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Brunton, Thomas Lauder, Sir, 1844-1916.
Royal College of Surgeons of England

Publication/Creation

London : Printed by W.I. Richardson, 1892.

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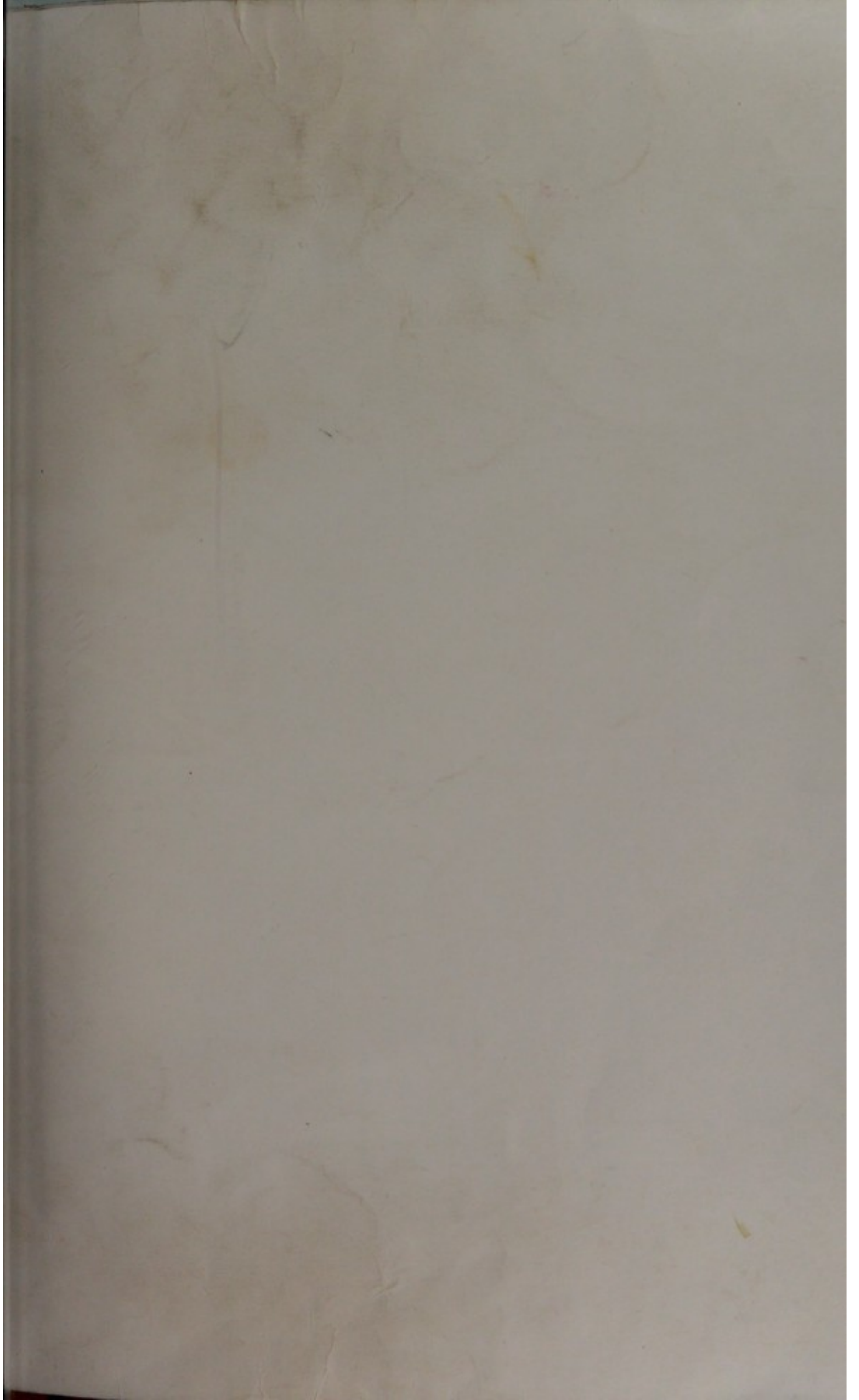
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ON IMPURITIES

T. LAUDER R.

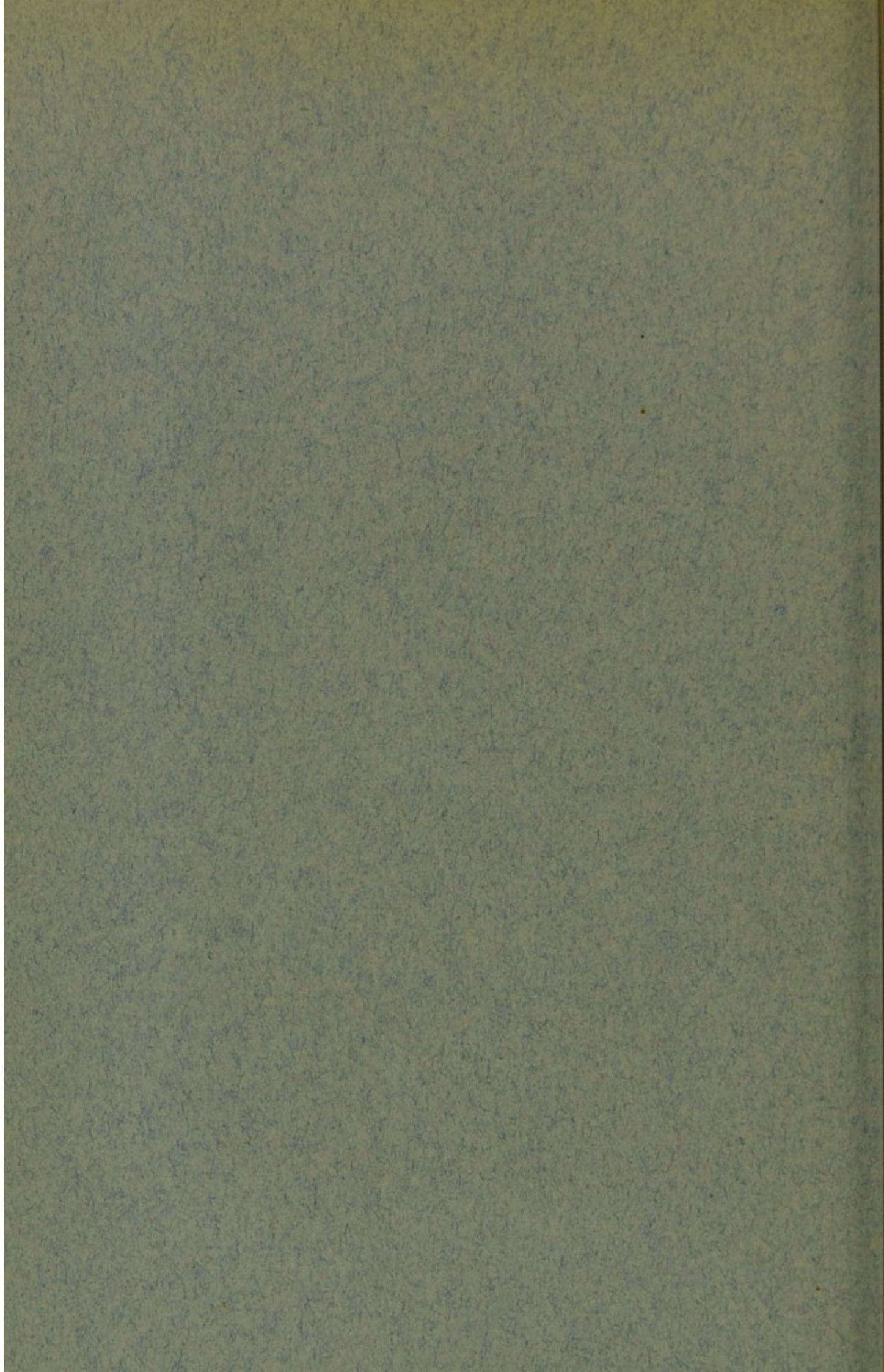
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ON IMPURITIES AND MISTAKES.



BY

T. LAUDER BRUNTON, M.D., F.R.S.



[*Reprinted from the PHARMACEUTICAL JOURNAL,*
December 24, 1892.]

ON IMPURITIES AND MISTAKES.

BY T. LAUDER BRUNTON, M.D., F.R.S.

GENTLEMEN,—I must begin to-night not only with thanks but with an apology. With thanks for your doing me the honour of asking me to address you, and with an apology for the nature of the address. My subject ought to be "Impurities and Mistakes," but when I came to consider the matter I found that I had committed myself a very common mistake, one that we all of us have probably committed in our childhood, but that we certainly ought to avoid in our maturer years. It is that of trying to teach my grandmother to suck eggs, of attempting to address you on a subject that you knew much more about than I. If anything more had been needed to convince me of my folly it would have been the "Ordo rerum" which Mr. Martindale has kindly sent to me. I felt at first inclined to write and ask your President to allow me to change the subject of my paper, but I think that, as a rule, it is a good thing when you have got into a difficulty to face it fairly and not to evade it, unless you are driven to do so by dire necessity. Moreover, it seems to me that there are three classes of people in the world—those who learn by their own mistakes—these are the ordinary people—those who learn not only from their own mistakes but by the mistakes of

others, and those are the wise—and those who will learn neither by their own mistakes nor those of others, and those are the foolish. I trust that all of you belong to the wise class, and that my mistake may prove useful to you and prevent you from getting into a like difficulty. It is possible also that although you know much more about mistakes and impurities in regard to drugs and dispensing than I do, I may have more opportunities than you for seeing the same subject from another point of view, and that my experience may thus be useful.

I had intended to deal with mistakes as made by chemists, by nurses, and by physicians, but I shall deal very briefly with all of those, and give more attention to the subject of impurities.

In speaking of mistakes by physicians my memory carries me back a good many years to a mistake which I made in a prescription about seventeen years ago, and which, if it had not been corrected by the chemist, might have proved very serious. In writing a prescription I put "Extractum opii ℥ii." The quantity was correct for what I had intended to prescribe, viz.: the liquid extract of opium, but I had omitted to put the "liq.," and I had also omitted to put "fl." before the sign for drachms, so that the prescription as it stood actually meant 2 drachms of the solid extract. Fortunately the chemist noticed the omission and brought the prescription back to me, and I inserted the "liq.," thus making it all right. This mistake has been a lesson to me ever since, and I do not think I am likely to fall into the same error again, or to be careless in drawing a distinction between liquid and solid extracts in the case of any active drug.

In regard to nurses' mistakes, I was much shocked to see a notice in a paper of a highly respectable nurse

having been imprisoned for manslaughter, she having caused the death of a baby under her charge by giving it three drops of laudanum. It is quite possible, I think, that the laudanum may have been all right, but I have hunted in vain for a long time to find the original case in which the death of a baby is recorded from one drop of laudanum. At last I found it in turning over some second-hand books in a shop in Baker Street. I read the case, and found it there noted that the laudanum had been standing for a considerable length of time on the mantelpiece in a bottle which was only stopped by a piece of rolled up paper. This imperfect stopper would naturally allow the spirit to evaporate, so that the residue was really not ordinary laudanum, but a solution of opium of unknown and probably great strength. I did not buy the book at the time, and on going back the next day to purchase it I found to my great sorrow that it had been sold. I had not noted its name exactly, and I have not been able to hear of it since. I suppose such a mistake is of less common occurrence now than it used to be, but bad corks or paper stoppers are certainly things to be avoided in the case of all poisonous tinctures.

Another mistake is one that I should hardly have credited, had I not seen it for myself. In my text-book on 'Pharmacology and Therapeutics' I recommended as a useful way of giving chloroform to relieve pain that a piece of blotting paper should be put in a tumbler, and as much chloroform put upon it as would simply wet the paper, leaving none, however, free in the tumbler. The great risk is that the patient should get hold of the bottle himself, as he may spill it on the pillow, and thus cause fatal chloroform narcosis; but after recommending this plan to a patient, I was astonished one day to see the nurse hand to the patient

a tumbler, half full of a clear liquid, with a paper at the bottom of it. I thought that she had only made a mistake with the tumbler, and was merely going to give him some water to drink and had forgotten to take out the paper; but to my horror I found that she was offering him half a tumblerful of chloroform; and if his hand had been shaky and he had spilt this upon the bedclothes, the consequences might have been very serious. Ever since I have recommended that before the chloroform tumbler is handed to the patient it should be turned upside down, so that only as much of the anæsthetic as has been soaked up by the paper shall remain in the tumbler.

In regard to the mistakes in dispensing strychnine instead of quinine and so on, we have read enough in the papers, and you possibly know all the cases a great deal better than I do. The mistakes we generally hear of are those in which the patient has either been killed or seriously injured, and we do not so often hear of a druggist's mistake curing a patient. Yet an instance of this was recorded by Dr. Claiborne, of Petersburg, Virginia, who had been treating a case of persistent eczema in a child for nearly a year and had run through all the local and constitutional remedies he had ever seen used or had heard of being used, and at the last the little boy was worse than ever. Dr. Claiborne hurriedly wrote two prescriptions, more in the hope of getting the father to consult somebody else than with any expectation of curing the child. In a fortnight the father came back to say that the boy was nearly well and the repetition of the last prescription would probably completely cure him. Dr. Claiborne begged him to get it made up again without delay. "But," says the father, "the druggist says he has put it up wrong, and I have been using it wrong all the time,

and he will not renew it without a note from you. The note was accordingly given, the wrong prescription was renewed, and in a few days the patient was well, and his skin as smooth and soft as velvet. The prescriptions ordered by Dr. Claiborne were the following:—First, Oil of cade, 4 drachms; *sapo viridis*, 4 drachms; alcohol, 1 ounce. To be applied twice a day. Secondly, Unguent. oxid. zinc. 2 ounces; ol. of cade, 2 drachms. To be kept on the eruption, regardless of the stage or character of it, all the time. The mistake which the compounder of the prescription made was to substitute the oil of cajuput for the 1 of cade.

It is not every mistake that is so happy in its results as the one I have just mentioned, and undoubtedly it is much better to find out precisely the proper curative drug and apply it knowingly than do it by mistake.

This, I think, bears also on the question of impurities, for I believe that some good results are often attributed to certain drugs when they are really perhaps more due to the impurities, or, at least, the action of the drug is aided by the presence of an impurity in it. More especially is this the case, I think, in regard to preparations of mercury. I had no idea to what an extent grey powder contained mercuric oxide until, in conjunction with Professor Leech, I had to conduct a practical examination at Victoria University. Amongst the substances that we gave to be tested was grey powder, and we had considerable difficulty in getting a specimen of this substance quite free from mercuric oxide. The reason of this, as Professor Leech informed me, was the general substitution for the old pestle and mortar of a rotating pan, which is driven by machinery, and in which cannon balls roll round

and round so as to mix the chalk and mercury thoroughly. By this process a much greater amount of oxidation occurs than by the old method. I am not at all sure that the presence of the oxide may not have a good deal to do with the utility of the grey powder, and probably instead of expunging it altogether it might be better to have a quantitative standard of the amount of oxide which the grey powder should contain, or else to retain the present requirement that the grey powder should be quite free, and let a definite preparation of oxide be added as required by each prescriber. A similar process occurs in regard to calomel, and there are in the market some very minute pilules containing calomel, apparently made up with sugar of milk, which are very active. These pilules contain only one-twentieth of a grain of calomel, and yet five of them taken at night and followed by a saline in the morning are usually quite sufficient to act as a cholagogue in cases of biliousness. I once prescribed ten of these to a doctor who was suffering from hepatic disease. He scouted the notion of taking them, and said he usually took ten grains of calomel at a dose, and what was the use of giving him ten of those which only contained half a grain. I said, "Very well, try the little pilules; they wont do you any harm, and if they are not sufficient you can then have your ten grains of calomel the next time." I went to see him again next day, but his tone had entirely changed, and instead of scoffing at them he said: "Oh, doctor, ten grains of calomel never turned me out like these little pilules!" From their activity I suspected that they contain some corrosive sublimate, and my suspicion was confirmed by Mr. Wallas, of Messrs. Allen and Hanburys, who kindly analysed them for me. I do not know how they are made, but I should

think that probably they are prepared by the aid of a copper basin and iron balls in somewhat the same way as grey powder, so that the calomel undergoes some oxidation with the formation of a trace of perchloride and a trace of peroxide. I have made comparative trials with pilules containing one-twentieth of a grain of pure calomel, and I have not been so pleased with their action as with that of these commercial pilules. At the same time it would be better if one knew precisely what one was doing, and had pilules guaranteed to contain a definite dose of calomel with a definite dose, however small, of corrosive sublimate or mercuric oxide, or both. It was, I believe, the tendency of mercury to pass into the mercuric condition by prolonged trituration that led Hahnemann into one of his errors, and to attribute the increased power of the drug to some occult dynamisation instead of to definite chemical change. It is quite true that we do not know the intimate nature of this chemical change, and we cannot say whether mercury in its mercurous and mercuric state should be regarded as really two elements which, though convertible into one another, are distinct from each other, just as heat and mechanical energy are quite distinct, though convertible into each other. But we do know the conditions under which the mercurous will become converted into mercuric preparations, and we can regulate definitely the amount of conversion, and thus ascertain precisely what we are giving to our patients.

There is another metal, viz., bismuth, whose impurities, if not dangerous, are excessively disagreeable; and my attention has been very forcibly attracted to it lately by the circumstance that the out-patient room at St. Bartholomew's was smelling like an onion bed. This impurity is tellurium, and although this

metal has recently been recommended as a cure for night sweats in phthisis, the oniony smell which it imparts to the breath of patients is enough, I think, to deter them from making themselves a nuisance to their friends, when other remedies can be found free from such an objection. So characteristic is the smell that four or five years ago I saw a patient in consultation, and I at once suspected the impurity. I asked the doctor to send a specimen to Professor Dunstan, who kindly examined it and found the tellurium. There is, at present, a great deal of this bismuth containing tellurium in the market; for it is not only at St. Bartholomew's that we have been troubled by it. About a fortnight ago I went to a consultation in the country, and, while examining the patient, I noticed the tellurium smell and asked the doctor whether the patient had been taking bismuth. I was assured that he had not, and I could not understand how it was that I smelt the tellurium so strongly. On driving back to the train with the doctor, however, I soon found the reason. He had been suffering from dyspepsia, for which he had been taking bismuth. He had gone to one of the best firms in London for bismuth, in order to be sure that the drug was pure. I had got a whiff of his breath while examining the patient, and accordingly attributed to the latter the smell which had come from the breath of the former. This smell is very persistent, and I have noticed it in the breath of a patient at St. Bartholomew's more than four weeks after she had ceased to take the drug. The human body seems to be a much more delicate reagent for tellurium than the test given by the Pharmacopœia; for I have been informed by the dispenser at St. Bartholomew's that although the bismuth had been tried by all the tests of the Pharmacopœia and been pro-

nounced quite pure, yet it gave rise to the disagreeable smell of which I have complained.

Another article whose impurities are of the utmost importance is alcohol. It is hardly possible to estimate how much of the mischief wrought by alcohol in this country may be due to impurities in the spirits or wine drunk and how much to the ethylic alcohol which they actually contain. It is a matter of very common observation that the best wines and the purest spirits are less liable to disagree with the person who takes them, and are especially less liable to cause headache than wines or spirits of the commoner sorts. So much is this the case that many people fear to touch sherry, which is frequently fortified with very impure spirit, and in consequence the sale of sherry has fallen off so greatly that I was informed by a London wine merchant two or three years ago that the great Spanish wine growers had petitioned to be made virtuous by Act of Parliament. They sent a petition to the Cortes asking that a duty so high as to be actually prohibitive should be put upon the introduction of impure foreign spirit into Spain. "For," said they, "the impure spirit with which the sherry has been fortified has so impaired its reputation that it is hardly possible to find buyers for the produce of the last ten years. If this spirit continues to be imported at a cheap rate it will continue to be used by the smaller growers, and the whole growth of wine throughout the country will consequently suffer, as the occasional sufferings which customers may experience from such an impure wine will tend to keep up the prejudice against sherry in general, notwithstanding the efforts of the larger growers to raise its character." But it is not merely the individual who consumes the impure wine or spirit who suffers in

consequence, for many of the violent attacks upon defenceless wives and children which appear in our police reports are attributed, and I think not entirely without cause, to impurities in the spirit the men have drunk. A proposal was made about two years ago to lessen such violence by keeping all spirits in bond for at least two years before it was allowed to be consumed. A Commission of the House of Commons was appointed to investigate the subject and report upon it. The conclusion they came to was that such a measure would not only involve very great expense and loss but would be ineffectual to produce the desired result. I was called upon to give evidence before this Commission and, therefore, to make myself acquainted with the impurities likely to occur in alcohol, and especially in potable spirits. Pure alcohol ought to contain no nitrogen, but nitrogen is an element which even in small quantities imparts energy to organic compounds in a remarkable way and greatly increases the activity of carbon and oxygen, whether it be present in organic alkaloids or in gunpowder. There are certain compounds of nitrogen which have a great power to produce headache, such as nitro-glycerin in minute quantities, and the headaches which it gave me made me hesitate about using it on patients, so that although Dr. Tait and I* investigated its physiological action in 1876, the credit of actually introducing it into practice belongs to Dr. Murrell, who employed it a year or two afterwards.† The violence of the headache which impure spirits or wines may produce leads one to look for the possible

* Brunton and Tait, *St. Bartholomew's Hospital Reports*, 1876.

† Murrell, *Lancet*, 1879, vol. 1, p. 80, etc.

presence of some nitrogenous compound in them Trimethylamine has been found in Austrian wine by Professor E. Ludwig, but it seems doubtful whether this body, although nitrogenous, is likely to cause headache or not. More important impurities are those which belong to the aromatic series, and Krämer and Pinner, in 1870, found a mixture of volatile bases belonging to the picoline series, and amongst these collidine. Guareschi and Mosso found pyridine in 1883. Although this substance was, I believe, proposed as an adjunct to alcohol for the purpose of rendering it undrinkable without destroying its utility in the arts, yet I believe that this proposal was not made until after the date of the researches I have mentioned, and the presence of picoline bases in the alcohol examined by Krämer and Pinner, Guareschi and Mosso, could not be thus explained. I have not seen any satisfactory explanation of the presence of any such alkaloidal bases in alcohol, but the recent researches of Brieger and others have shown that albuminous substances when decomposing yield alkaloids, the nature of which varies according to the state of decomposition. As wheat, barley, maize, and other grains, and potatoes, contain more or less vegetable albumin or gluten we may expect that decomposing grain, if fermented and distilled, would contain some alkaloidal substances in the distillates. Lombroso and Dupré obtained from decomposing maize a poisonous oil and alkaloid. The alkaloid apparently acted exactly like strychnine, the oil caused paralysis. How far these bodies pass over in the distillation of alcohol I have not been able to find out.

But in all alcohol, however good the material from which it has been made may have been, there are certain impurities which are to a considerable extent

removed in the process of distillation, and to these impurities the term "feints" is given. It is usually supposed that much of the injury done by ethylic alcohol is due to an admixture of amylic alcohol, but it is more probable that its injurious action is due rather to bodies not belonging to the paraffin series in which the carbon atoms are arranged in an open chain, but rather to those of the aromatic series, like pyridine or picoline, in which they are arranged in a closed chain, or those of the intermediate furfuran series, in which there is also a chain consisting of four instead of six carbon atoms. The physiological action of bodies of this series was investigated by Professor Curci, of the University of Catania, who kindly sent me his paper on the subject. He found that furfuran C_4H_4O produces first a brief period of excitement, followed by drowsiness and sensory paralysis, in which the animal still preserves consciousness and involuntary movement, but this is succeeded by motor paralysis, stoppage of respiration, and death. Its action appears to be exerted first of all on the spinal cord. It attacks the sensory sooner than the motor powers, and in this respect it resembles the substances of the paraffin series such as ether.

Furfur-alcohol has an action somewhat like furfuran, but causes greater excitability. In a small dog weighing about five pounds, $\frac{1}{2}$ drachm in about three minutes caused great excitement, apparently pleasant, with much friskiness, the dog barking and jumping about. This was succeeded by inco-ordination of movement like that of drunkenness, so that when jumping its legs yielded and it fell forward, then turned about with its head in the air, and stared with an astonished look as if it had some pleasant hallucination. It was constantly in motion, barking and frequently falling

forward. In a few minutes more this jolly state of intoxication seemed to pass into another less agreeable form, and although still excited the dog became quieter, vomited, and then became less able to stand, fell about on one side or other. After this it shook rapidly and repeatedly as if from electric shocks, and then had convulsions both tonic and chronic, with slight dilatation of the pupils and projection of the eyes. It beat its head against the furniture, an action which it is difficult to explain, unless it is possible that the poor creature was suffering from a headache, such as many human beings experience on the morning after a bank holiday. After a little while it got all right again.

So far as I know, the effect of this drug has not been tested upon man, and so we do not know whether it has the same power of producing rapid intoxication, followed by staggering and headache, that it seems to produce in the dog.

The next body, furfurol, is the aldehyde of the series. It is much more toxic than furfur-alcohol, and has quite a different effect upon the cerebrum. Instead of producing the pleasant jollity and excitement of furfur-alcohol, it seems to produce a kind of delirium, in which the animal seems at once suffering and furious. It howls and wishes to bite, as if it were mad, and this effect is succeeded by paralysis. Whether this substance is allied to the actual poison existing in the nerve centres in rabies, and whether it has anything to do with the outbreak of fury leading to outrage or murder, which one reads of occasionally in the papers here, remains a subject for farther investigation.

The other substances of the series are less interesting. Furfurcarbonic or pyromucic acid acts chiefly by weakening and paralyzing the heart. Furfurine

causes an epileptic form of convulsions, foaming at the mouth and death; while furfuraldoxim is a convulsant, like furfurine, but has also a powerful action on the glands, producing hypersecretion.

While giving evidence before the Commission it occurred to me that the end that it had in view, viz., that of diminishing the injury caused to the population of this country directly and indirectly by the impurities of alcohol might be gained in a much easier way than by either keeping the whole bulk of spirits for a length of time or subjecting the entire bulk of spirits to any chemical process for the purpose of mellowing it. I have heard of one plan by which a whiskey merchant was accustomed to convert new, raw, and fiery whiskey into old and mellow whiskey, to the great advantage both of his customers and his own pocket. The plan simply consisted in putting a bottle full of whiskey on a shelf and an empty bottle on a shelf below it. He then put one end of a thread of stocking yarn into the full bottle and the other end into the empty bottle. The whiskey was slowly sucked up by the thread which acted as a syphon and conveyed the whiskey from the full bottle into the empty one. A good deal of evaporation occurred on the passage so that he got only about two-thirds of a bottle instead of a whole one, but the product was mellow instead of fiery, and the increased price which his customers were willing to pay much more than compensated for the loss of material. During the process of distillation of spirits the impurities are separated in the form of feints, and it appears to me that instead of dealing with the whole bulk of spirits, the feints might be subjected to special chemical treatment, which would remove, destroy, or alter any such bodies as furfurol, and thus prevent the de-

pression and fury which it appears to excite. At the same time any nitrogenous substances likely to cause headache might be removed or so altered in their chemical structure that their action might become beneficial instead of injurious.

I have already spoken of the intense headache which is sometimes produced by nitro-glycerin. The same kind of headache sometimes occurs also after the inhalation of nitrite of amyl, but this is not invariable, nor does it occur in all persons. Moreover, I am inclined to think that it does not occur in all specimens of nitrite of amyl, though I am unable to tell you what specimens produce it.

Those who are opposed to experiments upon animals say that such experiments are useless. They even declare that Harvey did not discover the circulation of the blood through experiments, although Harvey himself says so in so many words; and he, if anyone, ought to know. It was my good fortune to discover the utility of nitrite of amyl as a remedy for angina pectoris in 1867. I have seen it stated that this discovery was not made by experiments upon animals by people who object to such experiments *in toto*. I ought to know the facts as well as anyone, and my application of the substance as a remedy in angina pectoris was due to experiments upon animals. The first observation upon the action of the drug was no doubt made by Professor Guthrie, who noticed that while working upon it his face flushed. By experiments upon animals, Dr. B. W. Richardson came to the conclusion that it was a general anti-spasmodic and might be useful in tetanus, and that it was also a powerful excitant of the circulation, quickening the heart and dilating the vessels, so that it might be useful in syncope. So far as I know, he made no experiments upon the tension of the blood

within the vessels, as measured by the manometer; and although his conclusions in regard to syncope are correct, yet one might have been inclined to think that from his placing it amongst stimulants of the circulation, the drug would not be useful in cases where the heart-beat was already excessively rapid and the pulse tension very high, as I found it to be in angina pectoris. My friend, Professor Arthur Gamgee, however, made some experiments upon animals with the manometer, and he showed that, notwithstanding the rapidity of the heart-beat, the tension within the blood vessels became greatly diminished by the drug; and in some of these experiments I assisted him and thus became acquainted with his results. It so happened that at this very time I was house physician in the infirmary in Edinburgh, and had under my care a patient, in whom I was much interested. The poor fellow used to get an attack of angina pectoris every night, and he sat up usually for a couple of hours in the greatest agony, but bearing his pain like a martyr, never uttering a word of complaint and showing the utmost gratitude for all the attempts to relieve him, useless though those attempts might be. Night after night I went to the ward about 2 a.m. and took tracings of the pulse to try and see if possible from whence the pain came. When the pain came on the pulse became very rapid and the tension rose extremely. It then occurred to me that if I could lower his tension I might relieve his pain, and that nitrite of amyl was the very thing to do it. Just as I had come to this conclusion he said to me, "I am much obliged to you, sir, for all you have done, but it is all quite useless, and I want to go home." I said, "Well, I want to try one thing more, and if it does not relieve you, you can go out to-morrow." That night, as soon as the pain came on I gave him a whiff from a small

bottle of nitrite of amyl, with which my friend Dr. Gamgee had provided me. In less than a minute the pain had disappeared, and it did not return. Every night the same thing was repeated. I did not prevent the onset of the pain, but I could limit its duration to three-quarters of a minute instead of to two hours. Every night that unfortunate man had been undergoing pain which I think was greater than that of most experiments upon animals, even if these experiments are not done, as they usually are, under the influence of anæsthetics, and this he suffered not once as an animal would, but night after night for months together. I should say that in a week or, to put it in wide limits, in the course of a fortnight, that that man suffered more pain than all the animals put together that were used to acquire the knowledge of the action of nitrite of amyl upon blood pressure, which not only relieved that one patient but has relieved very many since that time. To anyone who has seen the sufferings of patients and of animals under experiment it seems almost incredible that people who profess themselves to be humane should so lightly disregard the real sufferings of their fellow creatures and expend their commiseration on those of animals, even if the latter were real instead of being, as they often are, purely imaginary.

As an example of this I may perhaps be allowed to mention some experiments of my own in regard to digitalis. It is most disappointing to a doctor when called to a case in which the life of a patient is trembling in the balance, to find that a drug which has usually proved trustworthy entirely fails to have its wonted action. His case is then as bad as that of the soldier whose sword breaks in his hand at the critical moment of a conflict. Now it has been found that in

cases of inflammation of the lung, when the temperature is high and the patient in danger, digitalis sometimes fails entirely to exert its usual action in slowing the pulse. I was anxious to find out the reason of this, so as if possible to prevent the remedy failing us in our hour of need, and I made a number of experiments upon rabbits for this purpose. The rabbits were deeply narcotised with chloral, so that they felt absolutely nothing from the beginning to the end of the experiment. They were rolled in cotton wadding and laid upon a tin pan, like those used for warming the feet in bed, though somewhat longer. Above the animal was laid an indiarubber bag of hot water similar to those employed either for warming the feet or other parts of the body. Between this bag, this pan, and the animal's skin was a very thick layer of cotton wool, so that it was impossible that the skin could be burned in the very least. Being narcotised, however, and the heat from the body being not only prevented from escaping but increased by the hot water, the animal's temperature gradually rose until death occurred from hyperpyrexia. The condition of the animal was precisely like that of a patient in a comfortable bed, with this difference, that the animal was absolutely unconscious, whereas the patient dying from hyperpyrexia is conscious, at least in the earlier stages, and thus suffers more than the animal. These experiments were described by Miss Cobbe in the *Zoophilist* as "baking alive," and she drew graphic pictures of the sufferings of the animals, these sufferings existing only in Miss Cobbe's imagination (*Zoophilist*, Nov. 1, 1884).

But I have digressed from the subject of nitrites and the causes of the variation in their action. I show you here the effect of nitrite of amyl upon the pulse,

a straw having been attached to the lever of the sphygmograph that the little paper flag on the end may make the pulse beat visible to you all.

The physiological action of the different nitrites has been most carefully examined by Professors Dunstan and Cash in a paper which they sent in to the Royal Society, and they find that the higher the nitrite stands in the homologous series the more rapid and powerful is its action, and the lower it is the more enduring is its action.

It occurred to me that hydroxylamine might possibly have an action like the nitrites, and on testing it with Mr. Bokenham we found that it was so, and that the fall of blood pressure produced by it could hardly be distinguished from that produced by nitrite of amyl. I have tried hydroxylamine on patients and find that it also relieves cardiac pain. As nitroglycerin, which is really a nitrate, has a similar action to nitrite of amyl and hydroxylamine it would appear that the effect we produce may not be directly dependent upon the chemical substances which we administer, but on those which are formed out of them in the organism itself. This may lead to the variation of the action of a drug in different patients or in the same patient at different times, but I have already detained you so long that I cannot enter upon this question just now. Nor can I even discuss the chemical changes which occur in plants in the process of growth, and which yield bodies having such remarkably diverse actions that now and again we meet in the same plant, not only with alkaloids having varieties of strength, as in aconite, but with alkaloids having directly antagonistic actions, like those in jaborandi, where pilocarpine produces intense excitement of all the secreting glands, while jaborine pre-

cisely antagonises this action and paralyses the secreting nerves, thus completely arresting secretion. Thus it might happen that a specimen of jaborandi containing a large quantity of alkaloids might appear to have no action whatever on account of the proportions of the two alkaloids, being so evenly balanced as to antagonise each other. This field of investigation is such a wide one and is of so much practical importance, that I think it is quite sufficient for me to indicate it to you, because if we are to attain what we desire and cure sick and suffering humanity, physician and chemist must work together, and it will depend very greatly indeed upon the chemist whether the physician succeeds or fails. In your hands, therefore, rest, to a great extent, the lives, the health, and the happiness of your fellow countrymen, and I trust that in the future we may none of us be found failing in our duty, and that we may have the pleasure of knowing that our work has been useful to our fellows.

LONDON:

PRINTED BY W. I. RICHARDSON, 4 AND 5, GREAT QUEEN STREET,
LINCOLN'S INN FIELDS, W.C.



