

Hand-book of the Clinical Research Association, Limited.

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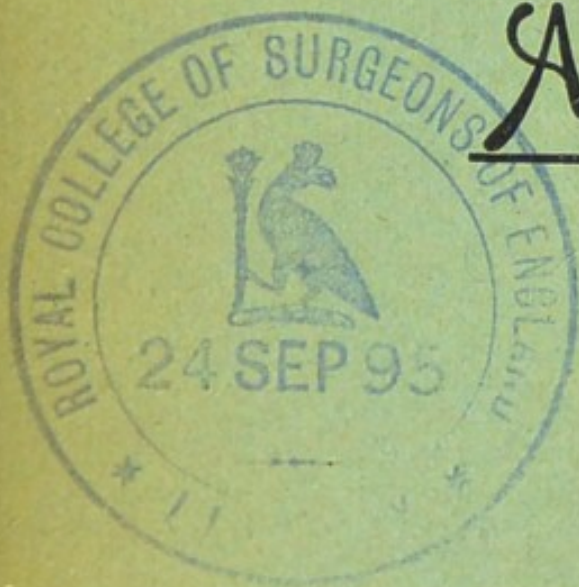


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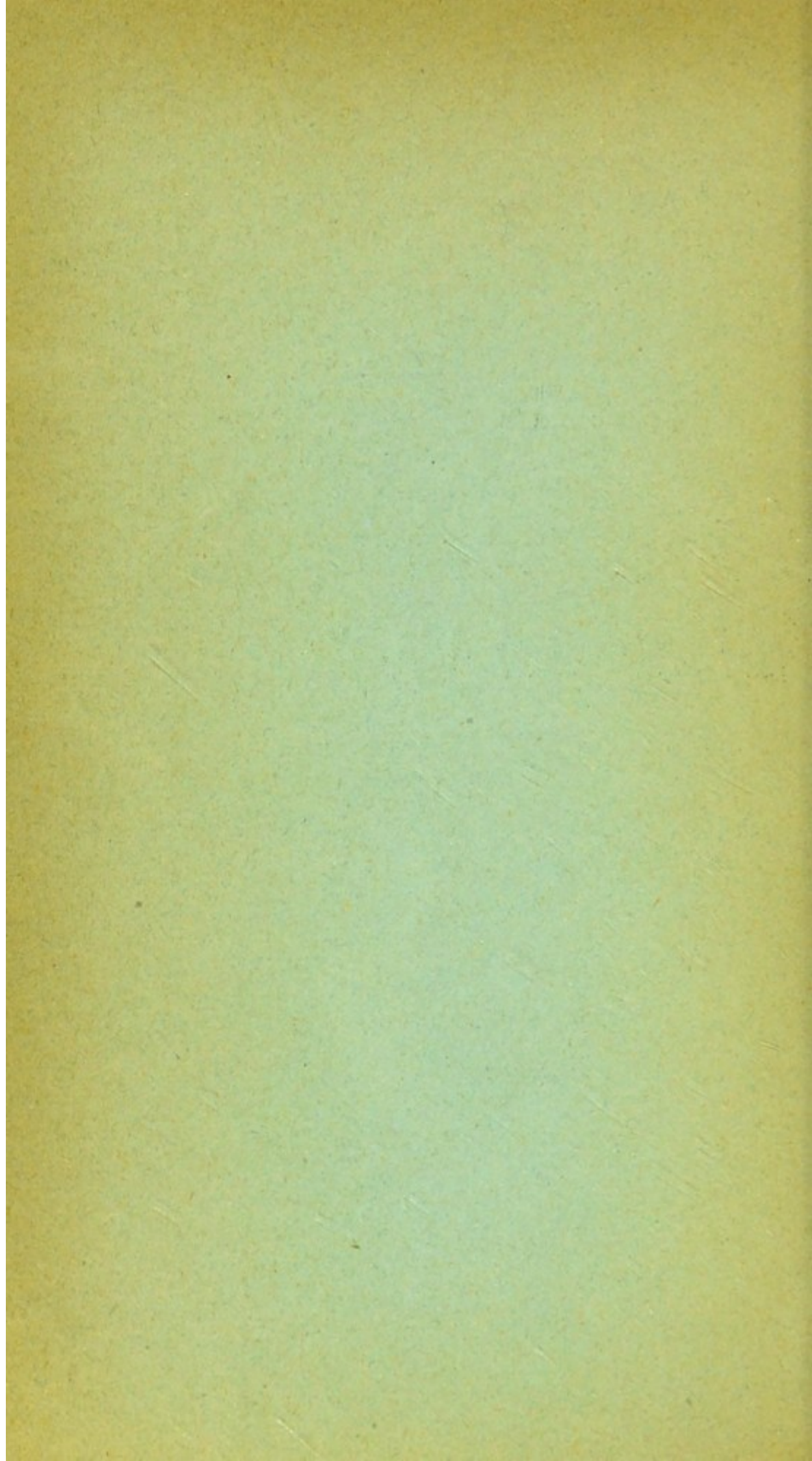
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HAND-BOOK
OF THE
Clinical Research
Association,
LIMITED,



1, SOUTHWARK STREET

LONDON BRIDGE, S.E.



THE
Clinical Research Association,
LIMITED.

UNDER THE PATRONAGE OF

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THE CLINICAL RESEARCH ASSOCIATION.

IT is a fact already widely recognised in all Schools of Medicine that a Clinical Laboratory is an essential adjunct to the wards of a large hospital. In such laboratories are daily carried on under the supervision of Members of the Staff with the co-operation of numerous willing Students investigations not only desirable in order to further our knowledge of medicine, but essential for the accurate diagnosis and successful treatment of obscure and dangerous diseases.

It falls to the lot of but few private practitioners to possess the leisure, facilities, and assistance to enable them to provide for their patients the advantages that must accrue from investigations carried on in such an institution. When these researches become absolutely necessary, the practitioner must either conduct them himself with much loss of valuable time, or put himself under an obligation to some

less busy colleague. In many cases where the research would tend rather to the advancement of general medical knowledge than to the special benefit of the patient, it must perforce be abandoned. It was to remedy this unsatisfactory condition of affairs that, in the autumn of 1894, with the good wishes and approval of some of the most eminent physicians and surgeons in the United Kingdom, the Clinical Research Association was originated. Much thought was bestowed upon the best way of founding an association which should deserve the confidence of the profession, and should possess a thoroughly stable organization. Conferences took place between representatives of the body of private practitioners who would be likely to make use of the association and of those engaged in scientific work such as would fit them to conduct the required researches, and at the same time advice was sought from those skilled in business administration.

As a result of these negotiations the conviction was reached that no voluntary association would have an assured prospect of permanence, and that it was wiser to form a limited liability company, to carry on the work on sound financial lines. It was thought better that those actually engaged in the work of research should have no direct pecuniary interest in the association other than as salaried officials, and with that understanding the association was able to secure as its laboratory directors gentlemen holding high rank as pathologists, as chemists, and as bacteriologists. At the same time it was deemed desirable that the control of the policy of the association should be in the hands of those who were interested in the advance of scientific medicine, and with that object it was arranged that a majority of the Directors of the Company should be medical men actually in practice.

With regard to the provision of funds for carrying on the work, after the preliminary expenses had been met, it was decided at the commencement, at least, to avoid asking the Members to pay an annual subscription, as such a method of payment would obviously be unfair to those who should make only occasional use of the Association's services. It is still felt that this course is a wise one, and it will be followed until the end of 1895, by which time it will have been ascertained if the amount of work sent to the Association promises to be sufficient to cover expenses at the present low scale of charges. In any case it has been determined that all medical men who join the Association before that date shall be considered original subscribers, and shall be exempt from any subscription should it be subsequently found necessary to institute one.

The warm welcome which was immediately accorded to the Association by the profession generally, and by private practitioners in particular, shewed the pressing need of some such institution. The steady growth in the number and variety of the investigations required leads those responsible for its management to believe that the work done in the laboratory is giving general satisfaction; and they take this opportunity of acknowledging the numerous letters of encouragement and thanks they have received from all sides.

The response to the original circular letter addressed to the profession last September shewed the Board of Directors that the premises provisionally fitted up for the work of the Association would be inadequate, and steps were taken to provide more suitable accommodation. This was secured before the end of the year, and it is hoped that the laboratories and offices at present

occupied will allow for the development of the Association for some time to come.

The great variety of the investigations that the Association was asked to undertake, and the numerous enquiries with regard to the best methods of forwarding materials to be examined, and as to the cost of the examinations, necessitated, within a few months of the opening of the Laboratory, the issue of a more complete scale of charges and more detailed instructions for the transmission of specimens. The present hand-book is a still fuller guide for the use of members of the profession who may desire to avail themselves of the services of the Association.

MEMBERSHIP OF THE ASSOCIATION.

There is no entrance fee or annual subscription at present.

All Medical Practitioners who subscribe five shillings to the Association before the end of 1895 will receive in return for their Subscription a box of eighteen bottles and postal packages, will be enrolled as original members, and will be exempt from any entrance fee or annual subscription, should it be subsequently found necessary to institute one.

SCOPE OF THE ASSOCIATION.

The object of the Association is to assist medical practitioners in the prevention, diagnosis, and treatment of disease, and in the investigation of the causes, progress and results of morbid processes, whenever help to this end may be gained by accurate reports on the results of microscopical, chemical, or bacteriological examinations. With

this object in view the work of the Association's Laboratory is placed under the control of Directors skilful in these methods of investigation, under whose immediate supervision all kinds of morbid products—excretions, secretions, or effusions, vomit, fæces, and blood, as well as water, milk, or any article of diet suspected of being the cause of disease—are carefully examined and reported upon. Pathological specimens are described, dissected, or mounted in museum jars, and drawings, photographs, micro-photographs, and lantern plates prepared.

The cost of conducting the more commonly required investigations is indicated in the scale of charges given in the succeeding pages, and the Secretary will be pleased to answer any enquiry as to cost in other cases. In fixing the scale every attempt has been made to keep the charges as low as is compatible with reliable results, in recognition of the fact that in many cases the practitioner is unable to charge a fee to his patient for such investigations.

Appreciating the advantages of a post-mortem examination in almost all cases, and the great difficulties of conducting one in a private house without skilled assistance, the Association sends out attendants experienced in the mechanical work to help such medical practitioners as may desire it.

TRANSMISSION OF SPECIMENS.

For the busy practitioner a ready means of packing and despatching specimens for examination is essential. For this purpose the Association provides bottles of various sizes, some filled with preservative fluid, and each contained within an addressed postal box which is easily and securely fastened by gumming, and is then ready for

transmission by hand or through the post. Eighteen such bottles and boxes, six intended for urine, six for sputum, diphtheritic membrane, &c., and six for portions of tumours or solid tissues for histological examination, and accompanied by instructions for sending specimens, are forwarded post free for Five Shillings. The proportion of bottles for different purposes can be varied to suit the requirements of practitioners. To each bottle is attached a label on which should be stated the sender's name and address, and the nature of the investigation required.

In cases where a series of examinations has to be made for one patient, as, for example, in diabetes, Bright's disease, or chronic phthisis, the Association, at the request of the medical attendant, forwards a supply of bottles and postal boxes to the patient; but in no circumstances is a report sent to anyone but a medical practitioner.

Large pathological specimens and those which from their nature cannot conveniently be sent by post are collected by the Association's messenger from practitioners residing within four miles of London Bridge upon due notice being given, and for examining such specimens a small extra charge is made to cover the cost of transit.

For the transmission of *Blood* for the estimation of the amount of hæmoglobin, number of corpuscles, &c., of *diphtheritic exudations* for bacteriological examination, and of *drinking water* for analysis, special apparatus is sent immediately upon application. Further particulars will be found under these several headings in the following pages.

DIRECTIONS FOR SENDING SPECIMENS.

GENERAL INSTRUCTIONS.

By attention to the following instructions the practitioner will ensure the safe transit of his specimen, and a prompt report upon the result of the investigation.

Every specimen should be securely fastened, fully addressed, and have firmly attached to it a label, clearly written, indicating the sender's name and full postal address, the patient's initials, the nature of the material, and the investigation required. For these purposes the bottles and blank labels sent out by the Association will be found well adapted. (*See page 22.*)

The nature of the investigation should be explicitly stated, it being understood that the Directors of the Laboratory do not undertake to express an opinion as to the nature of the case under investigation, but will confine their report to the result of microscopical, chemical or bacteriological examinations of the materials submitted to them.

If it is desired that a report by telegram should be sent, the specimen should be marked "urgent," and instructions to that effect written on the label. For such reports, except in cases of Diphtheria, which are always treated as urgent, an extra fee of 2/6 will be charged.

If the specimen is sent by post it is necessary to pay attention to the following postal regulations.

"No package containing liquid or glass may be sent by Letter Post, but must be sent by Parcel Post."

"All packages sent by Parcel Post must be marked Parcel Post and handed into the Post Office over the counter. If put into a letter-box in the ordinary way, such a parcel will be surcharged on delivery."

Packages sent to the Association in contravention of these regulations are frequently delayed many hours in transit.

The examination of every Specimen received at the Laboratory before two o'clock is commenced on the day of its arrival, and when possible a report is despatched the same evening.

In cases in which the examination of the specimen takes too long to allow a report to be sent within three days of arrival, its receipt is acknowledged, and if possible the date on which the report may be expected is intimated.

TELEGRAPHIC ADDRESS.—The registered telegraphic address of the Association is "Tubercle, London."

URINE.

SELECTION AND PREPARATION OF SPECIMENS.—In sending specimens of urine for examination, it is recommended that the quantity passed in the morning before breakfast should be chosen, in preference to any other portion of the day's excretion. It is, however, of still greater advantage, even for the purposes of qualitative examinations, to submit a specimen from the whole quantity passed during the 24 hours, as many pathological constituents vary greatly in amount at different periods of the day. Where quantitative results are required such a procedure becomes still more desirable; and, if the daily excretion of any constituent is to be estimated, it is obviously necessary that the entire 24 hours' quantity should be mixed and measured, and a specimen from the

whole sent for analysis. It is, moreover, requisite in the latter case to shake up the urine thoroughly before pouring off the sample, in order that a due proportion of any previously formed deposit should be included.

QUALITATIVE EXAMINATIONS.—Under the head of “General Qualitative Examination” the urine is tested for sugar, albumen, and blood, these being the routine clinical tests as applied at the present day. It may be noted that in the examination for sugar the reduction test is, in all doubtful cases, supplemented by the fermentation and phenyl-hydrazine tests; cases where glycuronic acid, and copper-reducing substances, other than sugar, occur, are thus eliminated. Again, in testing for albumen no one process is relied upon in cases where there is the slightest doubt, and the same may be said of the examination for blood. It is hoped that the examinations made by the Association may thus be of value to those who, while accustomed to apply the ordinary tests for themselves may meet with cases of doubt or difficulty. Under the head of “General Qualitative Examination” a microscopic examination of the deposit is made as a matter of routine, except where countermanded. For this purpose the urine is in all cases centrifugalized. Where a copious deposit of phosphates or urates exists this is dissolved before the centrifuge is used so that a subsequent search for casts, etc., becomes more certain.

EXAMINATION FOR MICRO-ORGANISMS.—In the examination of the deposit above referred to no attempt is made to detect special organisms. When required the urinary residue is examined for tubercle-bacilli or gonococci.

For *tubercle bacilli* it is advisable to send several ounces of the urine passed, including all deposit. The urine is centrifugalized to obtain as reliable a result as possible

but on account of the organism being diffused through so large a quantity of fluid, it is clear that several examinations are advisable on which to found an opinion should the case be suspicious or the early results negative.

By similar means *gonococci* may be detected in the urine in cases of gonorrhœa, but if at all possible, it is well to send one or two cover-glass preparations of the pus as it exudes from the urethra, taking care that the layer of discharge is not too thick.

QUANTITATIVE EXAMINATIONS.—The best available method of estimation is adopted for each constituent, and a careful uniformity of working is observed, so that if a series of determinations is required in any case, the results will be strictly comparable. The fees for the estimation of each of the commoner urinary constituents will be seen on reference to the schedule: other determinations can be made at charges which will vary with the difficulty of the process.

GENERAL REMARKS.—The significance of the commoner variations from the normal is too well known in the case of urine to need comment; but it may not be out of place to suggest here certain less ordinary lines of investigation which may be of value to Practitioners, and which the Association is prepared to undertake. It should, however, be premised that only a few instances can be given from the large number of aids to diagnosis which modern research has supplied. *Reaction of Urine*.—An actual determination of the grade of acidity is frequently of great importance. Sir William Roberts has shown that hyper-acidity is the chief predisposing cause in the deposition of uric acid gravel or calculus. The knowledge that a tendency to such hyper-acidity exists may therefore lead to correct treatment at an early stage in the disease.

Pigmentation—The detection of abnormal pigments is frequently of diagnostic value. The question of bile pigments need hardly be referred to; but the observation, say, of an excess of urobilin may fix the attention upon the liver in many cases otherwise obscure, and the same pigment when in excess, may, in other cases, rightly suggest the occurrence of internal hæmorrhage. The presence, again, of the urobilin absorption band in the fresh urine of an anæmic patient is highly characteristic of pernicious anæmia, and may clear up the diagnosis in a doubtful case. In this connection may be mentioned the importance of excess of indican as pointing to putrefactive changes in the bowel or elsewhere in the body; the evidence of the existence of toxæmia from such a cause being strengthened if the ethereal sulphates of the urine are found in excessive quantity. *Uric Acid*.—A knowledge of the amount of this substance excreted is of the utmost importance in following the progress of a case of gout, and in the treatment of so-called lithæmic conditions with their manifold discomforts and dangers. The information thus gained is made more definite by a knowledge of the relative as well as the absolute excretion of uric acid; for instance, by knowing the “urea-uric-acid ratio.” On the other hand in dealing with trouble occurring on the distal side of the renal tubules it is the actual percentage which should be known; *cæteris paribus* an increased percentage means increased danger for the subjects of uric acid gravel or stone. An estimation of the rate at which a given specimen deposits its uric acid is of value in such cases. Where calculus is suspected the urine should be examined for xanthin and cystin. *Oxaluria*.—Any tendency to this is generally discovered during the microscopical examination by the presence of large numbers of calcium

oxalate crystals, but a quantitative determination of oxalic acid may be of importance; many obscure lumbar pains associated with nervous symptoms, are found to have no objective accompaniment other than oxaluria of high grade (V. Jaksch and others). Diabetics may show marked oxaluria when sugar is for the time absent from the urine. *Peptonuria*.--The proof of the presence of peptone is frequently of great value in the diagnosis of deep-seated suppuration. To make an examination for this constituent not less than 10 or 12 ounces are required. Lastly in cases of *Suspected Poisoning*, concealed morphia habit and the like, the detection of such toxic substances in the urine is of obvious importance.

SPUTUM.

The more solid portion of the expectorated material is best adapted for examination. In order to obtain this it is well when possible to collect the sputum in a covered spittoon for 12 hours, and to select the denser portion. This should be sent in a small clean wide-mouthed bottle, such as those provided by the Association for the purpose, and should not be mixed with any preservative fluid.

It should be borne in mind, when the presence of the *Bacillus Tuberculosis* is suspected, that one negative result does not disprove the diagnosis of Phthisis. The breaking down of a tuberculous focus may bring about the presence of bacilli in sputum pronounced free from them a short time before. It is well therefore in cases of suspected Tuberculosis when a negative result is reported, to have two or three examinations made at short intervals.

When a special report is required on the general microscopic characters of the sputum or upon the

presence of organisms other than the *Bacillus Tuberculosis*, a request should be made to that effect, so that particular attention may be directed to the subject.

DIPHTHERIA.

For Bacteriological examination in suspected cases of Diphtheria, portions of the exudation may be forwarded to the Laboratory, or the medical attendant may himself make the culture directly from the suspected case by means of the apparatus provided for the purpose by the Association.

If it is desirable to send a portion of the exudation, this should be removed by means of forceps, a spatula, or similar instrument, sterilized either by heating to redness in a spirit flame, or by boiling in water for a few minutes. The exudation thus removed should be placed in a perfectly clean wide-mouthed bottle without any preservative.

In most cases the apparatus provided by the Association will be found suitable for this examination. It consists of a specially prepared culture tube, and a sterilized swab for making the inoculation, enclosed in a metal box. This apparatus is readily used, and is especially serviceable when the amount of membrane is small or difficult to detach; or when there is no visible membrane, as in the case of a very early inflammation of the throat, in the laryngeal variety of the disease; or when it is desired to ascertain the duration of the infectious period after the disappearance of the membrane.

Sets of apparatus, accompanied by printed directions for use, will be forwarded immediately upon application.

All cases of Diphtheria are considered "urgent," and a telegraphic report is sent as soon as the diagnosis is clear, usually in 26 hours after the receipt of the material,

DRINKING WATER.

CHEMICAL ANALYSIS.—For this purpose not less than a Winchester quart of the suspected water should be sent for examination.

The bottle should be thoroughly cleaned by rinsing with strong sulphuric acid and afterwards several times with water—preferably with the water of which a sample is to be examined. The bottle should be securely stoppered. A suitable bottle, properly cleaned and packed in a basket will be sent on application to the Secretary.

The extent of the chemical examination usually made and the cost thereof are indicated in the scale of charges.

BACTERIOLOGICAL EXAMINATION.—The Association will also test the quality of water from the Bacteriological point of view, by the enumeration of micro-organisms present.

For this purpose it is advisable to obtain the water from the source as directly as possible, *e.g.*, in a water supply immediately below the filter beds. The water should be received into a carefully sterilised glass-stoppered bottle. As the organisms increase in number with great rapidity in water at ordinary temperatures, the sample should be sent to the Laboratory as expeditiously as possible.

When this examination is contemplated, it is desirable that the Secretary should be informed of the fact.

If it is thought necessary to obtain a report as to the character of the organisms present, a more extended investigation will be necessary; before proceeding to such an examination the opinion of the Directors should be ascertained as to the advisability of the proposed investigation.

The Association is also prepared to undertake other

Bacteriological investigations. As the precautions necessary to obtain trustworthy results require to be carried out carefully, it is requested that the Secretary be informed of those which have been taken. If desired, instructions will be sent for the conduct of the preliminary stages on the character of the required investigation being explained.

HISTOLOGICAL EXAMINATIONS.

TUMOURS AND OTHER TISSUES FOR HISTOLOGICAL EXAMINATION.—Place in the bottle of preservative fluid provided for the purpose a piece of the affected tissue, *not exceeding one inch in length and half-an-inch in thickness*. In the case of tumours, select from the edge of the new growth, and where possible include the adjacent healthy structure in the section. Those parts of a tumour in which caseous or other degenerative changes exist should be avoided. The most suitable fluid for such specimens consists of equal parts of methylated spirits and water. When an immediate report of the nature of a tumour is required, a portion of the growth in its fresh state should be sealed up in gutta-percha tissue or wrapped in lint wetted with water, placed in an empty bottle, and tightly corked. It can then be examined by fresh sections, or rapidly hardened, cut, and stained. Though this method serves a very useful purpose for speedily determining the nature of a suspected growth, yet it must be remembered that the results are never so satisfactory as when the tissue has been slowly fixed and embedded—a process that involves a delay of at least ten clear days. It is particularly requested that when a rapid examination is desired, a statement to that effect be made on the label of the bottle, in the absence of which the longer method of hardening will be adopted.

Delicate tissues such as *brain* or *spinal cord* should not

be placed in spirit. Satisfactory results are best ensured by hardening small fragments of the diseased tissues in Müller's fluid, or in a very weak solution of bichromate of potassium. *Eyes* should be dealt with in the same manner. It is well to prick the eye with a needle in several places to allow the hardening fluid to reach the interior of the organ.

MUSEUM PREPARATIONS, &c.

Specimens obtained post-mortem, or removed by operation, may be sent for pathological examination. A full report on the morbid anatomy of the specimens suitable for publication will be forwarded. If desired, they will be dissected, the important features displayed, and the tissues permanently mounted in suitable glass jars, so that they may be preserved in a museum, or exhibited at a medical society. Such preparations should be well washed with cold water to remove the excess of blood, then wrapped in cloths saturated with perchloride of mercury solution, and despatched with as little delay as possible, in order that the investigation may be begun before the morbid appearances have been destroyed by decomposition of the tissues. To obtain a satisfactory permanent preparation it is very important that the tissues or organs should *not* be placed in methylated spirit immediately after removal, because they are liable thus to become hardened in the least advantageous position.

BLOOD.

THE EXAMINATION OF BLOOD.—Careful experiments conducted on behalf of the Association have shown that it is possible to transmit blood to the Laboratory for enumeration of the corpuscles and estimation of hæmoglobin. Special apparatus for this purpose will be sent on application, accompanied by all instructions for its use.

SCALE OF CHARGES.

SPUTUM.

SPUTUM.				£	s.	d.
Presence of Tubercle Bacilli Report	2	6	
		Slide and Report	...	3	6	
Other Micro-Organisms	...	Report	...	3	0	
		Slide and Report	...	4	0	
General Microscopical Exam-						
ination	Report	...	5 0
				Slide and Report	...	6 0
Lung Tissue	Report	...	4 0

URINE.

Qualitative Examination for Blood, Albumen and Sugar	3	6
Qualitative Examination for Blood, Albumen and Sugar, with Microscopic Examination of Deposit	5	0
Microscopic Examination of Urinary Deposit ...	3	6
Quantitative Estimation of Sugar, Albumen, Uric Acid, or Urea each	2	6
Ehrlich's Typhoid Reaction	2	6
Spectroscopic Examination of Urine for the "Pernicious Anæmia" Band	2	6
Tubercle Bacilli or Gono- cocci in Urine, each ... Report	5	0
Report and Slide ...	6	0
Indican	2	6
Peptones	5	0
Qualitative Examination of Calculi	10	6

BLOOD.

Enumeration of Red Discs	5	0
Estimation of Hæmoglobin	5	0
Estimation of proportion of Leucocytes to Red Corpuscles	5	0

PUS.

	£	s.	d.
Tubercle Bacilli Report	2	6	
Slide and Report ...	3	6	
Gonococci and Actinomyces Report	4	0	
Slide and Report ...	5	0	

VOMIT AND FÆCES.

Presence of free Hydrochloric Acid in Vomit ...	2	6	
Microscopic Examination	3	6	

HAIR AND SKIN.

Examination for the Parasite of Ringworm, Favus, Tinea Versicolor, Erythrasma, each	2	6	
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TUMOURS AND DISEASED TISSUES.

Simple Histological Exam- ination Report	3	6	
Slide and Report ...	5	0	
Search by Special Stains for Micro-organisms of Tubercle, Anthrax, or Actinomyces, each			
Slide and Report ...	5	0	
Brain and Nerve Tissue, Special Stains Slide and Report ...	7	6	
Structures of the Eye... .. Slide and Report ...	7	6	

CULTIVATION EXPERIMENTS.

Bacillus Diphtheriæ in Membrane Report by Telegram	7	6	
Anthrax Bacillus in Serum or Blood Report by Telegram	5	0	

POST-MORTEM EXAMINATIONS.

An Attendant experienced in the mechanical work will be sent to assist Medical Practi- tioners at Autopsies. Fee if within five miles of London Bridge	10	6	
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Above this distance an extra charge of 6d. for each additional mile will be made. These charges include railway fare. The Attendant will provide Instruments and all necessary apparatus.

DRINKING WATER.

Chemical Analysis consisting of the Quantitative Determination of total Solid Residue, Chlorine, Nitrates, Free and Albuminoid Ammonia, Oxygen required, Hardness (total), and Qualitative Tests for Nitrites, Lead and Copper	1	11	6
If two or more samples sent by the same person at one time, each... ..	1	1	0
Bacteriological Examination, Enumeration of Micro-organisms present... ..	1	11	6
Presence of special Micro-organisms, from... ..	3	3	0

POISONS.

Detection of Poisons in Articles of Food and in Vomit. METALLIC POISONS only, including Antimony, Arsenic, Barium, Lead, Mercury	10	0
Strychnine, Brucine, Morphine	15	0
Hydrocyanic Acid (or Alkaline Cyanides), Oxalic Acid, Mineral Acids or Caustic Alkalies, Phosphorus	15	0
Detection of any or all of the above	2	2 0
Examination for one specified Poison in the above group	10	6
Examination of Wall paper or of Fabrics for Arsenic, each	7	6

FOOD ANALYSIS.

Analysis of Milk for Quality	10	6
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PACKING BOXES.

Each containing One dozen bottles for Sputum
 or Tissues for Histological Examinations
 and Half-a-dozen bottles for Urine, with
 labels and postal packages 5 0

MODES OF PAYMENT.

Practitioners may either forward the amount of the charge for each examination with the Specimen by crossed Postal Order, or they may send a larger sum by Cheque which will be credited to their account, notice being sent to them when the sum is exhausted.

Members may if they prefer it have quarterly accounts furnished of the Association's charge for work done on their behalf.

A discount of 15 per cent. from the scale of charges is allowed to Provincial Hospitals and Local Sanitary Authorities.

LIST OF SUBSCRIBERS.

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