

A probationary essay on the antidotes to arsenic : submitted ... to the examination of the Royal College of Surgeons of Edinburgh ... / by Donald Mackenzie.

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Publication/Creation

Edinburgh : Printed by Her Majesty's Printers, 1839.

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A

PROBATIONARY ESSAY

ON THE

ANTIDOTES TO ARSENIC;

SUBMITTED,

BY AUTHORITY OF THE PRESIDENT AND HIS COUNCIL,

TO

THE EXAMINATION

OF THE

Royal College of Surgeons of Edinburgh,

WHEN CANDIDATE

FOR ADMISSION INTO THEIR BODY,

IN CONFORMITY TO THEIR REGULATIONS RESPECTING THE ADMISSION

OF ORDINARY FELLOWS

BY

DONALD MACKENZIE, M.D.

EDINBURGH:

PRINTED BY HER MAJESTY'S PRINTERS.

1839.

PROBATIONARY ESSAY

ANTIDOTES TO ARSENIC

BY AUTHORITY OF THE FELLOWSHIP AND HIS COLLEGE

THE EXAMINATION

Magd College of Edinburgh

WHEN CANDIDATE
FOR ADMISSION INTO THEIR BODY
IS REQUIRED TO EXHIBIT A PROOF OF HIS KNOWLEDGE
OF THE NATURE AND PROPERTIES OF THE
ANTIDOTES TO ARSENIC

DONALD MACKENNIE M.D.

EDINBURGH:
PRINTED BY HENRY COLVILL & CO. LTD.

1884

TO

ROBERT CHRISTISON, M.D., F.R.S.E.

PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS,

PROFESSOR OF MATERIA MEDICA IN THE UNIVERSITY OF EDINBURGH, &c.

THIS ESSAY

IS RESPECTFULLY DEDICATED,

IN GRATEFUL ACKNOWLEDGMENT OF HIS VALUABLE

INSTRUCTION AND KIND ATTENTION,

BY HIS

FRIEND AND PUPIL,

THE AUTHOR.

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TO

RICHARD SMITH, M.D.

THE FOLLOWING PAGES ARE RESPECTFULLY INSCRIBED

BY HIS FRIEND,

THE AUTHOR,

AS A SMALL TOKEN OF GRATITUDE FOR THE KIND ASSISTANCE
RENDERED TO HIM IN THE COURSE OF HIS PROFESSIONAL
STUDIES.

RICHARD SMITH, M.D.

THE UNIVERSITY OF CHICAGO PRESS

BY THE AUTHOR

THE ACTOR

A TRAGEDY IN FIVE ACTS, BY THE AUTHOR

CHICAGO: THE UNIVERSITY OF CHICAGO PRESS

1904

PUBLISHED BY THE UNIVERSITY OF CHICAGO PRESS

CHICAGO: THE UNIVERSITY OF CHICAGO PRESS

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INTRODUCTION.

UPON revising the records of the various cases of poisoning which have taken place during the present century, it must be obvious to the most casual observer, that in the great majority of such cases the poisonous article employed, not only in this country, but also on the continent, was arsenic ; * and this is sufficiently accounted for by the great facility with which this substance may be obtained and administered. Another reason for this is, that arsenic is very generally used for the purpose of destroying noxious animals, when, from a proper want of care, it often falls into the hands of per-

* From a table drawn up by MM. Chevalier and J. Bois de Loury, it appears that out of 94 cases of poisoning, which occurred in France during a period of seven years, the arsenious acid was used in no less than 54 of these cases. *Annales d'Hygiène publique, &c.* T. xiv. p. 401.

sons ignorant of its deadly nature, and is by them mistaken for some other substance, and frequently swallowed. It is therefore very desirable that it should be determined whether or not there is any antidote which may, by chemical combination or otherwise, suspend its action.

With a view to the decision of this question, I have chosen this subject instead of a more practical one, as I consider that an experimental enquiry into the antidotes of a substance of so much importance as arsenic would be better received from me by the College, as a probationary essay, than a mere compilation from the works of authors, who detail the symptoms, pathology, and treatment of the various diseases to which the human body is liable ; of which I, from being a young member of the medical profession, can have but a very limited experience, and on which, most certainly, I can bring forward no new views. My principal motive, however, was, that the last discovered and only true counterpoison for arsenic, viz., the hydrated sesquioxide of iron, so much extolled by the toxicologists of the continent, more particularly by those of Germany and France, had been declared by two English surgeons to be utterly useless, (which had consequently shaken the confidence placed in it by medical men,) as far as I can judge, upon somewhat superficial grounds.

Prior, however, to investigating this point, I

shall give a short sketch of the antidotes which were in use previous to the discovery of the properties of the sesquioxide of iron, detailing the manner in which they act, the nature of the compound, if any, which they form, and the reasons for which they have been abandoned. I shall then detail the experiments I have made, for the purpose of finding out if the sesquioxide possessed the property of neutralizing arsenious acid. Some may think that the number of the experiments are few, when compared to the importance of the subject, but I beg such gentlemen to recollect that I am not exploring a new path, but merely following the footsteps of the experimentalists mentioned in an after part of this paper,* (who have investigated the subject in a most scientific manner) for the purpose of discovering whether or not, as has been asserted, they had overrated the powers of this substance as a counterpoison.

* Vide page 18.

ON THE
ANTIDOTES TO ARSENIC.

In the present state of our knowledge, no antidote has been discovered which, by “exciting in the system an action contrary to that established by the poison,”* may counteract the constitutional symptoms caused by arsenic. Dr. Bunsen, indeed, thinks that the sesquioxide of iron may be of advantage by acting on the constitution, but he has adduced no proofs in favour of such an opinion.† I shall therefore proceed at once to detail the various mechanical and chemical antidotes which have been administered for the purpose of acting locally on the arsenic.

And first, with regard to those substances which, by the fineness of their powder, envelope and prevent the poison from acting on the stomach; for which purpose charcoal, clay, magnesia, and cinchona, have been employed.

* Christison on Poisons, p. 33.

† Lancet 1834-5. Vol. i. p. 27.

From some experiments which were performed by M. Bertrand of Montpellier on the lower animals, he inferred that charcoal was a good counterpoison for arsenic; and so convinced was he of its efficacy, that he had no hesitation in swallowing five grains of the white oxide intimately mingled with it. He experienced no other bad effects than as he himself describes it, "*une sensation de chaleur, une peu douloureuse dans la région epigastrique, avec beaucoup de soif sans autre accident notable.*"* Four hours and a half after taking the above dose, he was perfectly well, the thirst and slight pain being entirely gone. But no other experimentalist has obtained the same results as M. Bertrand; and M. Orfila has clearly proved, that although the charcoal is sometimes of advantage when intimately mingled with the poison, yet it cannot be relied upon when given a short time after the arsenic has been swallowed; for there is a great difference between exhibiting the two substances mingled together, and taking the charcoal a little while after the arsenic, which is the proper method of testing the efficacy of any antidote.

I have placed charcoal among the number of the mechanical antidotes, although M. Bertrand considers that it acts as a decomposing agent. He

* *Annales Cliniques de Montpellier*, T. xxxii. p. 275.

says, "En comparant les effets morbides et organiques qu'entraîne nécessairement avec elle l'ingestion de l'acide arsenieux avec ceux des expériences que je viens de relater, l'on voit que c'est à l'aide de la formation de sels insolubles ou d'une réduction métallique que l'action délétère de ce dangereux toxique se trouve annihilé ou modifié."* But this supposition of M. Bertrand is evidently erroneous, as charcoal cannot decompose the arsenious acid except at a red heat, a temperature which, it is almost needless to say, the two substances are not exposed to in the living body. M. Orfila proved by several experiments that charcoal only acts mechanically in the same manner as potter's clay, or fine sand †.

Another antidote, viz. magnesia, was found useful by M. Mandel;‡ and cases in which it is said to have acted beneficially are related in several periodicals;|| but if it afforded any advantage, which is by no means distinctly proved, it must have acted merely in a mechanical manner, as no chemical action takes place between it and arsenic.

* Op. Cit. p. 227.

† Traité des Poisons, T. i. p. 430.

‡ Annales Cliniques de Montpellier, T. xvii. p. 1—16.

|| Lond. Med. and Phys. Journal, vol. xlv. p. 466 and 545.

Do. Do. Do. vol. xlix. p. 117.

London Med. Repository, vol. xxx. p. 288

Powdered cinchona bark has also been mentioned as an antidote; but it is evident, from what has been already said upon the employment of charcoal for the same purpose, that it can be useful only when swallowed along with the arsenic. This indeed happened in the case of an American physician, who recovered after having taken sixty grains mixed with a considerable quantity of bark.*

Having said so much upon the mechanical antidotes, I shall now proceed to examine the chemical, or those substances which act by combining and forming an insoluble compound with the arsenic.

Although at one time the alkaline sulphurets were imagined to be excellent antidotes in poisoning by arsenic, it has been satisfactorily shown that no reliance can be placed upon them. Indeed M. Orfila, from his researches on the subject, came to the conclusion that they were decidedly useless, and that so far from counteracting the irritant action of the poison, the compound formed acted much more rapidly than the arsenious acid itself. “*En effet,*” says he, “*les animaux meurent dans un temps aussi court, et même plus court quand on leur administre ce prétendu contre-poison, que lorsqu’ils prennent l’acide arsenieux seul.*”†

* American Journal of Med. Science, vol. ix. p. 61.

† Traité des Poisons, T. i. p. 422.

The reason of this was discovered by Berzelius,* who says, that the sulphurets of arsenic act as *sulphur acids* when there is any free alkali in the fluid, as in the present instance; and that the compounds formed are arsenio-sulphurets of potassium, which are very soluble, and—as the compounds of arsenic prove prejudicial in the ratio of their solubility—very quick and powerful in their effects.

MM. Orfila† and Renault‡ have also found that the sulphuret of arsenic, formed when sulphuretted hydrogen comes in contact with the oxide in solution, is decidedly poisonous, although it is not nearly so active as the oxide; and also, that although sulphuretted hydrogen may be somewhat useful in all cases where the arsenic has been dissolved in water, it affords no benefit whatever when it has been administered in the solid form, because it takes a long time to combine with it when in that state. As arsenic is generally exhibited in the form of fine powder, we must come to the conclusion, that, in the great majority of cases, it is of no avail whatever.

The manner in which the insoluble sulphuret of arsenic proves deleterious, is by being decomposed, sulphuretted hydrogen being given off, and oxide of arsenic formed. This decomposition,

* Turner's Chemistry, by Liebig, p. 715.

† Op. Cit. T. i. p. 451.

‡ Sur les Contrepoisons de l'Arsenic, p. 33.

which was first pointed out by M. Decourdemanche,* has been found to take place, though slowly, even in cold water, but much more rapidly when acted on by the gastric fluids. “ Professor Orfila † made some experiments on dogs with the native orpiment and realgar, and with the sulphuret procured by sulphuretted hydrogen gas, (which are all pure sulphurets;) and he found that in doses, varying from 40 to 70 grains, they all caused death in two, three, or six days, whether they were applied to a wound, or introduced into the stomach.” ‡

Another antidote which has been recommended is lime water; but it has deservedly fallen into disuse, because the compound formed, viz., the arsenite of lime, although insoluble in water, is perfectly dissolved, or rather decomposed by the fluids of the stomach, and is consequently equally poisonous as the arsenious acid itself; for no antidote can be of any utility which does not form a compound insoluble in the fluids secreted by the alimentary canal. “ Hence the absolute inutility of vinegar, sugar, butter, and other oily substances, bitter decoctions, and many other antidotes once vaunted and now justly forgotten.” ||

* Journal de Pharmacie, T. xiii. p. 207.

† Journal de Chimie Méd. T. ii. p. 153.

‡ Christison on Poisons, p. 274.

|| Do. do. p. 332.

Having now detailed and shown the inefficacy of the principal counterpoisons which were formerly employed, I shall proceed to examine the action of the hydrated sesquioxide of iron in obviating the deleterious effects of this most fatal poison.

Drs. Bunsen and Berthold, two physicians of Göttingen, presented to the public a treatise * on the efficacy of this substance in cases of poisoning by arsenic, in which they mention that they found it to be an excellent antidote, as it formed with arsenious acid a compound not only insoluble in water, but also in the juices of the stomach. These opinions were supported by the result of experiments on several of the lower animals, to which they found that they could exhibit arsenic, without any prejudicial effects, in a dose quite sufficient to destroy life, provided, at the same time, they administered a sufficiency of the antidote.

These opinions of Drs. Bunsen and Berthold have been corroborated by the experiments of MM. Miquel and Soubeiran †—Orfila and Lesueur ‡—Bouley, jeune ‡—Renault and Lassaigne—and Drs. G. Borelli and C. Demaria of Turin; § but

* Das Eisenoxydrat ein Gegengift des Arsenigen Saure.

† *Lancet*, 1834-5, vol. i. p. 517.

‡ *Annales d'Hygiène publique*, T. xiv. p. 134.

§ *British and Foreign Med. Rev.*, vol. i. p. 595.

they have been declared erroneous by Mr. Brett* and Mr. Orton,† who state that they found the peroxide of iron to be of no avail in counteracting the poisonous properties of arsenic.

There are two methods of preparing this substance, viz., by the addition of ammonia to the persulphate or perntrate of iron. The hydrated sesquioxide immediately precipitated is to be collected on a cloth filter, where it is to be carefully washed with boiling water, until most of the sulphate of ammonia is removed, which will be ascertained by the water used in washing not affecting reddened litmus paper.

The permuriate of iron does not answer for the preparation of this substance, as, on the addition of the ammonia, there is often thrown down along with the sesquioxide a considerable quantity of chloride of iron.

The hydrated sesquioxide ought to be kept in the state of a magma, as it is found to unite with arsenic more readily in that condition than after it has been dried. Dr. Bunsen indeed says, that no action takes place between the anhydrous sesquioxide and arsenious acid. It should be carefully excluded from the air, as it is apt to absorb carbonic acid. By taking a given quantity of the magma, and evaporating it to dryness over a

* Medical Gazette, vol. xv. p. 220.

† Lancet, 1834-5, vol. i. p. 232.

vapour bath, the real amount of sesquioxide present will be ascertained. M. Henry says, that for every thirty-six parts of sulphate of iron, you will obtain twelve of the sesquioxide.*

The quantity of the antidote, requisite to neutralize a given portion of the poison, has been differently stated. Dr. Bunsen recommends from two to four drachms, with sixteen drops of ammonia, to be given for every six or eight grains of arsenic; while MM. Orfila and Lesueur give a much larger quantity. They however do not give any ammonia, as it is of no advantage. M. Bouley gives thirty-two parts, and Drs. Borelli and Demaria four and a half, for every portion of arsenic; but the quantity most generally chosen is that recommended by MM. Miquel, Soubeiran, and Nonat, who administer the antidote in the ratio of twelve to one of the arsenious acid.

Dr. Von Specz of Vienna, from some experiments which he made with the rust of iron, and haematite, (red iron ore,) instead of the hydrated sesquioxide, was of opinion, that, when there is none of the latter to be procured, the two former will be found of advantage. He thinks that the rust of iron comes very close to the hydrated sesquioxide in its property as an antidote, and then “sed longo intervallo, haematite, which, in consequence of its slow operation, may be used without

* Journal de Pharmacie, T. xxi. p. 100.

any beneficial result where the poison is exercising a very powerful action on the system.”*

EXPERIMENT I.

Three grains of arsenious acid were dissolved in about an ounce of water, and then a quantity of the magma of the hydrated sesquioxide, equal to thirty-six grains, was mingled with it. The mixture was immediately filtered, and tested with ammoniaco-nitrate of silver, ammoniaco-sulphate of copper, and sulphuretted hydrogen, none of which gave the characteristic precipitates.

This experiment proves that all the arsenic had united with the sesquioxide of iron, and had formed an insoluble compound with it, which Dr. Bunsen says is an arsenite of iron. I repeated this experiment several times, and always with the same result, which shows that Mr. Brett was wrong in stating that an “excess of peroxide of iron will not neutralize arsenious acid, even when the last is in solution, and the time allowed very considerable.”†

Having thus proved that, when a solution of arsenic and the sesquioxide of iron come in contact, they combine and form an insoluble com-

* British and Foreign Medical Rev., vol. iv. p. 239.

† Medical Gazette, vol. xv. p. 222.

pound, I proceeded to make a few experiments on animals, with a view to determine whether, when arsenic is introduced into the stomach in the solid form, the antidote combines with it and prevents it acting.

Some persons have objected to the propriety of extending to man the opinions founded on experiments performed on the lower animals. This indeed cannot be done in all cases. But in the present instance, no objections can be urged upon sufficient grounds, as arsenic produces the same symptoms, and the same morbid appearances on the lower animals, as it does in man, no matter through what channel it may have been introduced, whether by a wound, ulcer, or by the serous and mucous tissues.

EXPERIMENT II.

At a few minutes past 4 P. M. I injected, by means of an oesophagus tube, into the stomach of a large mongrel dog, eight grains* of arsenious acid in fine powder, and immediately afterwards a quantity of the magma of the hydrated sesquioxide, containing one hundred grains, suspended in about

* This quantity of arsenic is more than sufficient to kill a large dog in about $2\frac{1}{2}$ hours when vomiting is prevented. *Journal de Pharmacie*, T. xxi. p. 99.

five ounces of water. The oesophagus was then tied to prevent vomiting.

This animal presented none of the appearances which so large a dose of arsenic always produces. It was killed at about three o'clock on the following day.

AUTOPSY IMMEDIATELY AFTER DEATH.—The peritoneum was perfectly healthy throughout the whole of its extent. The mucous membrane of the stomach presented slight redness at its inferior portion towards the great curvature. There were several inflamed spots along the course of the duodenum, but they were very few and faint in the jejunum and ileum. The coecum and large intestines were healthy, but the rectum, at its termination, was considerably reddened. The other organs in this cavity were natural.

The heart and lungs presented no abnormal appearances.

EXPERIMENT III.

On the 30th March, at 1 p. m., seven grains of arsenic were administered to a very small mongrel dog, and five minutes afterwards the antidote in the ratio recommended by M. Bouley. A ligature was then tied round the oesophagus to prevent vomiting.

The animal was rather weak after the operation, but it soon became stronger. It was visited at $\frac{1}{2}$ past eight in the evening, and the ligature round the oesophagus was removed. No vomiting took place. On the following morning it was quite healthy, and there were none of the symptoms present which characterize poisoning by arsenic. The food which had been laid before it on the previous evening remained, as far as I could judge, untouched. However, during the course of the day, it both eat and drank, and, in short, continued perfectly well until the 5th April, on which day it was killed.

AUTOPSY.—The peritoneum was healthy. In the stomach there was slight redness, considerably diffused, which extended to within about two inches of the pylorus, and the mucous membrane was coated in several places with false membrane. The small and large intestines exhibited the same appearances as in the last experiment.

The lungs were healthy; and the only morbid appearance in the heart was a very slight ecchymosis at the left auriculo-ventricular opening.

EXPERIMENT IV.

At about $\frac{1}{2}$ past 4 P. M., twelve grains of arsenious acid were introduced into the stomach of a

middle-aged mastiff, and ten minutes afterwards the antidote, (in the proportion of twelve to one,) diffused in about eight ounces of water. The oesophagus was then tied.

The dog continued pretty well up to the time it was killed, which was about twenty-four hours after the exhibition of the poison.

DISSECTION.—The appearances in the stomach and intestinal canal were the same as in the last two experiments, but a little more strongly marked. The other organs in the abdomen, as also those in the thorax, were quite healthy.

EXPERIMENT V.

At 9 o'clock A. M., seventeen grains of arsenic, suspended in about two ounces of thin syrup, were injected into the stomach of a terrier, and after the lapse of fifteen minutes the hydrated sesquioxide was administered in the same ratio as in experiment third, and the oesophagus tied.

The ligature round the oesophagus was removed at about 7 P. M. of the same day, and no vomiting took place. This dog continued to do well up to the time it was killed, which was on the sixth day after the poison had been administered.

AUTOPSY.—Peritoneum healthy. The stomach presented very slight redness, as also did the duo-

denum; and there were here and there small pieces of false membrane effused. The remainder of the small intestines, the coecum, and large intestines, presented scarcely any abnormal appearances, and, with the exception of a few very small red spots, and slight diffused redness near the anus, might be said to be perfectly healthy.

The other organs were natural.

EXPERIMENTS VI. AND VII.

At 10 A. M. ten grains of arsenic, diffused in about an ounce of the thin part of rice broth, were administered to a sheep dog about six months old, and, twenty minutes afterwards, the sesquioxide, in the ratio recommended by M. Soubeiran, was also injected, and the oesophagus tied.

At 11 A. M., ten grains of arsenic, suspended in an ounce of milk, were administered to a small terrier dog, and, after twenty-five minutes had elapsed, the antidote was given, as in the last experiment.

These two dogs continued well, and were killed on the third day of the experiment.

DISSECTION.—The appearances of inflammation in the stomach and intestinal canal were, if any thing, somewhat greater than in experiment five,

and corresponded pretty accurately with those related in experiment three.

The other organs were healthy.

All the foregoing experiments tend to prove that Dr. Bunsen, and the other gentlemen mentioned in page 18, did not err in ascribing so much value to the use of the hydrated sesquioxide of iron, precipitated by ammonia, in cases of poisoning by arsenic, as Messrs. Brett and Orton asserted that they did; and they show that those gentlemen were wrong in stating that no confidence could be placed in its properties as a counter poison.

In all of the experiments, slight inflammation was found in the stomach and intestinal canal, but that does not invalidate the efficacy of the antidote, because, whenever arsenic comes in contact with the mucous membrane, it adheres to it, and soon becomes enveloped in a coat of mucus, which effectually prevents the antidote acting upon it, and consequently causes inflammation, more or less severe, according to the quantity thus covered up. This was very well shown in experiments two, three, and four, where the arsenic came more in contact with the coats of the stomach, from its being suspended only in water, the inflammation being greater in them than in experiments five, six, and seven, where it was diffused through a thickish fluid, even although more time elapsed

between the administration of the poison and antidote in the latter than in the former.

I have not thought it necessary to make any experiments with a view to determine how long, after the poison has been swallowed, the antidote may be of avail, as it commences its action much more quickly in one case than in another. In some indeed it commences to act almost immediately, but, on the average, not until after the lapse of half an hour.

There are a considerable number of cases where this antidote was used with success, related in the following periodicals, viz. :—

Gazette Médicale, Août 22. 1835.

Literary Gazette, 1835, p. 556. Two cases.

Lancet, 1834-5, vol. i. p. 516.

Lancet, 1838-9, vol. i. p. 54.

Ditto ditto, p. 327.

Medical Gazette, vol. xix. p. 177.

British and Foreign Med. Rev., vol. i. p. 572. Six cases.

Ditto ditto ditto, vol. vii. p. 563.

Upon being called to a case, the practitioner ought, if vomiting has not taken place, to administer an emetic, while he is procuring the antidote. This will prove useful, by evacuating the stomach of a considerable quantity of the poison. Of course, it would be wrong to give an emetic in

those cases in which vomiting has been produced by the action of the arsenic, and all that is necessary to be done is to give milk, which "should be drunk both before and after vomiting has begun, as it appears to be the best substance for enveloping the powder, and so procuring its discharge."* Whenever the antidote is procured, it ought to be given every two or three minutes in dessert or table-spoonful doses, mingled with a little water. Some have recommended syrup or mucilage to be used instead of water ; but it is of no importance which is employed. If the antidote is vomited up, which very frequently occurs, it should be given until the vomiting, and other bad symptoms, have entirely ceased. Indeed, the quantity ought not to be regulated by the amount of the arsenic swallowed, but rather by its effect on the symptoms.

The prognosis will be more favourable, the less the time which elapses between the administration of the poison and the antidote, and the thicker the fluid in which the arsenic was suspended, because less of it will adhere to the mucous membrane of the stomach, when diffused in such a vehicle as soup or milk, than when it is taken only suspended in a little water.

From the experiments which I have related, I conclude,

* Christison on Poisons, p. 335.

That the hydrated sesquioxide of iron should be resorted to in all cases where arsenic has been swallowed, as it is a chemical antidote of great avail, in poisoning by that substance.

FINIS.

ON

ENLARGEMENT OF THE HEART.

ARGUMENT OF THE JURY

The second group of the evidence is

ARGUMENT OF THE JURY

WILLIAM ROBERTSON, JR.

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