activity is no doubt the presence of bodies which we call metabolic, which are shed into the tissue spaces by the active cells; the cause of the similar phenomena in the case of inflammation is the presence of bodies which we call toxic in these same spaces. Whether a scientific truth underlies the apparent similarity depends upon the, as yet unascertained, relation of these two classes of bodies. In the meantime so long as we have anything to learn from such comparisons they are worth drawing, and I hope in my next lecture to deal with a comparison which is at least something more than a coincidence.

REFERENCES.

¹ Recent Researches in Physiology. ² Report of the British Association. ³ A. V. Hill, *Journ. of Physiol.*, xlii, p. 23. ⁴ Weizsäcker, *Journ. of Physiol.*, xlviii, p. xxxviii. ⁵ Weizsäcker, *Pflüger's Archiv*, cxli, p. 457. ⁶ Fletcher and Hopkins, *Journ. of Physiol.*, xxxv, p. 296. ⁷ Loewy and Caspari, *Biochemische Zeitschr.*, xxvi, p. 405. ⁸ Oinuma, *Journ. of Physiol.*, xliii, p. 364; Barcroft and King, *Journ. of Physiol.*, xxxix, p. 374. ⁹ Barcroft and Kato, *Proc. Roy. Soc.*, 1915 (in press). ¹⁰ Back, Cogan, and Towers, *Proc. Roy. Soc.*

EPIDEMIC CEREBRO-SPINAL FEVER:

THE PLACE OF THE MENINGOCOCCUS IN ITS ETIOLOGY.

A BACTERIOLOGICAL STUDY.

(Interim Report.)

BY

EDWARD C. HORT, F.R.C.P. EDIN.,

DIRECTOR OF THE CONSTANCE TROTTER RESEARCHES, AND PHYSICIAN TO THE ADDINGTON PARK WAR FEVER HOSPITAL;

C. E. LAKIN, M.D., M.R.C.P.,

ASSISTANT PHYSICIAN TO THE MIDDLESEX HOSPITAL;

AND

T. H. C. BENIANS, F.R.C.S.,

PATHOLOGIST TO THE PRINCE OF WALES'S HOSPITAL.

(From the Bacteriological Laboratory of the Addington Park War Fever Hospital.)

In a preliminary note on the bacteriology of epidemic cerebro-spinal fever we recently recorded the following facts:¹

1. That from the blood, cerebro-spinal fluid, and urine of acute cases we had frequently isolated, and as far as possible identified, the so-called meningococcus of Jaeger.

2. That from the filtrate of a fresh catheter specimen of urine from a severe case we had obtained a slight growth, a single colony of which was composed of the following morphological types:

- (a) The meningococcus of Jaeger.
- (b) The meningococcus of Weichselbaum.
- (c) A Gram-negative rod-shaped granulating organism, each granule consisting of a pair of cocci with flattened opposed surfaces. This organism for convenience of reference will be referred to as the "biscuit bacillus."
- (d) Various Gram-positive forms.

3. That in stained preparations from deposits of fresh catheter urine from acute cases with fever we had sometimes found:

- (a) Gram-negative cocci, lying free in pairs and tetrads, and morphologically indistinguishable from the meningococcus of Weichselbaum.
- (b) Clusters of much smaller Gram-negative diplococci.
- (c) Minute and large Gram-negative bacilli.
- (d) Various Gram-positive forms.

In the same note we also discussed the unsatisfactory nature of the epidemiological and bacteriological evidence usually relied on by those who consider that the meningococcus of Weichselbaum is the primary infective agent in epidemic cerebro-spinal fever.

As a result of these observations, themselves suggested by recent bacteriological work in typhus fever, it was suggested by one of us (E. C. H.) that the *Meningococcus intracellularis* might prove to be merely a late non-infective phase in the life-history of the true infective agent, and that for reproduction of the disease this must be present in its earliest forms.

According to this theory the earliest phases might lie outside the range of vision, in which case their morphology would be indeterminable, and it would be impossible to say whether the meningococcus of textbook fame is derived from a coccal ancestor or not. On the other hand, the earliest phases of the causal organism might lie within the range of vision, in which case it should be

possible to determine whether the meningococcus is always a coccus, or whether it is derived from bacillary ancestors. In the latter event only could true pleomorphism be proved, though as regards infectivity it would be immaterial whether the earliest phases were coccal or not, provided that the relatively large diplococcus of Weichselbaum were incapable of reproducing the disease. And this appears from animal experiments to be the case.

Since the publication of our first note we have repeated in other cases the observations there quoted, and have obtained the same essential results. We now, however, wish to record further experiments, with special reference to the question whether a filter-passing organism is or is not present in the blood, cerebro-spinal fluid, urine and naso-pharyngeal secretion of acute cases, leaving the question of its infectivity to animals to a later occasion.

The following observations are selected from a large number of experiments, and are admittedly incomplete owing to the absolute necessity for control microscopical examinations at every step, and the heavy expenditure of time and labour involved.

CEREBRO-SPINAL FLUID.

Case I (E. C. H.).

A specimen of cerebro-spinal fluid was obtained from an acute case, death ensuing forty-eight hours after lumbar puncture. A slope of inspissated serum was inoculated from the centrifuged deposit of the fresh fluid, and gave, after incubation for forty-eight hours, a good growth of Gram-negative meningococcal organisms. Further identification was not possible owing to pressure of work, but *post-mortem* examination by one of us (C. E. L.) proved the case to be one of sporadic cerebro-spinal fever with meningitis.

Post-mortem Notes.

An examination of the body was made twenty hours after death, and showed the characteristic appearances of a case of cerebro-spinal fever. A swab taken from the nasopharynx by West's method showed the presence of a Gram-negative coccus, but whether this was the meningococcus or *Micrococcus catarrhalis* was not determined. On removal of the calvaria the dura mater exhibited a slight degree of vascular injection, and when this membrane was stripped off creamy pus was found ascending to the vertex along the course of the cerebral vessels and extending between the convolutions of the brain. At the base the exudate was collected around the optic chiasma, the tuber cinereum, the crura, and the ventral aspect of the pons, while posteriorly it was found upon the upper surface of the cerebellum. The tympanum on each side and the ethmoidal sinuses were laid open, but no sign of disease was disclosed.

On cutting into the lumbar portion of the spinal dura mater a quantity of purulent fluid escaped, and a creamy purulent exudate was observed lying upon the posterior aspect of the cord in the dorsal and lumbar regions. No pus was found upon the cervical portion of the cord. It was noticed that while the consistence of the lumbar and dorsal segments of the cord was markedly diminished, that of the cervical portion was still firm.

Examination of the viscera afforded little indication of morbid change. There was slight cloudy swelling of the kidneys, and fatty change was commencing in the liver. The lungs were congested. The spleen was not enlarged; its cut surface was smeared over two nasagar plates, and from these a growth was obtained of *B. coli*, streptococci, and a Gram-negative coccus.

The remainder of the fluid not required for centrifuging was incubated for one night, and films made from loopfuls of the uncentrifuged incubated fluid showed a few Gram-negative cocci, both free and intracellular, a film from the deposit of the fresh unincubated fluid showing intracorpuseular organisms only. Three c.c.m. of the cerebro-spinal fluid which had been inoculated for one night were then diluted with twice the volume of autoclaved normal saline made with water previously filtered at low pressure through a new Chamberland bougie. After sterilization in the autoclave the saline was again thoroughly boiled. The diluted cerebro-spinal fluid was then passed, by the aid of a medium exhaust, through a new Berkefeld filter. (The methods employed for assembling, sterilizing, and testing all filters used in these experiments will be detailed in a separate note.) On the completion of filtration, which lasted twenty minutes, the filter was removed from the filter flask through a large spirit flame, and 2.0 c.c.m. of the filtrate were taken up, still through flame, in a sterile Pasteur pipette guarded with wool. The point of this was again flamed, and the contents of the pipette were slowly discharged under the lid of a

nasgar plate, tested for sterility by previous incubation for three days. The inoculum was finally spread over the surface of the medium with a sterile glass rod. Examined after incubation for forty-eight hours the plate showed isolated semitranslucent colonies of a greyish colour, with stippled surfaces and well-defined margins, as seen under a low-power lens. One of these colonies contained Gram-negative diplococci resembling meningococci and Gram-negative "biscuit bacilli." After incubation for another period of twenty-four hours a fine semiconfluent growth of extremely minute transparent colonies was also seen, the growth giving a bluish haze. Under the lens each colony near the edge of the growth was greyish in colour, showed a stippled surface and was irregular in outline. Stained films from the central bluish haze, in which the colonies were too small to be seen with the naked eye, showed

- (a) Gram-negative diplococci indistinguishable from the meningococcus of Weichselbaum.
- (b) Slender Gram-negative bacilli.
- (c) Gram-negative "biscuit-bacilli."
- (d) Gram-negative and Gram-positive diplobacilli. Many of these were oat-shaped; in others one-half of the organism was coccal, the other half being bacillary in form.

Attempts to isolate individual types (a), (b), (c) by the method of dilution failed. In first subculture Gram-negative forms were seen, but disappeared in subsequent cultures. On the original plate the growth was easily detached, and emulsified freely. The organisms cultivated from the filtered cerebro-spinal fluid in this case corresponded well with the organisms found in a single colony cultivated from the filtered urine of the case we described in our last note.

We now return to the unfiltered cerebro-spinal fluid, the various events in its laboratory history being tabulated as follows:

EXAMINATION OF CEREBRO-SPINAL FLUID.

Fresh Fluid.

Deposit shows: (a) Intracorpuseular Gram-negative diplococci. (b) No free organisms.

Incubation 24 Hours.

Film from uncentrifuged deposit shows: (a) Intracorpuseular Gram-negative diplococci. (b) A few free organisms of the same morphology.

Incubation 48 Hours.

Film from uncentrifuged deposit shows: (a) Enormous numbers of free Gram-negative diplococci. (b) Pus cells undergoing autolysis.

Incubation 72 Hours.

Film from uncentrifuged deposit shows: (a) Large numbers of free Gram-negative diplococci. (b) A few small clusters of extremely minute Gram-negative organisms of indeterminate morphology. Some clusters contain one or more well-stained normal sized diplococci. At first sight these clusters suggested masses of degenerated meningococci. Further examination, however, suggested minute organisms on the point of growing into the range of vision.

Incubation 116 Hours.

Film from uncentrifuged fluid shows a large number of large clusters composed of definite Gram-negative organisms, minute coccal and bacillary forms being seen with a 1.5 apochromatic lens.

EXAMINATION OF SOLID MEDIA.

Inspissated serum inoculated from centrifuged deposit.

Inspissated serum shows slight growth. Nasgar plate A inoculated from incubated cerebro-spinal fluid.

Inspissated serum shows good growth of Gram-negative diplococci. Nasgar plate A no colonies. Nasgar plate B inoculated from incubated cerebro-spinal fluid.

Nasgar plate A shows minute greyish colonies, single colonies showing small Gram-negative and Gram-positive diplobacilli.

Note.—After incubation of the cerebro-spinal fluid for 48 hours a slope of ascitic-glucose-agar was inoculated. This gave a growth of a Gram-negative bacillus, behaving in a similar manner to the organism described in Case vi (v. below). Nasgar plate B no colonies. Nasgar plate C inoculated from incubated cerebro-spinal fluid.

Nasgar plate B no colonies. Nasgar plate C no colonies. Nasgar plate D inoculated from incubated cerebro-spinal fluid.

EXAMINATION OF CEREBRO-SPINAL FLUID.

Incubation 168 Hours.

Observations of incubated cerebro-spinal fluid now discontinued.

EXAMINATION OF SOLID MEDIA.

Nasgar plates C and D found to be contaminated with spore-bearing organisms covering the medium. Nasgar plate B (2B₁) shows extremely minute colonies, invisible to the naked eye, which were easily detached and emulsified. Films showed: (a) Gram-negative diplococci; (b) Gram-negative "biscuit bacilli"; (c) clusters of minute cocco-bacillary organisms; (d) Gram-positive forms.

Unfortunately, no normal cerebro-spinal fluid was available for subculture from the incubated infected cerebro-spinal fluid; and in this case, therefore, complete evidence could not be obtained by subculture of multiplication of the minute cluster-forming organisms seen in films prepared from the unfiltered unincubated fluid.

Case II (E. C. H.).

Cerebro-spinal fluid from a severe case, which subsequently proved fatal, was incubated for forty-eight hours and a film was then prepared from loopfuls of the uncentrifuged fluid. This showed:

- (a) Enormous numbers of Gram-negative diplococci, morphologically indistinguishable from the meningococcus of Weichselbaum, the flattening of the opposed surfaces being unusually distinct.
- (b) A few Gram-negative bacilli.
- (c) Gram-positive organisms, otherwise meningococcal in form, the flattening of the opposed surfaces being again very distinct.

In a film prepared after another twenty-four hours the same appearances were seen, except that only a few Gram-negative bacilli were found in the incubated fluid. A nasgar plate inoculated after incubation for the first period of twenty-four hours showed in seventy-six hours yellow colonies and a bluish haze composed of colonies invisible to the naked eye. With a low-power lens these small colonies were greyish, with stippled surfaces and slightly irregular outlines. A film from a single large yellow colony showed Gram-negative rounded diplococci of the *cinereus* type, whilst a film prepared from the bluish haze showed extremely minute Gram-negative diplococci mixed with larger Gram-negative organisms indistinguishable from the meningococcus. Attempts to isolate these completely failed. Gram-positive forms were also present.

After incubation of the cerebro-spinal fluid for eleven days no meningococci could be seen, in accordance with our general experience that the first crop of meningococci disappear from incubated cerebro-spinal fluid within four to five days of its collection. Examined, however, on the twelfth day, large numbers of extremely minute, well staining Gram-negative cocci and diplococci, mixed with Gram-positive members, were to be seen in films prepared from the uncentrifuged fluid. Many of the forms were so minute as to be scarcely recognizable as organisms without the aid of a 1.5 mm. apochromatic lens and a No. 8 ocular.

Examination of the next three cases, which are still being studied, was carried out in the following manner. From the centrifuged fluid, as soon as possible after recovery from the body, films were made, and nasgar, blood-agar, and glucose-ascitic-agar were inoculated from the deposit. The remaining uncentrifuged cerebro-spinal fluid was then incubated for twenty-four hours, after which time further films and cultures were made, the whole process being repeated on successive days.

Case III (T. H. C. B.).

FILMS DIRECT FROM THE FLUID.

(a) Fresh Fluid.

Many leucocytes show intracellular Gram-negative organisms resembling meningococci; also a few Gram-negative organisms of diplobacillary form.

CULTURES FROM THE FLUID.

Typical meningococci in culture and in films.

FILMS DIRECT FROM THE
FLUID.

- (b) *One Day's Incubation.*
Same as above, but meningococci much more numerous.
- (c) *Two Days' Incubation.*
Gram-negative debris; no formed elements seen.
- (d) *Three Days' Incubation.*
Degenerating pus cells and Gram-negative diplococci seen.
- (e) *Four Days' Incubation.*
Gram-negative debris seen; no formed elements seen.

CULTURES FROM THE
FLUID.

A few scattered colonies of typical meningococci in culture and in films.

No growth.

No growth.

No growth.

Case IV (T. H. C. B.).

- (a) *Fresh Fluid.*
Many leucocytes and numerous Gram-negative, intra- and extra-cellular diplococci.
- (b) *One Day's Incubation.*
Enormous numbers of meningococci, principally extracellular. Pus cells degenerating.
- (c) *Two Days' Incubation.*
Gram-negative granular substance in clumps.
- (d) *Three Days' Incubation.*
Gram-negative granular material. Also (a) A few definite Gram-negative diplococci. (b) Large Gram-positive cocci in groups.
- (e) *Four Days' Incubation.*
Gram-negative granular material, and degenerating pus cells. Also (a) Gram-negative diplococci. (b) A group of large Gram-negative cocci.

Abundant growth of typical meningococci.

Free growth on glucose-ascitic agar. Films show a small Gram-negative coccus in pairs and groups.

No growth.

Abundant white growth on glucose-ascitic agar of Gram-positive cocci in groups and masses; often in pairs and definitely flattened. One or two Gram-negative forms.

Same as in (d).

Case V (T. H. C. B.)

- (a) *Fresh Fluid.*
Pus cells and numerous meningococci, both intracellular and free.
- (b) *One Day's Incubation.*
Appearance as in (a).
- (c) *Two Days' Incubation.*
Débris entangling meningococci.
- (d) *Three Days' Incubation.*
Gram-negative debris entangling a few meningococci. Also Gram-positive bacilli suggesting diphtheroids.
- (e) *Four Days' Incubation.*
Gram-negative debris. Also (a) Clumps of Gram-negative cocci; several of the cocci are typically flattened in their opposed surfaces, when in pairs. (b) Numerous Gram-positive organisms suggesting diphtheroids.

Typical meningococci; abundant growth.

A few colonies of meningococci (? films).

No growth.

Growth of Gram-positive organisms suggesting diphtheroids.

Growth same as in (d).

Case VI (T. H. C. B.)

In this case films from centrifuged fresh cerebro-spinal fluid showed pus cells containing Gram-negative cocci. These were also lying free in pairs and groups. There were also present numerous small, slender Gram-negative bacilli. Cultures on blood-agar showed numerous dew-drop colonies. In film preparation from these only meningococcal forms were present. The uncentrifuged remainder of the cerebro-spinal fluid was incubated for three days. The centrifuged deposit of this now showed short Gram-negative bacilli, each bacillus presenting a central constriction, which in many cases gave the impression that the organism was an elongated diplococcus. There were also numerous single Gram-negative cocci and a few Gram-positive larger diplococci. Cultures from this deposit on nasgar produced a growth of small, rounded

colonies with irregular margins and finely granular surfaces, when viewed with a low-power lens. These colonies gave a marked bluish sheen by transmitted light. Films showed short, stout, Gram-negative bacilli, with a central constriction; where two lay side by side the appearance was that of a tetrad. This organism gave slight acidity in glucose, but did not ferment lactose, saccharose, maltose, or mannite. It did not alter litmus milk; did not grow on gelatine at 22° C., and gave a very slight, pale growth on agar. The organisms showed marked oscillatory movements in a hanging-drop preparations. From a second specimen of cerebro-spinal fluid withdrawn from the same case one week later, an organism with identical morphological, cultural, and biochemical reactions was obtained.

BLOOD.

First Case (E. C. H.).

Six c.cm. of venous blood were collected from a severe case of cerebro-spinal fever in which a successful cultivation of Weichselbaum's meningococcus had been made from the cerebro-spinal fluid. The blood was discharged direct from the collecting syringe into a sterile flask closed with a rubber cork, and containing 50 c.cm. of a sterile 1.2 per cent. solution of sodium citrate in filtered tap water. The flask and its contents were autoclaved before use. Within two hours of collection 6 c.cm. of citrated blood were withdrawn from the flask by perforation of the rubber cork, the collecting needle and syringe being thoroughly sterilized before use. The specimen of citrated blood abstracted from the flask was then diluted with five to six times its volume of autoclaved normal saline, and about 5 c.cm. of the mixture were then filtered through a new Berkefeld bougie. The filter flask and its contents were then incubated for forty-eight hours. At the end of this time the previously clear filtrate was markedly turbid, and films prepared from the uncentrifuged filtrate showed great numbers of Gram-negative diplococci, indistinguishable from the meningococci of Weichselbaum. A nasgar plate previously tested for sterility was inoculated with the filtrate, but in spite of the heavy infection of the filtrate the plate showed no growth within the limits of observation (six days). A second nasgar plate inoculated from the filtrate after another twenty-four hours of incubation also remained sterile, as did a third plate inoculated from the filtrate after forty-eight hours. A fourth plate, however, inoculated after seventy-six hours' incubation of the filtrate, showed numerous minute colonies. These colonies contained minute Gram-negative diplococci and small Gram-negative bacilli. The bacilli readily took up the counter-stain (neutral red), but the cocci refused this, as well as a counter-stain of dilute fuchsin, being only brought into view in fresh films after counter-staining with carbol fuchsin. The fresh urine of this case was inoculated on to nasgar plates, and after incubation for five days numerous minute colonies were seen, containing Gram-negative diplococci mixed with Gram-negative bacilli, resembling the "biscuit bacilli." In subculture these did not survive.

Second Case (E. C. H.).

A specimen of venous blood from a fatal case was collected two days before death, and was received into citrate and filtered as described above. The filtrate was clear, and remained so for twenty-four hours at blood temperature. After incubation for an additional twenty-four hours the filtrate was turbid, and became progressively so. Stained films from loopfuls of the filtrate showed, however, no organisms, even after centrifuging. Only Gram-negative debris was present, suggestive of broken-down organisms. A nasgar plate, tested for sterility by previous incubation, was inoculated with 2.0 c.cm. of the filtrate, and was incubated for forty-eight hours. The plate then showed a small number of isolated semitransparent colonies. Single colonies gave in stained films a mixture of minute Gram-negative bacilli. A subculture from one of these gave on the following morning a good growth of small colonies, single colonies now showing Gram-negative and Gram-positive bacilli. Meanwhile the filtrate had been continuously incubated, and on the fourth day film preparations showed large numbers of clusters of what appeared to be very minute Gram-negative organisms of indistinguishable morphology. A subculture of this

into a filtered specimen of normal human blood in saline showed in forty-eight hours a growth suggesting involution forms, which were rounded, ovoid, and dumb-bell shaped. Gram-negative and Gram-positive forms were both present. A control specimen of filtered normal blood in saline gave no organisms. During this period of forty-eight hours the incubated filtrate was examined twice, and the clusters of indeterminable morphology at the end of this time appeared to have broken up into very minute Gram-negative diplococci, many of them showing flattened opposed surfaces. They refused, however, to stain with dilute fuchsin, and could only be demonstrated by immersion in carbol-fuchsin. After incubation for a further period of forty-eight hours enormous numbers of Gram-negative diplococci of varying size were present in the filtrate, and now stained readily with dilute eosin or fuchsin or neutral red. A subculture on nasgar, inoculated at the beginning of this period of forty-eight hours, gave after incubation a profuse growth of extremely minute greyish colonies, with stippled surfaces and irregular margins. In film preparations minute Gram-negative diplococci were seen in pairs and tetrads mixed with Gram-positive forms of the same small size. In both flattening of the opposed surfaces was well marked. At the end of this period of forty-eight hours fresh subculture from the filtrate was made, the plate showing after forty-eight hours in the incubator a thin bluish haze and large numbers of semi-confluent greyish colonies. Films made from the haze and from the isolated colonies showed Gram-negative diplococci with flattened opposed surfaces, Gram-positive forms being also present. The fresh urine of this case was also filtered, but through a new Chamberland F bougie, the filtrate being enriched by secondary filtration through the same bougie of normal human blood in saline. After incubation for one night films prepared from the filtrate showed minute Gram-negative organisms of indeterminable morphology, rounded Gram-negative diplococci, Gram-negative bacilli, and Gram-positive forms.

We are fully alive to the fact that all bacteriological experiments involving the use of filters must be scrutinized with the greatest care, whether the primary object of experiment is determination of the presence or absence of filter-passing organisms, or of the occurrence of a genuine pleomorphism. And we also recognize that to establish a true relationship between the various organisms (excluding the gonococcus) which present a family likeness to the meningococcus of Weichselbaum, itself no fixed type, is an extremely difficult matter. Finality in attempting to bring into line the various types of organism we have constantly met with in our meningitis work is, in fact, impossible at present. And this particularly applies to the thesis whether a particular type may present both Gram-positive and Gram-negative phases, as appears to be the case with the meningococcus of Jaeger.

Contaminations, in short, in experiments of this nature are a perpetual menace to accurate observation, and it is well to remember that their presence or absence is always easier to assert than to prove. None the less, the consistent employment of a scrupulous technique justifies, we believe, an appeal for independent and searching inquiry. And in the meantime we think we have produced sufficiently good evidence to justify further study, with particular reference to the following points:

- (a) The presence or absence of a filter-passing organism in the body fluids of acute and subacute cases of cerebro-spinal fever.
- (b) Its relationship to the disease.
- (c) Its relationship to the meningococcus of Weichselbaum and to the various types of organism we have isolated from the body fluids, especially when these are incubated before subculture.
- (d) The reciprocal relationship of these latter organisms to each other.

We desire to record our thanks to the following for their generous assistance in our work: Dr. F. Foord Caiger, Dr. W. J. J. Stewart, Dr. T. R. C. Whipham, and Dr. Romanes.

REFERENCE.

¹ BRITISH MEDICAL JOURNAL, March 27th, 1915.

CLINICAL LABORATORY METHODS IN
METABOLIC DISEASES.*

By ALBERT DE THIERRY MOUILLOT, M.D.,

EX-PRESIDENT, BALNEOLOGICAL AND CLIMATOLOGICAL SECTION OF
THE ROYAL SOCIETY OF MEDICINE.

NOTES ON DUFF HOUSE.

DUFF HOUSE was built by the first Earl of Fife in 1745. The architect was William Adam, and the house is designed in the same style as Wentworth Woodhouse, but in Duff House the wings planned were never built, owing, it is said, to a dispute between the Earl and his architect. The house was the residence of the Fife family until a few years ago, when the late Duke presented it, with its park of 165 acres, to the twin burghs Banff and MacDuff. The municipal authorities of these burghs let the mansion to a syndicate which opened it as a hotel. This hotel was not successful, and in 1913 the building was taken by some gentlemen who were anxious to open in Great Britain an institution for the study and treatment of certain diseases of metabolism on lines similar to those of some well-known Continental sanatoriums.

Duff House is just outside Banff, a town 50 miles from Aberdeen on the Moray Firth.

No systematic weather records except those of rainfall were taken until 1914, when Mr. A. J. Leigh, B.Sc., was appointed Meteorological Observer, but since then daily reports of rainfall and sunshine have been telegraphed to South Kensington. From these reports it would appear that the climate is decidedly good. The sunshine is the highest in Scotland, reaching in the summer as high as 37 per cent. of the possible. The number of hours of bright sunshine recorded in 1914 was 1,400. The rainfall amounted to 27.5 inches in that year, and I can testify to the fact that whilst I was in Banff, during December, 1914, and January, 1915, the weather contrasted very favourably with reports which reached me from other places. It is remarkable that the mean temperature is only 3° F. lower than that of places on the south coast, though Banff is over 600 miles north of them.

The scenery, both river and sea, is interesting, and specially brilliant sunsets were frequent during my visit. The facilities for sport are good. The shooting was excellent, and the fishing on the River Deveron is said to be good. There is an eighteen-hole golf course in the park, the soil of which is sandy, and the course, though not a first-class one, has the merit of drying quickly. Indoor the patients have the use of a full-sized billiard table, and can play card games in the lounge, and one way or another time passes very quickly there.

To the naturalist the district is specially interesting, owing mainly to the variety of bird life. The Scottish naturalist Edwards, whose interesting life was written by Smiles, lived in Banff, and made his wonderful natural history collections in the neighbourhood.

The management was fortunate in obtaining the services of a well-known and experienced chief medical officer, who has gathered round him a very keen and able staff, consisting of chemists, an x-ray specialist, masseurs, matron, and nurses.

The chemical laboratory struck me as very complete, and Mr. Leigh and his assistant, Mr. Sanders, seemed to find plenty of work to do in conducting the analyses required. The chemists have done very useful work in making analyses of many of the foods sold as suitable for diabetes. It is greatly to be hoped that this work will be published for the general information of the profession, as I know that some quite unsuitable articles of diet are often recommended for such cases.

The x-ray department, under the direction of Mr. Marxer, is also well equipped. The work done in this department is mainly screen work on patients who were having bismuth or barium meals, but a great many negatives are taken, and already a most interesting collection of plates has accumulated, showing unexpected and unusual causes of intestinal trouble, and sometimes unwished-for results of gastro-enterostomies and other short-circuiting operations. The diagrams indicating the position of the barium meal become part of the dossier of the patient.

* A paper read at Harrogate Medical Society on March 26th, 1915.