

eliminated by giving the students the entire bones, and so the second time an assistant holds a watch and each one is given but a very limited time in which to identify the bone. This will eliminate a few more and then we have permitted the contestants to feel only a limited part of each bone and as a final test we have taken bones from the comparative anatomy laboratory and this usually floors more of them, as most of the men have not had a course in comparative osteology. Students who have passed the test are permitted to turn around and thus see what bone is being given to those farther down the line and this makes the test more interesting for all.

This may or may not contribute much in teaching gross anatomy, but it does help to teach the freshman that anatomy and its application in medicine and dentistry requires the training of the fingers as well as the eye. It also helps to stimulate interest in the history of anatomy.

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HOW MANY FIGURES ARE SIGNIFICANT?

THE discussion of this subject ought to prove interesting to all research workers, teachers and students. It is one of the hard subjects to teach and a harder subject to follow out in practice. The ordinary school boy and girl is usually driven by the teacher to carry out all his calculations in science to an unwarranted extent, the only deciding factor apparently being the number of decimal places. The teacher thinks more of the accuracy of the arithmetic than of the truth of the statement. It takes a long time in the university to replace these ideas (or lack of ideas) in the student's head by a little of the common sense of the theory of measurements. The research worker trained without a course in this subject often wastes his own time and wearies the patience of his readers with an absurd number of "significant" figures in his numerical work. Professor Kelley has done well in calling for a statement on definite and uniform practice. As a mere tyro in this subject and one whose experience lies largely with elementary students I should be inclined to use less significant figures than Professor Kelley. Unless the variates follow the Gaussian Law of Error, and in practice this is rarely the case even when a large number of variates are used, I do not like to quote results with more than a two figure probable error or standard deviation. I don't think the results warrant a greater accuracy than this. In Professor Kelley's first case (*SCIENCE*, Dec. 5, 1924, p. 524) I should say Mean = 82 and standard deviation 13; in the second case, Correlation coefficient .75 and its probable error .02. In the second case I give only one significant figure to the

probable error because of the variation likely to occur in another independent calculation of the correlation coefficient from a different but equally reliable set of data.

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LABORATORY APPARATUS AND METHODS

STAINING PARAMECIUM IN THE CLASS-ROOM

A VERY simple, inexpensive and practical method of showing trichocysts, cilia and nucleus of *Paramecium* was recently demonstrated to students of general biology by the writer, through the application of two different colored inks to the slide of living material.

One or two drops of solution containing the culture is placed on each student's slide, and time is allowed for the study of specimens in their usual activities. When the trichocysts and cilia are to be observed and compared the cover-slip is removed, and a dab or two of Sanford's red ink is carefully stirred into the culture by means of a tooth-pick or pin-head. The slip is then replaced. The swimming and "tumbling" of the slightly opalescent specimens are more pronounced. In about four minutes a fountain-pen containing Waterman's blue ink is applied to the edge of the cover-slip. One can see the expulsion of the trichocysts when the animal plunges into the encroaching wave of blue. In a flash the cytoplasm turns a deep red with purplish tinge, the cilia a flame color and the trichocysts a deep blue—without disruption of the specimen. Various shades may be obtained by the students, depending upon the amount of inks used, and the length of time allowed before applying the blue. Incidentally, the nucleus takes on a more concentrated hue than does the surrounding cytoplasm.

This method can be employed by the students themselves and can be repeated several times during the laboratory period with generally uniform success.

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SPECIAL ARTICLES

TRYPARSAMIDE TREATMENT OF AFRICAN SLEEPING SICKNESS¹

THE problem of sleeping sickness in tropical Africa is a source of great concern. The disease is be-

¹ From the laboratories of the Rockefeller Institute for Medical Research, New York.

coming more common in many regions long known to be affected and is spreading to regions previously supposed to be free. There are two ways known of combatting the disease: The destruction of breeding places of the tsetse-fly which is the intermediate host of the trypanosome parasite which incites the disease, and the cure of persons already suffering from it. The former undertaking is formidable in a tropical country only sparsely settled and, as yet, very little brought under control of Europeans with knowledge of sanitary measures and power to put them into force. At best, a long period of years must elapse before effective beginnings in that direction can be made.

The actual cure of the disease by means of drugs is something within present possibility. It may be conjectured that by this means the number of infections may be reduced through diminution of sources from which the tsetse-flies become contaminated. One speaks circumspectly upon this point since it still remains unknown whether wild animals serve as reservoirs for the *trypanosoma gambiense*.

Laboratory experiments covering the years 1914 to 1917 led to the production at the Rockefeller Institute for Medical Research of tryparsamide (the sodium salt of N-phenylglycineamide-p-arsonic acid) by Jacobs and Heidelberger (1) and to the determination of its biological action by Brown and Pearce (2). The promising curative results obtained in various species of animals infected with pathogenic trypanosomiasis, by Brown and Pearce, led to the application of the drug to the treatment of human trypanosomiasis, or sleeping sickness, in the Belgian Congo in 1920. The cooperation of the Belgian medical officers has made it possible to keep under observation, for upwards of three years, many of the patients treated by us during our visit. In this way we have gained a knowledge of and insight into the manner and duration of action of tryparsamide which otherwise it would have been very difficult, if not impossible, to secure.

In order to arrive at the real value of any drug in the treatment of human trypanosomiasis two conditions of therapeutic action must be fulfilled: First, its direct destructive or trypanocidal effect as determined by the microscopical examination of the blood and of fluid aspirated from lymph glands, and next, the degree of curative action on cases in the advanced or cerebrospinal stages of the disease. The first effect is more easily achieved than is the latter. Atoxyl, tartar emetic, Bayer 205 and other less well-known drugs have been proven to possess trypanocidal action and thus are of more or less value in the early or acute phases of the disease; no drug, unless it be tryparsamide, has shown a marked therapeutic action in the late stages of the affection.

The results of the first clinical investigations with tryparsamide by Pearce (3), based upon the treatment of 77 patients in Léopoldville, Belgian Congo, demonstrated that tryparsamide caused (1) a prompt disappearance of trypanosomes from the blood and lymph glands, (2) a rapid improvement of the abnormal cerebrospinal fluids of advanced patients which in the majority of cases amounted to a restoration to normal, and (3) a marked improvement of both physical and mental states. Van den Branden and Van Hoof (4), who have continued the observations and treatments in Léopoldville, reported in October, 1923, the condition of 55 patients first treated three years previously. The period of observation after treatment extended from six months to two years and seven months. Twenty of these patients were early cases with normal cerebrospinal fluids; all were alive and in good health when last seen with negative blood, lymph gland and spinal fluid examinations. Thirty-five patients were advanced cases of various types, including several with pronounced lethargy. Three very advanced patients had died. Thirty-two patients were alive and well with negative blood and lymph gland examinations; in 16 the spinal fluid was normal while slight abnormalities persisted in the others. The amount of tryparsamide administered to this group of patients varied greatly under the conditions governing the early investigations and ranged from 2.0 to 82.0 grams. In the light of our present knowledge, however, it appears that many of these patients were insufficiently treated so that the excellent results obtained are all the more striking.

A second group of patients treated with tryparsamide by Chesterman (5) working at Yakusu, near Stanleyville in the Belgian Congo, has recently been reported. The therapeutic results obtained are of special significance because all of his cases were well advanced in the latter stages of the disease and the amount of drug administered was limited, while the period of observation following treatment extends from 18 months to two and one-half years. Only a single course of treatment was given consisting of 8.0 to 27.0 grams. Chesterman reports that 15 out of 37 patients, or 40.5 per cent., have remained well and without sign of relapse for periods averaging over two years from the end of treatment, and he expresses the opinion that the failures were due in many instances to faulty or insufficient dosage. The physical and mental improvement of Chesterman's patients was marked, as was the case with the Léopoldville group.

Only preliminary reports are at present available from the French physicians now using tryparsamide in Africa. Letonturier, de Marqueissac and Jamot

(6), who have reported on 14 patients treated in the Cameroons, are most impressed with the action of the drug in advanced patients and state that to their knowledge no other drug is endowed with such a power of meningeal penetration or has such a beneficial effect upon the clinical symptoms of advanced patients.

In New York City two Americans in the advanced stages of sleeping sickness have been successfully treated with tryparsamide. One patient, whose history has recently been reported by Morgan (7), had relapsed 2 months after treatment with Bayer 205 with the typical symptoms of an advanced infection including lethargy; her condition was extremely grave. Tryparsamide was administered intravenously in three courses over a period of 13 months and she has been given a total amount of 63.0 grams. Clinical improvement was observed after the initial dose of the drug and by the end of the first course of ten doses both the physical and mental condition appeared normal. Since this time she has resumed her household and social duties which have only been interrupted by the additional treatment administered. Physical examinations have continued to be negative, the last one being 6 months after the cessation of treatment. The condition of the second American was fortunately not so critical. Two courses of tryparsamide amounting to 53.0 grams were administered by Dr. K. M. Lewis (8) with prompt clinical response and a rapid restoration of the normal state of the cerebrospinal fluid. The patient's condition was reported to be satisfactory 10 months later.

From various reports, both published and unpublished, dealing with the therapeutic results obtained with tryparsamide in African sleeping sickness, the system of treatment at present recommended is the administration of 24.0 to 30.0 grams in early cases and from 50.0 to 70.0 grams in advanced cases. The treatment for advanced patients should be given in two or three courses separated by intervals of 2 or more months, and each course should consist of eight to ten weekly doses. The size of the individual dose most frequently used is 3.0 grams and the intravenous route of administration has so far been followed almost exclusively.

Tryparsamide is now being widely used in the Belgian Congo at the request of the Colonial Government, and it has recently been supplied to the British and French colonies in tropical Africa. The results of its use under various conditions of field administration and in different parts of Africa will be published from time to time. The chronic nature of African sleeping sickness and its tendency to relapse are formidable obstacles in obtaining authentic cures and it is the realization of these facts that has led

us to emphasize the necessity of continued observation of treated patients for long periods of time. However, if future reports are as encouraging as those briefly summarized above and if the treatment of the native population in infected districts can be carried out on a large scale, it is probable that the control of African sleeping sickness may eventually be accomplished.

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THE PANCREATIC RESPONSE TO CARBOHYDRATE INGESTION

IN the course of studies on the relation of blood sugar concentration to food ingestion, we have been impressed with the variety of responses by the body mechanism for glucose storage. The subjects were healthy students working in the chemical laboratory. The morning meal was taken immediately after the first blood sample was drawn. Analyses were made by the Folin-Wu method.

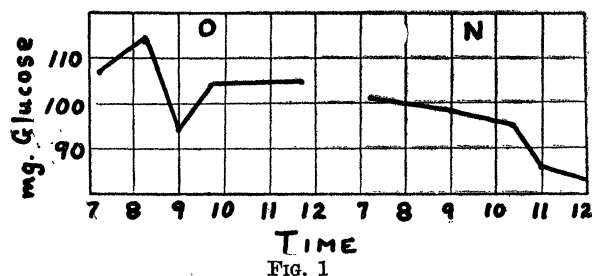


Fig. 1

In Fig. 1 the curve of subject O presents what seems the commonest type of reaction. During the period of relatively low blood sugar concentration there was a definite sense of hunger. This we correlate with the observations reported by Bulatao and Carlson.¹ The curve of subject N is of a different

¹ Bulatao, E., and Carlson, A. J., *Am. J. Physiol.*, 1924, lxi, 107.