children were at school with the exception of the baby, who was asleep. As no complaint was made as to the state of his health I did not examine it. On the following night, at 7, I was sent for to see

CASE II.—E.D., a female infant, aged 14 months. Her throat was in a very similar state to that of her sister, and she died at 11 p.m. Next morning in daylight I examined the throats of the other members of the household and found two more children affected.

CASE III.—E.D., a girl, aged 5 years. She was first seen at 8.30 a.m. on February 27th. The left tonsil and uvula were covered with characteristic membrane which had also just commenced to invade the soft palate. Antitoxin was sent for and 15 c.cm. were injected into the loose tissue between the scapulæ at 5.30 p.m. By this time there was a patch of membrane on the inner side of the right tonsil, and it had also spread somewhat forward on the soft palate. Temperature 100.5°, pulse 120, small and regular. February 28th, 8.30 a.m. Palate free from membrane, while that on the tonsils and uvula seemed to have lost some of its vitality, and to be attached rather loosely. Temperature 99°, pulse 120. There was at 6 p.m. no membrane on either the right tonsil or the uvula, while that on the left tonsil was hanging in shreds. Temperature 99°, pulse 116. On March 1st the temperature was 98°, pulse 96. There was no membrane to be seen, and a sound surface was present where the patches had been. The patient felt hungry. In this case I did not repeat the injection as I required all the antitoxin I had for the following case, and the result of the first injection seemed so striking that I thought repetition unnecessary. From March 1st to 5th the patient made capital progress, eating well and apparently convalescent. On March 6th she was seized with headache and shivering. Temperature 102.4°. The urine, which showed at first traces of albumen, was now pretty well loaded with it. The heart sounds were regular but feeble, pulse 140; eyelids and face somewhat puffy. Iron and diuretics were administered, and by March 13th, a fortnight from the commencement of the diphtheritic attack, the urine was free from albumen. There have been no further complications, and the patient is now convalescent and able to be out of doors.

CASE IV.—T. H. D., a boy aged 10. On February 27th, at 6 p.m., both tonsils and uvula were covered with membrane. There was a sanious discharge from the nostrils and a good deal of inflammation and swelling of their mucous membrane. The angles of the jaw were much enlarged. Temperature 101°, pulse 144. Antitoxin (15 c.cm.) was injected between the scapulæ. February 28th, 8.30 a.m. Temperature 100°, pulse 140. There was not much change in the patient's state except that the nostrils were less swollen and inflamed. The urine was free from albumen. Ten c.cm. antitoxin injected. At 6 p.m. the membrane had commenced to come away in shreds. Temperature 99°, pulse 120. From this time forward the boy made an uninterrupted recovery. On March 1st an erythematous rash appeared on both thighs, which lasted for three days, but caused no inconvenience. It disappeared without treatment.

CASE V.—A. D., a girl aged 7, sister of the other four children. I had been examining her throat daily. On March 2nd there was a large patch of membrane on the left tonsil and the side of the uvula adjoining. Temperature 100.2°, pulse 100. No albuminuria. Fifteen c.cm. antitoxin immediately injected between the shoulders. On March 3rd the uvula and half the tonsil were clear. Temperature 98.6°, pulse 100. On March 4th no trace of membrane was visible. The child made a good recovery. No sequelæ.

CASE VI.—A girl, aged 11 years. I first saw her on the morning of March 11th. The left tonsil and uvula were covered with membrane. Temperature 101.4°, pulse 118. At 9 p.m., with the assistance of Dr. Burns, of Lower Edmondton, I injected 20 c.cm. of antitoxin into the loose tissue over the abdomen. By this time the membrane had spread very much, and, as Dr. Burns remarked, had come "quite forward to the teeth." Temperature 101°, pulse 120 and fairly strong. There were traces of albumen in the urine. Respiration was laboured. On March 12th, at 8 a.m., the palate was nearly clear of membrane. Temperature 99.6°, pulse 100. The child could not yet take much nourishment. At 6 p.m. only the uvula and tonsils were still covered. Temperature

99°, pulse 100. On March 13th there was not much change in the state of the throat. Temperature 100°, pulse 100. I injected 10 c.cm. antitoxin in the interscapular region, as I found that the injection over the abdomen had caused slight inflammation, which prevented the patient from being able to bear the pain of being propped up for the purpose of taking nourishment, etc. Next morning the temperature was normal, and the right tonsil and adjacent side of the uvula were clear. On March 15th Dr. Burns again saw the patient with me, and was gratified to find that only a small patch of membrane on the uvula was now visible. Temperature normal. On March 16th the temperature and pulse were normal, and there was no membrane to be seen. The child has since continued to make satisfactory progress. There have been no complications. The urine is free from albumen, and she has practically quite recovered. In all the cases a mixture of tinct. fer. perchlor. and glycerine was given.

THE APPROACHING REVISION OF

THE BRITISH PHARMACOPŒIA.

IX.

DOSAGE OF THE BRITISH PHARMACOPŒIA, WITH SUGGESTIONS FOR UNIFORMITY.

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THE objections to the dosage in the present issue of the *British Pharmacopœia* are threefold:

1. The doses of many substances are inaccurate, in a few instances even dangerous, and in some so small a dose is given that the drug has no effect. This objection may be briefly summarised by the word "inaccuracy."

2. The doses of the different preparations of a remedy are frequently formulated without any reference to their strengths: thus, under the name of the crude drug or salt, a certain dose is given, and when the infusion, tincture, or liquor of the substance is referred to, it may be found that its official dose represents many times more or less of the amount of the drug or salt. This might be defined as "inconsistency."

3. The doses of the members of the great Galenical groups, such as the powders and tinctures, vary so widely as to constitute a grave difficulty in prescribing. This might be defined as want of uniformity, or, if the word be permitted "in-uniformity."

It is the object of the present article to point out a few examples of this official inaccuracy, inconsistency, and in-uniformity, though the writer is conscious that, especially on the question of dosage, he enters upon highly debatable ground; but the greatest good must result if the views herein expressed will elicit such ripe and invaluable criticisms as those from the able pen of Professor Burney Yeo in a recent number of the *BRITISH MEDICAL JOURNAL*.

The objections to the *British Pharmacopœia* dosage are not taken from the standpoint of fault-finding. Therapeutics is a progressive science, and many of the official doses simply prove that they were formulated upon the basis of the knowledge of the day, which has now broadened and become more accurate.

1. The aconite preparations claim notice first: thus the maximum dose of the extract is given as 1 grain and of the tincture as 15 minims; before the action of the drug was properly investigated these doses were sometimes administered, though with risk. Aconite is a drug now chiefly employed in the treatment of acute inflammatory conditions, in small and often repeated doses, and if this quantity of the tincture was prescribed to be taken say four or six times a day, serious consequences might be expected. Physicians treat such cases successfully by the exhibition of doses of $\frac{1}{2}$ minim to 1 minim, often in the aggregate not exceeding 10 or 15 minims from the beginning to the end of the acute

affection. Dr. Lauder Brunton suggests "that it would be a distinct advantage if the maximum quantity of a drug to be given in a day was indicated as well as that for each dose." Such an arrangement would be valuable in the case of remedies like aconite. A young physician, knowing that this remedy is nearly always used in often-repeated doses, looks up the *British Pharmacopœia*, and ordering, say, the medium dose of 10 minims every hour or every two hours, might have a fatal result. The dose of 1 gr. of the extract is even more serious, and if the revisers would place the maximum dose of these potent agents at the present minimum amounts they would not make any serious mistake. The same remarks apply to the tincture of *veratrum viride*, though it is used in America in heroic doses.

The maximum dose of both extracts of *colchicum* is fixed at 2 grs., an amount bordering upon the dangerous, especially if administered two or three times a day in gout. It is difficult to see why two extracts of this drug should take up the valuable space of the *British Pharmacopœia*.

Another serious overdose is that given for the alcoholic extract of *gelsemium*, that is, 2 grs., which is dangerous. Poisonous symptoms have been reported from smaller amounts. Moreover, *gelsemium* is a drug used chiefly for neuralgia, in frequently repeated doses, and a fatal result might soon follow if the maximum amount was prescribed every few hours, as is the rule with drugs used for the relief of severe pain.

Before leaving the extracts it is worth while pointing out that the dosage of the two extracts of *belladonna* might be easily muddled up by both the dispenser and the prescriber, and lead to serious results; that of *extractum belladonnæ* is given as $\frac{1}{4}$ to 1 gr., whilst that of the *extractum belladonnæ alcoholicum* is only $\frac{1}{8}$ to $\frac{1}{4}$ gr. If the former be retained a distinctive adjective, such as *viride*, should be appended to its present title.

The dosage of the iron preparations requires complete revision if that of *ferrum redactum* (that is 1 to 5 grs.) is to be taken as a basis.

The dose of the hypodermic injection of apomorphine is given as 2 to 8 minims. This is rarely given, except as an emetic; the minimum for this purpose is useless and the maximum is too high. It is not safe to exceed $\frac{1}{10}$ gr. hypodermically. It may be noted that the dose of the drug by the mouth is not given, and this is a serious mistake, since the difference is so remarkable: ten times the lethal hypodermic dose has been given by the mouth without causing vomiting.

The maximum dose of *liquor potassæ* is given as one teaspoonful; an exception might be made in the case of this corrosive liquid, and fatal results guarded against, by the addition of the warning that it should be largely diluted, or as in the case of *liquor ammoniæ* no dosage at all should be mentioned. This latter plan would prevent its being prescribed without consulting special authorities.

The dose of 30 grs. of boric acid and 10 grs. of antifebrin might be reduced with advantage; the former drug in this dose often causes serious gastritis, and the latter substance occasionally produces symptoms of collapse.

Nearly all the official pill masses are given in doses of 5 to 10 grs.—that is, 1 to 2 large pills; but, as Dr. Lauder Brunton has pointed out, these are quite too large or bulky for use. In almost every instance reduction in size can be accomplished by the exclusion of inert substances, and the resulting concentration will bring the dose down to 3 to 6 grs. All the pills containing aloes, if made with aloin, will be improved, and their dosage minimised, without sacrifice. Recent experience has proved that the maximum dose of *chrysarobin* will very often produce grave disturbance; it should be reduced from $\frac{1}{2}$ to $\frac{1}{8}$ gr.

It is manifest that it is a more serious matter to sanction a dangerous dose than to legalise one which is inadequate; nevertheless, a few examples of this latter error may be pointed out. An instance about which there cannot be any difference of opinion is seen in the *extractum filicis liquidum*, where the dose is given as 15 to 30 minims. All physicians agree that a dose smaller than 1 drachm is useless, and this erroneous official dosage has brought unmerited discredit upon one of our most valuable remedies, and annoyance and disappointment to the practitioner who follows the guidance of

the *British Pharmacopœia*. It would be safe to fix the dose at 45 to 90 minims.

Succus conii is given as $\frac{1}{2}$ to 1 drachm; 10 to 20 times this amount has been given without unpleasant symptoms, and it is safe to affirm that the drug is valueless in the official dose. In a previous article it has been pointed out that the dose of 6 grs. of the extract is inert, as many drachms have been swallowed owing to the faulty process by which the preparation is made.

In the case of drugs like male fern, where a single dose is expected to be followed by an obvious result, there is not so much room for a difference of opinion about the amount to be administered. This is evident in the official blunder of fixing the dose of Rochelle salt in the various revisions of the *Pharmacopœia* at $\frac{1}{4}$ to $\frac{1}{2}$ oz., and in the case of Epsom salt, where the maximum dose is also but $\frac{1}{2}$ oz. The maximum amounts in the cases of calomel and quinine are fixed at 5 grs. and 10 grs.; double these quantities are daily prescribed, and found necessary to produce the effects desired.

The official dose of iodide of potassium is 2 to 20 grs., but that of the less depressing sodium salt is only given as half this amount. This is the more regrettable since the iodide of sodium was introduced for exhibition in those diseases like tertiary syphilis where large doses had to be taken for long periods, and it was found desirable to avoid the depressing effects of the potassium base by substituting sodium for it. It is difficult or impossible to conceive why the dose of *pulv. opii co.* is fixed at $\frac{1}{2}$ to 5 grs.; all its constituents are inert in this dose save the opium. This, however, might be more correctly mentioned as a typical example of the next variety of error.

2. In the consideration of what has already been defined as inconsistency in the official dosage, at the start it may be said that it is not reasonable to expect that in every case the dose of the various preparations should be made exactly to correspond upon the basis of their strength in the crude drug. Thus the dose of quinine being given as 10 grs. it would be unwise to expect that the dose of the tincture should be the equivalent of this, that is, 10 fluid drachms. The alkaloid is intended in such doses to be exhibited for its antiperiodic or antipyretic action, whilst the tincture should be reserved for its tonic properties. No one should argue that the dose of paregoric should be calculated from the amount of opium contained in it, as is the case in settling the dose of laudanum. After making all possible allowances upon this score, it will be found that the *Pharmacopœia* contains very many inconsistencies, which could have been easily avoided by the exercise of a little care and arithmetic. An example will make this obvious: thus the extract of *nux vomica*, which is now standardised so as to contain 15 per cent. of total alkaloids, has its maximum dose fixed at 1 gr., which represents less than $\frac{1}{4}$ gr. of alkaloids. Upon turning to the tincture of *nux vomica*, it will be found to consist of this standardised extract dissolved in alcohol and water, and its maximum dose is given as 20 minims—a quantity which corresponds to only $\frac{1}{4}$ gr. of the alkaloid. If the dose of the extract be correct, then that of the tincture of this powerful drug should be nearly 70 minims.

The dose of iodide of arsenic is given as $\frac{1}{10}$ gr., whilst the dose of its liquor is 30 minims—a quantity representing $\frac{1}{4}$ gr., or ten times that of the iodide. The maximum dose of oxide of antimony is 4 grs., but when mixed with twice its weight of inert phosphate of lime in the *pulvis antimonialis* it is only $\frac{1}{2}$ grs.

The dose of *gelsemium rhizome* is fixed at 30 grs. (maximum); the maximum dose of the tincture only contains $2\frac{1}{2}$ grs. of the rhizome. Ergot has a dose of 30 grs.; the amount of the drug in the fluid extract is correctly and consistently made to contain 30 grs., whilst that in the dose of the infusion is 22 grs., and in the tincture only $7\frac{1}{2}$ grs. Nearly all the essential oils have a maximum of 4 minims, but when dissolved in alcohol their maximum is a little over 1 minim in each dose.

The maximum dose of aloes in the decoction is $8\frac{1}{2}$ grs., in the pill 5 grs., in the vinum 4 grs., and in the tincture $2\frac{1}{4}$ grs.

If we investigate such potent agents as digitalis, the maximum dose of the leaf is $1\frac{1}{2}$ gr.; the infusion dosage is made to correspond with this, but the dose in the tincture represents 4 grs. Thus in some instances the proportional dose of

the tincture is one-third that of the crude drug, whilst in others it is three times greater.

The maximum dose of jaborandi is fixed at 60 grs., in the infusion at 43 grs., in the tincture at 13½ grs. In contrasting the dosage of the tincture with the crude drug it may be said that, owing to speedier absorption, a smaller dose of the tincture is required, but the dose is increased in the case of digitalis as just mentioned. The instance of hydrastis in the 1890 additions is instructive: the dose of the liquid extract represents 30 grs. of the rhizome, and that of the tincture represents only 6 grs., both being fluid preparations. The same is true of ergot and other drugs.

Only the most obvious of the numerous inconsistencies have been pointed out as examples. Indeed, anyone who takes up the *Pharmacopœia* and pursues this line of investigation cannot fail to be struck with the defects evident upon every few pages; and he probably will lay down the volume with the conviction that it is "a mighty maze without a plan," and will cease to wonder why it is regarded with such disfavour by all but those responsible for its contents.

3. The third defect in the official dosage is a more important one, inasmuch as it is more difficult to remedy, and it cannot be considered apart from a subject which opens up the most serious of all the many difficulties to be met by the revisers. This is the question of uniformity. Doubtless it is most desirable to have the strength of all the members of each Galenical group quite uniform; for example, it would be a very great gain to have all tinctures made 1 in 10, or some other convenient percentage. It would be equally desirable, or more so, to have the doses of all identical; but a moment's reflection will show that this is impossible. It may at the start be accepted that uniformity of dose and uniformity of strength are absolutely incompatible. If there must be a tincture of aconite and of calumba, each of the strength of 1 in 8, the dose of each must widely differ. If their doses be the same, it is manifest that their strengths must be far apart. It thus becomes a question of how far an approach to uniformity can be obtained. The question is, as already stated, a most difficult one; but it is not hopeless, though it has been evidently regarded as hopeless by the former compilers, judging from the motley character of their official patchwork, whose want of uniformity is its worst or most obvious fault.

Two courses seem open—either to make all the tinctures of one strength or all of such various strengths that their doses will be the same. In the case of the pill masses and the syrups, a fairly successful attempt was made, the dose of the former being fixed at 5 to 10 grs., whilst the great majority of the syrups were made so as to have a uniform dose of 1 drachm. It may be found by thoroughly practical pharmaceutical experts that in the case of, say, a group like the tinctures, there would be insuperable difficulties—arising from different solubilities, exhaustion, etc.—in establishing an absolutely uniform standard of strength. If so, there need be no insuperable difficulty as regards making them all of such strengths that the dose will, say, amount to 30 minims.

There are 75 tinctures; of these 37 are of the strength of 1 in 8; of the remaining 38, 8 are of the strength of 1 in 10, whilst 30 vary from a strength of 30 grs. to 10 ozs. in each pint. Apparently no attempt has been made at a uniform dosage, the dose varying from 5 to 15 minims in the case of several to 1 oz. in the case of rhubarb.

The want of uniformity in the dose of the powders is striking, and their strengths vary as widely; there is no difficulty which cannot be got over in making their strength so variable that the average dose would represent say 30 or 60 grains, except in the case of seidlitz powder. The doses of all infusions and decoctions could be easily made uniform by a rearrangement of their strengths. The liquors are a very complex group, and already an attempt has been made at uniformity in the strength of the alkaloidal solutions.

The recognition of the cause of the extraordinary want of any attempt at uniformity in the *Pharmacopœia* is the first step towards a solution of the difficulty. The writer has stated his opinion of this state of matters in a former article, when he ventured to suggest that it arose out of an attempt to reconcile the claims of the representatives of the old London, Edinburgh, and Dublin *Pharmacopœias* by the intro-

duction of preparations which were popular in the different divisions of the kingdom at the time when the *British Pharmacopœia* was compiled.

Any scheme for perpetuating those preparations which have only a historic interest must now be given up, and the work of revision commenced boldly. The idea of adhering to ancient formulæ so that synonyms may be introduced and prosecutions secured in the law courts against druggists, as has been recently contemplated, must be abandoned as tending to perpetuate old and introduce new incongruities. As a basis, then, for remedying the want of uniformity in dosage, it is clear that the best plan for the revisers to work upon is to aim at making a uniform dose for each group of Galenical preparations, and where this is found to be impossible the alternative should be accepted, and the preparations made of uniform strength. Always, it must be acknowledged, a few exceptions may be inevitable, no matter which plan be followed. In the new issue it is desirable to give the doses in the present weights and measures, and also in their metric equivalents. It would be greatly appreciated by practitioners if the authorities could see their way to give the doses suitable for a child, say, of 1 year old, in the case of those medicines most frequently prescribed for children. This might be regarded as a serious innovation, but it would tend to make the new work popular.

CONGRATULATIONS TO SIR JOHN ERICHSEN, SIR RUSSELL REYNOLDS, AND SIR JOHN WILLIAMS.

On Wednesday evening, March 27th, a congratulatory dinner was given by the staff and old students of University College Hospital, London, to Sir John Erichsen, Bart., President of University College and Consulting Surgeon to the hospital; Sir Russell Reynolds, Bart., Consulting Physician to the hospital; and Sir John Williams, Bart., Consulting Obstetric Physician to the hospital.

The chair was taken by Lord REAY, G.C.S.I., and over one hundred and eighty sat down to dinner. Among the guests were Sir Richard Quain, Sir William Broadbent, Mr. Justice Charles, Sir William Mac Cormac, Sir William Roberts, Sir George Young, Surgeon-General Sir James Mouat, V.C., Mr. Thomas Smith, Mr. Howard Marsh, Dr. Champneys, Dr. Herman, Mr. Knowsley Thornton, and many members of the profession now holding various offices in London and elsewhere whose medical education was obtained at University College.

After the toast of "The Queen" had been duly honoured, Lord REAY proposed the toast of the evening, prefacing his remarks by a brief sketch of the progress of medical thought in the modern epoch. He quoted the saying of the Emperor Joseph, the consort of the Empress Maria Theresa, that the most valuable capital of a nation was men, and observed that the public relations of the medical profession rested upon the fact that its efforts were directed to the conversation of this capital. After a brief reference to the scientific work achieved in the laboratories of University College, and particularly to the brilliant discoveries of Professor Ramsay, of the new gas, argon, and of the still newer gas, helium, first recognised on March 22nd, and as to which a telegram was sent to M. Berthelot, the French chemist, on March 23rd, Lord Reay turned to the special object of the meeting. This was to give expression of the gratification felt by all University College men at the signal honour paid, not only to the individuals but to the College and the profession to which they belonged, by the conferring of baronetcies on their three guests. Speaking of Sir John Erichsen, he said that official recognition had followed the natural selection of the fittest by those best able to judge. In its relations to the medical profession the State was conspicuous by its absence—except when it created baronets. The profession was self-governed, and independent of the State, and this autonomy was a possession in which it might be envied by some other professions. It was felt as a reproach to London that he was not able to greet their three guests as members of the medical faculty of a true University of London. When that faculty was formed it