis of the part directly affected, and subsequently paralysis of the respiratory muscles, marked convulsions, unconsciousness immediately preceding death. In slow poisoning by snake virus these symptoms are retarded in their onset; but in fatal cases from small doses, the order of the symptoms, though postponed, corresponds pretty nearly with that in which an overpowering quantity has been injected into the tissues. These two dogs died much in the same way as they would have done had they been subjected to an extensive and deeply penetrating burn, implicating the subcutaneous tissue, viz., from exhaustion. Moreover, we may mention that there was a decided rise in the temperature of these dogs after the spikes had been inserted underneath the skin; whilst in cases of snake-poisoning, whether by minute or large quantities, no such disturbance of the equilibrium of the animal heat has been observed."

APPENDIX III.

HARMLESS NATURE OF THE SEEDS WHEN GIVEN BY THE MOUTH.

When the seeds are given by the mouth the poisonous symptoms do not develop. The seeds when eaten in large quantities are reputed amongst the Hindus to prevent fecundity. Dr. M. Thomson (1) states that the seed, "even when finely ground, does not seem to be a poison when given by the mouth. I have repeatedly given it to dogs in as large doses as two or three drachms, but with no ill effect." Dr. Center mentions that he administered the seeds to dogs in doses varying from ¾ to 1 oz. without poisoning symptoms (2). About ¼ ounce of the powdered seeds can be introduced into the stomach of cats without inducing poisoning symptoms, and children frequently eat the raw seeds without bad results.

APPENDIX IV.

ABRIC ACID; ITS MODE OF PREPARATION AND ITS PROPERTIES.

Abric acid was obtained by digesting the powdered seeds with boiling rectified spirit and evaporating the resulting tincture to a syrupy consistence on the water-bath. After 24 hours an abundant crop of white microscopic needle-shaped crystals was found adherent to the sides of the capsule, and a large amount of oil had also separated, which floated on the surface of the liquid. Water in small amount was now added to the contents of the capsule, and the mixture poured into a bottle and agitated with ether. The ether was then drawn off, while the aqueous stratum holding the crystals in suspension was thrown on a filter and the crystals washed with water. The crystals thus obtained were repeatedly shaken with ether to remove traces of oily matter; then boiled with dilute alcohol, and the solution filtered and allowed to crystallize. The crystals were snow-white and silky, interlaced in masses, and under the microscope were seen to consist of minute needles. To the taste they were faintly astringent,

(1) Report of Chemical Examiner, North-Western Provinces, 1874.
(2) Report of Chemical Examiner, Punjab, 1873.

but without bitterness or acidity. The aqueous and alcoholic solutions were acid in reaction. In cold absolute alcohol, ether, or amylic alcohol, the crystals were practically insoluble; in chloroform, slightly soluble; in boiling dilute spirits they dissolved and crystallized out before the solution was cold. In ammonia and solutions of caustic soda or potash, they readily dissolved and formed well-marked crystalline salts. In dilute acids the crystals were also easily soluble.

APPENDIX V.

The Therapeutic Value of Abrus-seed Infusion in Ophthalmic Medicine.

The seeds are reported by Dr. Moura (1) to have been used for many years in Brazil for the treatment of chronic granular conjunctivitis. It is in the chronic granular cases which have resisted other treatment that *abrus* is said to be of advantage; but unless carefully applied, he has found it not unfrequently happen that an eye otherwise capable of being saved has been entirely ruined by the careless application of a concentrated solution. He used a cold infusion of the seeds, deprived of their testæ, made in the proportion of 0·5 grammes (about 8 grains) to 10 grammes (100 minims) of water.

Dr. L. deWecker confirms Dr. Moura's statements (2). The preparation which has answered best in his hands, and which he is in the habit of using, is weaker than that used by Dr. Moura, being prepared by macerating 10 grammes (about 155 grains) of the decorticated and powdered seeds for 24 hours in 500 grammes (17 fluid ounces) of *cold* water, and filtering. He sums up his observations as follows:—

1. A weak cold infusion of the powdered *abrus*-seeds applied as a lotion rapidly produces a purulent ophthalmia of an intensity corresponding to the strength and number of applications.
2. The factitious ophthalmia thus produced disappeared in the course of 10 days or a fortnight without any therapeutic interference or danger to the cornea.

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(1) *Pharmac. Jour.*, p. 4, 1883.
(2) *Compt. Rend.*, xcv., 299.

3. This property possessed by the seeds of provoking a very intense ophthalmia of short duration could be utilised in ocular therapeutics in the treatment of conjunctival diphtheria, &c. It cures granulations rapidly.

The *symptoms* of abrus-ophthalmia are thus described: "Immediately after the first application the patient's eyes begin to run, and he feels a burning heat and heaviness of eyelids. Next day the inflammation is so intense that he can no longer open his eyes, the skin of the lids becomes swollen, tense, and of a violet colour, and conjunctival ecchymosis becomes more pronounced, accompanied with a more or less abundant muco-purulent discharge, and the patient complains of great pain."(1)

For therapeutic purposes the glycerine solution is to be preferred, as it adheres better to the surface of the mucous membrane, and it is therefore more certain in producing its effects.

APPENDIX VI.

DESCRIPTION OF THE ROOTS OF ABRUS PRECATORIOUS AND HOW THEY ARE TO BE DISTINGUISHED FROM TRUE LIQUORICE-ROOT (GLYCYRRHIZA GLABRA).

The resemblance of the root of *abrus precatorius* to liquorice was remarked by Sloane in 1700. It was introduced into the Bengal Dispensatory in 1844 as a substitute for liquorice, and into the Pharmacopœia of India in 1868.

Description.—The root is long, woody, tortuous, and branching. It usually occurs cut up into short lengths. The thickest pieces are of about the diameter of a man's finger, but most of it is much more slender. The cortical layer is extremely thin and of a light brown hue. The woody part breaks across with a decidedly fibrous fracture, exhibiting a light yellow interior. It has a faint, somewhat disagreeable, odour, and a bitterish acrid flavour, leaving a faintly sweet after-taste.

Microscopic Structure.—On a transverse section the bark exhibits some layers of cork cells, loaded with brown colouring

(1) *New Remedies*, June, 1883.

matter, and then, within the middle zone of the bark, a comparatively thick layer of sclerenchymatous tissue. Strong liber fibres are scattered through the interior of the cortical tissue, *but are not distributed so as to form wedge-shaped rays such as are met with in true liquorice-root. In the latter the sclerenchyme* (thick-walled cells) *is wanting.* These differences are sufficent to distinguish the two roots.

The microscopical structure of true liquorice-root is as follows: The corky layer is made up of the usual tabular cells; the primary cortical tissue of a few rows of cells. The chief portion of the bark consists of liber or endophlœum, and is built up for the most part of parenchymatous tissue accompanied by elongated fibres of two kinds, partly united into true liber-bundles and partly forming a kind of network, the smaller threads of which deviate considerably from the straight line. Solution of iodine imparts an orange hue to both kinds of bast-bundles, and well displays the structural features of the bark. The woody column of the root exhibits three distinct forms of cells, namely, ligneous cells (libriform) with oblique ends; parenchymatous, almost cubic cells; and large pitted vessels.(1)

(1) *Pharmacographia*, p. 158.