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ARTHRITIS DEFORMANS  
(ATROPHIC FORM)

With special reference to the Bacterial Content of  
the Urine and the Vaccine Therapy of the  
Disease.

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T H E S I S

----- presented -----

FOR THE DEGREE OF M.D.

---- by ----

CHARLES C. ILES.

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## DEFINITION.

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Arthritis deformans in its atrophic form (rheumatoid arthritis) is, perhaps, best defined as a chronic disease affecting many joints, principally the smaller ones. It occurs chiefly in the female sex, is due probably to the action of a toxin, and is characterised by changes in the cartilages and the soft structures surrounding the joints, thus causing great immobility and deformity.

## HISTORICAL.

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That arthritis is a disease of great antiquity is borne out by the fact that recently-unearthed bones from tombs of about 3700-1300 B.C. showed unmistakable evidence of the affection.

In examination of remains in Egypt, remains representative of all periods from early predynastic times down to the Fifth Dynasty after Christ, "the disease which showed itself with by far the greatest frequency in the bodies of all periods is rheumatoid arthritis". Virchow has left records describing the affection in bones unearthed from Pompeii.

From these remote times onwards through the Middle Ages to the present day, an almost continuous

series of historical records testifies that the disease has always been with us, and also that its clinical characters have remained unaltered through all the ages.

The aetiology and pathology of the disease have, however, been so shrouded in darkness that we find the various writers, in their information on the subject, making indiscriminate use of the terms rheumatism, gout and arthritis to designate this affection.

#### VARIETIES.

A satisfactory classification of the varieties of arthritis deformans has not yet been arrived at. As already stated, this is in great part probably due to the confusion that has existed with regard to the pathological and clinical identity of the different forms, and to the medley of inappropriate names which have been used at various times. Thus, again, we find the terms rheumatic arthritis, rheumatic gout, infective arthritis, applied to the disease.

The application of the term rheumatoid arthritis, as applied to the polyarticular variety, has become more strictly limited since Adams (1) made an attempt to differentiate the various forms of the disease.

It is now no longer possible to look upon the cases usually included under the names rheumatoid arthritis, osteo-arthritis and arthritis deformans as examples of a single disease.

This realisation that we are here dealing with a group of diseases, and not with a single affection, is in itself a great advance.

Modern research seems to confirm the opinion that the varieties of arthritis are most satisfactorily classified on a pathological basis, namely:-

Infective arthritis	e.g. gonococcal.
Atrophic arthritis	or rheumatoid arthritis
Hypertrophic arthritis	or osteo-arthritis.

Nathan (2) divides the cases into:-

1. Those that begin acutely e.g. Infectious.
2. Chronic cases e.g. atrophic and hypertrophic.

Personally, I disagree with those observers who relegate all forms of rheumatoid arthritis to the category of chronic diseases. I have seen it commence acutely, with local swelling and constitutional disturbance, and later pass into a sub-acute stage, with, finally, persistent but slow advance from joint to joint and leading gradually to more or less complete joint disability.

The term arthritis deformans is, perhaps, best used generically to include all the varieties of deforming arthritis.

Nomenclature:

Osteo arthritis, or hypertrophic arthritis, would perhaps be best restricted to the form where bone and cartilage are chiefly affected as distinguished from rheumatoid or atrophic arthritis, in which the changes occur for the most part in the synovial membranes.

Of course, it cannot be asserted that the above classification is altogether a pure category, as overlapping of the two varieties occurs, and cases of infective arthritis are doubtless included.

It is with the sub-acute form of the atrophic variety of arthritis deformans (rheumatoid or synovial arthritis) that I propose to deal chiefly in this paper.

#### ETIOLOGY.

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Various predisposing factors have been mentioned in connection with the malady, the chief of which are, perhaps, worry and shock.

In two of the cases shortly to be considered, shock certainly seemed to bear a definite relationship to the onset of the disease.

The affection shows a marked predilection for the female sex, and the women attacked are usually between the ages of thirty and fifty.

Causative:

Regarding the actual causation of the disease, nothing is accurately known.

The infectious diseases, namely, influenza, scarlet, tonsillitis, measles and pneumonia have all been assigned places as causative agents.

As Hale White (3) points out, however, extensive statistics would be necessary to prove a relationship between arthritis deformans and previous infective processes, e.g. tonsillitis and measles, as these are so common, and, moreover, the relationship would be difficult to prove.

I may here point out in passing that in only one of my patients was a history of previous influenza obtained, but in this case the attack had been a severe one.

Theories:

In the old days, the humoral theory regarding the disease had most supporters, but this ultimately gave way to a neural theory, which, in its turn, is becoming supplanted by a bacterial theory.

Nature:

It cannot be denied that a number of infections, for instance, typhoid and gonorrhoea, may bring about a condition of the joints which may closely simulate rheumatoid lesions.

In arthritis deformans, however, the infections are of unknown origin. That the disease is an

infection is also shown in a number of cases by the therapeutic results, e.g. with guaiacol carbonate.

Septic  
foci:

Recently, for a time, much attention was directed to septic conditions of the nose, mouth, gastro-intestinal tract and uterus, through the frequency with which these disorders precede or accompany the disease.

Marked improvement, and sometimes even complete recovery, has been recorded in some such cases when the septic focus has been removed.

In the series of cases to be described, the patients, with two exceptions, were free as far as could be ascertained from definite foci of suppuration. Indeed, it appears to me that, in the majority of cases, careful inquiry and examination fail to reveal any such source of infection and previous to the onset of the illness, the patient may have been in perfect health.

#### BACTERIOLOGY.

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Organismal:

For some time past, the gradual trend of opinion with regard to the origin of arthritis deformans has been in favour of a microbic theory, at least in a large number of the cases of the disease.

Investiga-  
tions:

The earliest observations in this direction were those of Schüller (4), in 1892, upon cases of the villous form of the disease. He noted, in the joint exudations and inflamed synovial membrane, the occurrence of Gram positive organisms, some bipolar staining bacilli, and other resembling diplococci in appearance. Further, he showed that cultures of these germs, when injected into the joint cavity of a rabbit, produced, within three months, an arthritis resembling that found in the human joints.

Following this, Dor (5), in 1893, and Bouchard and Charrin (6), 1891-4, noted the presence of pyogenic cocci in the joints of arthritic cases.

In 1896 Bannatyne, Wohlmann and Blaxall (7), described in this connection a small Gram negative bacillus shewing bipolar staining, and closely resembling a diplococcus. They found that this organism was present in the joints of almost all the cases of rheumatoid arthritis, and they state that it also occurred in the blood in severe cases. They failed to find it, however, in the joints of patients suffering from the osteo-arthritic form of the disease, or in joints which were the seats of other forms of arthritis.

In following up the clue Painter (8), in 1901, was unable to confirm their results.

Chauffard and Ramond (9), in 1896, isolated from joints of a case a Gram positive diplobacillus which they succeeded in cultivating only in synovial fluid, where, however, it grew readily. Inoculation experiments were unsuccessful.

Soon afterwards, in 1898, von Dungern and Schneider (10) found a diplococcus, but the fact that their patient had suffered from rheumatic fever somewhat vitiates the results of their observations.

In 1902, Poynton and Paine (11) found post-mortem, in the knee-joint of a man suffering from rheumatoid arthritis, a diplococcus which they cultivated.

The interesting feature in their investigation is, that cultures, when injected into the blood stream in rabbits, produced a severe arthritis, with osteo-arthritic changes.

Post-mortem, no cardiac lesions were found, and the diplococcus was recovered from the affected joints of the animal.

They concluded that this organism was the cause of the arthritis in the case from which it was isolated, and of the condition, produced by experiment, in the rabbit.

Hale White (12), in 1902, found, post-mortem, in a case of rheumatoid arthritis in the synovial membrane of the left knee, a Gram positive organism which could not be identified with any of the more usual cocci.

It occurred singly, sometimes in pairs, but never in chains.

When injected intravenously into rabbits it caused no effect.

Guinea-pigs inoculated subcutaneously died in nineteen days.

In 1903, Gask isolated from the joints of a case of rheumatoid arthritis, a streptococcus.

Fayerweather (13) is probably the most recent investigator in this field.

In three cases he obtained an organism from the synovial fluid and tissues of the affected joints. Inoculation experiments on rabbits produced an arthritis similar in character to that present in the joints from which the organisms were derived.

In addition to these investigations, at various times other observers, working with cases of the disease, have failed to obtain growths from the fluid of the joints.

From this short summary it will be seen that different organisms have been associated with the disease, but until the bacteriological findings have more adequate confirmation, no organism can be definitely described as being the causative agent.

#### CLINICAL FEATURES.

Premoni-  
tory: In this affection, various premonitory symptoms have been described by different observers as occurring with comparative frequency. The chief of these appear to be indefinite or cramp-like pains in the limbs, tingling, and muscular wasting. In two of my cases presently to be described, the onset of the disease was preceded by severe backache and a curious sensation likened to a feeling of cold water trickling down the spine.

Safe it is to say, however, that in many cases premonitory symptoms are conspicuous by their absence.

Onset: There is no uniformity in the mode of onset of the disease. It may commence acutely with constitutional disturbance, or begin insidiously with the swelling of the joints, the patient otherwise appearing quite well.

In the sub-acute variety, constitutional

disturbance is rarely marked at any time. There frequently is, however, a moderate rise of evening temperature, along with irritability and depression.

The pulse-rate may be continuously high, e.g. 90-100.

Distribu-  
tion:

Taking a typical case of the sub-acute atrophic form of arthritis deformans, one finds that the disease usually commences with pain and swelling of one or more of the smaller joints of the hand or foot.

In the hands, the proximal row of the interphalangeal and the metacarpo-phalangeal joints appear specially liable to become affected.

The wrists, ankles, and jaw are often early attacked, but in the case of the latter joint the symptoms are frequently transitory and intermittent.

A number of joints may be attacked in succession, and often several are affected at one time, the distribution appearing in these cases remarkably symmetrical.

Features  
of the  
joints:

In the acute stages the joints develop fusiform swellings, due, chiefly, to the thickening of their capsules and ligaments and not to excess of synovial fluid.

This swelling becomes rendered more conspicuous by the intervening wasting of the muscles which occurs.

Pain is usually present but varies in intensity in different cases and appears to be influenced by weather conditions. It is worse on movement, but spontaneous pain, when the joints are at rest, does occur, especially when the patient is just dropping off to sleep at night.

The arthritis subsides in some articulations only to occur in others, and leaving a distinct change in the contour of the joint and a diminution in its power of mobility.

In the incomplete remissions which occur, pain greatly lessens and the swelling somewhat diminishes.

The patient, nevertheless, is liable to recrudescence attacks which exactly resemble the first, and result in fresh swelling in and around the already fixing joints.

The muscles atrophy, undergo contracture and permanent shortening, causing further impairment of mobility and ultimate striking deformity. The amount of this muscular atrophy is more than can be ascribed to mere disease. It is now usually regarded as a

Muscular  
atrophy:

reflex atrophy, and it is a significant fact that the tendon reflexes are usually found to be exaggerated in those cases in which they can be elicited.

Cutaneous: Trophic changes are seen in the skin, which, in the vicinity of the joints and indeed also in other parts, becomes atrophied, pigmented and glossy, whilst tender subcutaneous nodules can sometimes be felt at a distance from the articulations.

Progress: The disease may linger in the smaller joints for some time but in a large number of cases it gradually and persistently spreads, leading to a disability that marks the disease as one of the most terrible of human afflictions.

The varieties of ultimate deformity are too varied to be described, the most common being, perhaps, the ulnar deviation of the fingers and hand.

#### MORBID ANATOMY.

Lack of Material: Our knowledge of the morbid anatomy is necessarily very incomplete, as material upon which to base a description of the changes that occur in the joints of undoubted cases of rheumatoid arthritis, especially in the active stage, is very scarce. This is due chiefly to the fact that the disease has very

little tendency to shorten life.

It appears, however, that the changes commence primarily in the softer structures surrounding the joint, and not in the cartilage and bone as occurs in osteo-arthritis. Much fibrous thickening results in the capsule and ligaments, and the synovial membrane becomes swollen and pinkish.

Effusion  
uncommon:

Effusion of fluid into joints seems to be the exception rather than the rule, although the character of the swelling around the articulations frequently suggests its presence.

Out of four joint punctures I obtained fluid in only one case, and here the amount obtained did not exceed a fifth of a cubic centimetre.

Hypertrophy of the synovial fringes frequently occurs, and may lead to the erosion of the cartilage in places, and to the formation of loose bodies.

Except in cases of long standing, erosion of the cartilages is not so pronounced here as it is in osteo-arthritis, and when present is probably merely due to pressure changes. Morton (20) however, believes that absorption of the cartilage is a marked and early change.

Bony outgrowths and lipping also are rare, especially in acute cases, and osteo-phytes, when they do occur, are usually in the form of sharp spicules.

Later  
Changes:

In very advanced cases of the disease, changes in the cartilage may be seen, and ultimately all the constituent elements of the joints may become affected by a process of atrophy.

In these cases the joints have usually become fixed and the cartilages may then undergo complete degeneration and finally disappear.

This process is to be distinguished from the softening and absorption of the cartilage and subsequent eburnation of the bone surfaces that occurs in osteo-arthritis.

In my experience, creaking on movement of the joints occurs in both conditions in the later stages, but in rheumatoid arthritis, it is probably due to the thickened synovial fringes and ligaments.

To sum up, then, this atrophic form of arthritis deformans is one of synovial membrane and capsule, rather than one of bone and cartilage.

#### DIAGNOSIS.

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Arthritis deformans in an advanced stage can rarely be mistaken for rheumatism or gout. Whilst it can hardly be doubted that some rheumatic cases which leave behind them persistent swelling of joints

are mistaken for cases of rheumatoid arthritis, yet there do not appear to be any grounds for the belief that the two conditions are associated with each other in their causal relationship.

It is only in the early cases that a doubt may exist as to the accuracy of the diagnosis.

From acute rheumatism it is differentiated chiefly by the distribution, the persistence of the articular swellings, and the inefficacy of salicylates. The age of the patient and the previous history may also be of aid in distinguishing the two affections.

In gonorrhoeal arthritis, it is the large joints e.g. the knee, that are usually affected, whilst the finger joints frequently escape.

The diagnosis between rheumatoid arthritis and other infective arthritides, e.g. syphilitic, may prove more difficult, especially in early cases of the disease. Case 4, page 50, was probably one of this latter nature.

The distinction between the atrophic and hypertrophic forms of the disease is often difficult, and I should say, in the earlier stages of the disease, often impossible, except, perhaps, by X-rays.

Nor is this to be wondered at, for we do not

know but that the atrophic form may sometimes later develop hypertrophic tendencies and vice versa, leading to a certain amount of overlapping of the two affections

#### PROGNOSIS.

Of the diseases which do not tend to shorten life there are few in which the outlook is more unfavourable.

Cases do occur, however, in which the disease, after attacking two or three joints, may become arrested spontaneously, but only too often it is slowly progressive, deforming the joints and rendering the patient a helpless invalid.

We must consider the prospects of arrest of the active stage, for if this can be achieved early, the subsequent deformity is lessened.

In chronic cases, the amount of muscular atrophy and the occurrence or otherwise of fresh joint attacks, form the best basis for a prognosis.

#### TREATMENT.

General:

The treatment is very unsatisfactory. It has been chiefly on the lines of keeping the patient

in good health with a view to increasing resistance. Fresh air, good nourishing food, and a warm dry climate are indicated.

In the acute stages, rest of the affected joints should be insisted upon, whilst later, massage, exercise, and passive movements must be encouraged.

Mucous membranes should be carefully examined for foci of suppuration, and these, if present, removed.

Spa treatment often gives much benefit when the active stage has subsided and the damaged structures threaten to become permanently deformed, whilst hot-air and electric baths have proved of great service in many cases.

Treatment by medicines is not nearly so efficacious as might be wished. Guaiacol carbonate in increasing doses, combined with Iodides and continued for months, is, perhaps, the most valuable. For the relief of pain the drug I have found of most benefit is phenacetin.

Applications to the joints in the form of liniments, &c., do not prove of much service in this affection. Methyl salicylate is one of the most frequently used.

Tuberculin has been tried on the assumption that the disease is tuberculous in origin.

For increasing the amount of mobility of

Hydro-  
therapy:

Drugs:

Local:

Special:

stiffened joints, Fibrolysin has been used, and where fixation of an articulation has incapacitated the patient, orthopaedic measures have sometimes been found necessary.

Vaccines:

The only reference that I can find to vaccine therapy in this disease is that of Painter (14). From the knee-joint of a case of arthritis deformans, an organism resembling Schüller's bacillus was isolated, cultured, and a vaccine prepared. In use, however, Painter states that the vaccines effected no considerable degree of improvement in any case.

My own experiences of this branch of treatment in the disease will be found included in the description of the various cases.

#### PERSONAL INVESTIGATIONS ON THE URINE.

It is to the urine in arthritis deformans that I wish, more especially, to draw attention in this paper. Few, if any, observers appear to have devoted much attention to the urine in this disease, except in a few isolated cases, to make bare mention of the fact that albumin was or was not present.

Albumin:

Here I may mention in passing that in all of my cases, seven in number, albumin was absent.

Bacteri-  
ology:

To the bacteriology of the urine in arthritis still less appears to have been done, and I have failed completely to find any reference in medical literature to this branch of the subject.

Along with Dr. Warren Crowe of the Yel-  
verton Clinical Laboratory I have made, for some considerable time, a study of the urine by systematic microscopical and cultural examination.

The result of over two hundred such examinations (15) revealed an unsuspected prevalence of three, apparently distinct, varieties of cocci. In addition, it was shown, that while two of these organisms occurred with comparative frequency in the urine, their presence was not necessarily associated with severe bodily ailments, in fact, the reverse was generally the case.

On the other hand, the third variety which I shall here in future refer to as the diplococcus, was, at the time of publishing the report, found in only two cases out of the two hundred, namely:

- (1) A case of nephritis with "chronic rheumatic joints".
- (2) A case of arthritis.

Moreover, in one of these cases, if not in both, the organism did not occur in pure culture, but in association with one of the varieties above described.

Subsequent systematic examination of a further series of two hundred urines, including those of seven cases of arthritis deformans, has convinced me that the diplococcus is present in this disease, and in this disease almost exclusively.

#### THE DIPLOCOCCUS:

Diplococcus present: In the urine it is found that the organism occurs chiefly in the form of diplococci, although individual cocci do occur apparently from the separation of the pairs.

Chains are never seen when the organism is present in pure culture.

In length each diplococcus measures about  $3\mu$  whilst the width at the broadest part is about  $1\mu$ . Individual cocci are somewhat longer than broad and present a lanceolate appearance.

When stained each pair may appear as a single organism, but although various staining methods were tried the presence of a capsule could not be demonstrated.

The organism steins readily with the usual basic anilin dyes and retains the stain by Gram's method. It is non motile, has no flagella and does not form spores.

METHOD OF TAKING THE SPECIMEN OF URINE.

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Ordinary specimen

In order to minimise the risk of accidental contamination of the urine the following method of obtaining the samples was adopted. The patient was carefully instructed first to cleanse the meatus and surrounding parts, a solution of 1 - 1000 corrosive sublimate being used for this purpose.

The first part of the urine was allowed to escape and the remainder was received into a large, previously sterilised specimen tube which was then closed with a sterile paraffined cork.

The name of the patient, reference number, and date were then noted on the label affixed to the tube for that purpose. In all of the cases to be considered, at least two separate specimens were examined, and in three instances the second sample was obtained by means of the catheter.

Catheter specimen

With regard to the method of taking urine samples for bacteriological examination, however, it has been my experience, based on 400 specimens taken by one or other method, to find that catheter specimens are not more reliable than those taken in the manner described above.

## MICROSCOPIC EXAMINATION OF THE SPECIMEN

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Examination The sample having been obtained, the urine was first shaken up in the tube, 2. c.c.'s were withdrawn by means of a sterile pipette and centrifuged for five minutes, at a high speed in two sterile centrifuge tubes, which for the facility of description I shall call A. and B.

From A. after centrifugalisation, the supernatant fluid was pipetted off and the deposit transferred to slopes or plates of neutral red egg, and other media.

From tube B. a certain amount of the deposit was spread on a slide as a small film, fixed by passing through the flame and stained by Gram's method.

In some cases, where the urine had stood on the bench for a few hours, centrifugalisation was found unnecessary; a mere examination of the sediment showing the presence of the organisms.

A routine practice was made of culturing the urine irrespective of the apparent absence of the germs on microscopic examination.

## METHOD OF PREPARING NEUTRAL RED EGG MEDIUM

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Neutral red egg was invariably used as a medium for primary cultural examination

Egg Medium      As the methods described in text books for preparing egg as a medium for culture gave but indifferent results, I shall describe the method finally adopted as it gave the utmost satisfaction.

One dozen eggs, representing about one hundred tubed slopes, were usually found sufficient for one preparation.

Both ends of the egg are first sterilised by thoroughly flaming them over a bunsen burner after which they are chipped lightly with a pair of long sterile sinus forceps.

The egg is then placed, broad end downwards, resting on the mouth of a previously autoclaved two litre flask.

The sterile forceps are then introduced closed, into the egg from above, carried down the yolk and lower chipped end when they are suddenly opened, thus breaking the shell and causing the contents of the egg to be evacuated into the flask.

The empty shell is allowed to remain on

the mouth of the flask to prevent the entrance of dust, until it is replaced by the next egg.

When all the eggs have thus been added to the flask, the latter is plugged with an auto-claved rubber cork, fitted with two glass tubes, one of which reaches to the bottom of the flask whilst the other merely passes through the cork.

This assists later to mix the egg and also allows of pouring out the mixture without removing the stopper.

The neutral red is added in the form of a sterile 1% watery solution, 12 c.c.'s being used for every 100 c.c.'s of the egg.

In practice no additional water was found necessary, as the medium when set, remained sufficiently moist without it.

The contents of the flask are now thoroughly shaken until a homogeneous mixture is obtained.

This is then filtered by pouring it into a large tea-strainer, resting in a glass funnel, which latter is armed with a rubber delivery tube closed by a clip.

The mouth of the funnel is covered with the lid of a petri dish to prevent the entrance of dust.

The above apparatus must, of course, have been previously fitted together and auto-claved.

The wire strainer possesses many advantages over muslin, the chief being, that if it becomes clogged, it is a comparatively easy matter to free it without risk of contamination and even if this does occur, it can readily be re-sterilised over a flame.

After filtration the mixture is run into plates and large sterile test tubes, 5 c.c.'s usually being sufficient for each tube

These are then sloped in a Hearson's Incubator, a 90° C. capsule being substituted for the ordinary one at 37° C.

This is maintained easily at 80° - 85° C for half an hour after which the medium is set at a temperature of 90° C. for half an hour.

Subsequently the tubes may be incubated for 24 hours at 37° C. to determine the sterility of the medium.

#### MORPHOLOGY OF THE ORGANISM ON NEUTRAL RED EGG

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In a urine infected with the diplococcus there appear on the egg in about 20 hours at 37° C. small round, yellowish, granular colonies. They

are somewhat raised above the surface of the medium and at the end of 28 hours begin to exhibit a low dome-shaped central elevation, surrounded by two low and broad rings at short distances from each other, the outer one forming the margin of the colony. The margin itself has therefore a smooth and rounded off look. The above appearance is typically seen in 36 hours, and the colony may now be likened to one of the pieces used in the game of draughts.

Diagnostic

Shape, imaginary section



By the time the dome and rings have appeared, but not before this, the colony becomes tinged with red and shows a crimson aureola, striking a marked contrast with the surrounding yellow medium. From this point onwards, as growth proceeds, the colony loses its characteristic shape.

It becomes irregular and flattened, and the pink colouration gradually becomes less evident and disappears, the colony again assuming a yellowish appearance.

In subcultures, the colour is taken up more rapidly and may be evident before the 28 hours have elapsed, and before the dome and rings have appeared.

According to the number of the diplococci

Colour in  
Subcultures

present in the urine, the colonies may be few and scattered, or as I have sometimes seen, almost entirely covering the slope.

Subcultures on agar from egg show a much stronger growth than when the urine is primarily cultivated on this medium.

Microscopically, a slide prepared from one of the colonies shows cocci about  $1\mu$  in size, chiefly in pairs and short chains.

Involution forms, varying in size and not so definitely Gram positive, are frequently present, especially in the older cultures.

Capsules cannot be demonstrated.

#### AGAR STROKE

Primary culture on this medium yields a slow growth. In 30 hours, more or less isolated colonies appear. They are translucent, whitish and glistening, somewhat resembling the appearance of a streptococcal growth. Subcultures from egg grow much more rapidly. Microscopically, the cocci are smaller than those grown on egg. Short chains occur and involution forms are more common.

#### AGAR STAB

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Shows a somewhat similar growth along the track of the needle.

#### GELATIN STROKE

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Growth on this medium is very slow. In 48 hours, round, whitish colonies appear. They are usually somewhat isolated.

#### GELATIN STAB

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Whitish colonies appear slowly here also, along the stab. There is no invasion of the surrounding medium and no liquefaction.

#### POTATO

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No visible growth is present.

#### NASGAR

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The growth here shows larger rounded, translucent, whitish colonies with a slightly raised centre and edges, microscopically, the cocci appear larger, and involution forms are not nearly so common. In addition to this, the chains are longer than on any other of the solid media.

## BLOOD AGAR

On this medium, made according to Schottmuller's formula, viz:- two parts blood and five parts agar, the growth strongly resembles that of streptococci.

Around each colony marked haemolysis is present.

The organisms show fairly uniform staining by Gram and the chains are rather long.

## BROTH

Uniform turbidity occurs within 36 hours and there is a somewhat granular looking deposit.

Long chains of cocci are seen microscopically.

## LACTOSE BROTH

This medium becomes uniformly turbid. Frequently, fungus-like masses of growth are seen, and these, on microscopic examination prove to be long interlacing chains of the organism. Involution forms are rare with a growth in this medium, and the organisms are somewhat larger in size.

Further culture reactions are described on the table.

## STAINING REACTIONS

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From the media, which were always standardized to medium Alkalinity, films showed that the organism would readily take up any of the basic anilin dyes.

The Gram staining was usually definitely positive, but there was a certain amount of irregularity of staining in films prepared from the less nourishing media.

With Loeffler's methylene blue and a differential stain, no polar staining was observed, the organisms appearing blue and red, chiefly the latter.

By the Zeehl-Neelson method the counter stain was taken up.

## VIABILITY.

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The organism soon dies out in culture.

Direct bright sunlight will render a culture innocuous in one afternoon, whilst a temperature of 52°.C. for half an hour has the same effect.

## AGGLUTINATION & INOCULATION

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These reactions were not investigated.

It has been shown by Gordon (16) that the most satisfactory way to differentiate the streptococci and the staphylococci is by comparing their ability to decompose with an acid reaction various chemical compounds belonging to the carbohydrate glucoside and polyatomic alcohol series respectively: also by their power of clotting milk and reducing neutral red anaerobically.

It is this method that I have employed in testing and comparing with other organisms, the diplococcus under consideration.

The sugars employed were the best obtainable (Merck's) and the solution used was that recommended by Houston, namely.

Peptone 1%

Distilled water containing lemco 1%

Sodium bicarb 0.1%

10 c.c.'s per cent of a 10% watery solution of solid litmus.

The sugar was added in the proportion of 1%.

In the preparation of the medium, care was taken that the two solutions were separately sterilised.

\* and after cooling the sugar, solution was added to that of the peptone.

It is believed that this precaution is necessary in order to prevent the occurrence in the mixture of chemical changes, which would otherwise affect the validity of the tests.

The cost of these chemically pure sugars is very heavy, and in carrying out many hundreds of tests, a saving of solution is a matter for consideration. To this end the following method was devised and ultimately adopted throughout.

Method employed:

Sterile curly pipettes were taken and by means of rubber teats a number of about twenty were filled at the same time with one of the sugar solutions, the capillary end of each pipette being then sealed.

These were then numbered and could be stored for some considerable time without danger of contamination.

To inoculate the medium a teat having a hole in one side was adjusted to the pipette, the capillary end of which was snipped off with sterile forceps and a small amount of a broth culture of the organism sucked up.

After mixing the solution by means of an

air bubble, the end of the pipette was sealed in the flame and the tube numbered with a grease pencil and incubated **capillary** end downwards.

Anaerobic cultures were made in the same way, the tube being also sealed at the loop above.

For microscopic examination of the fluid the capillary end of the tube was snipped off, a teat affixed to the other end, and a droplet of the solution put on a slide, spread, stained and examined.

In practice this method is quicker than the ordinary one, and by its means, 5. c.c.'s of sugar solution suffices for six tests, that is less than 1. c.c. for each test, a saving of more than 4. c.c.'s of fluid solution.

The tubes were sufficiently inexpensive to be discarded after use.

In testing the diplococcus in this manner it was found that the sugar reactions were remarkably constant.

The inoculations were made from broth cultures, and, in cases where the sugar result was negative, egg subcultures were made from the tube in question. And if no growth occurred, a reinoculation of a fresh tube of the sugar was performed.

This precaution was necessary as it showed

whether or not, a successful primary inoculation of the medium had been carried out.

In order to eliminate the element of accidental contamination, egg subcultures were also made when the sugar result was positive, with a view to determine that the colonies presented the typical draughtsman-like appearance, so characteristic of this medium.

Controls: Control tests in the shape of uninoculated tubes, and others consisting of Houston's litmus solution without the addition of the sugar, were performed in each series of tests.

From the various solutions, slides were prepared and stained, and the organism identified microscopically.

It will be seen then from the above and from the table following that I have differentiated the diplococcus by a series of definite tests.

? Staphylococcus: Recently it was suggested to me that the organism with which I was working might be the *Staphylococcus epidermidis albus* described by Welch (17). In referring to the original article on wound infection by this observer, I find that he describes a non motile, aerobic, and facultative anaerobic coccus, staining by the usual methods, and

by Gram, and having as its natural habitat the skin.

He believes it to be *Staphylococcus pyogenes albus* in an attenuated condition, and its cultural characters and sugar reactions confirm this view.

It is, however, slower in liquefying gelatin and in coagulating milk and less virulent when injected into rabbits than the latter organism.

In using the sugar solutions as described, it is found generally speaking, that staphylococci act on glycerin more easily than on mannite, whilst the opposite holds good for the streptococcal group.

Again, the staphylococci rarely are seen to form acids with the glucosides, e.g., salicin and coniferin.

In addition to these tests we have with staphylococci, as distinguished from streptococci:-

The reduction of nitrate to nitrite.

The liquefaction of gelatin at 22°C.

The absence of chain formation.

The more copious growth on agar at 37.

The above then, were the tests upon which I relied more particularly in my efforts to differentiate the *staphylococcus epidermidis albus* from the diplococcus.

It is well-known that the staining

properties of the staphylococci and streptococci are useless as a guide for differentiation as they all stain well with the ordinary basic anilin dyes, are all Gram positive whilst none are acid fast.

The nitrate solution used was peptone containing .5% Potassium nitrate, inoculated and incubated for three days at 37° C.

By a reference to the table, it will be seen that in the tests the staphylococcus epidermidis albus follows those reactions characteristic of the staphylococci, whilst the diplococcus adheres more or less closely to those tests which distinguish the streptococci.

Probably the easiest method of differentiating the two organisms is by the appearances of the colony on Neutral red egg.

On this medium the growth of the staphylococcus epidermidis albus is much more rapid than that of the diplococcus.

In 12, to 14, hours, small pink colonies appear. They are round, smooth, raised, moist-looking and are devoid of any surface markings.

In twenty-four hours, they usually become confluent and as time goes on, develop into a staphylococcic-like smear.

I must mention here that the specimens which I believe to be staphylococcus epidermidis albus and upon which I base my description of growth on egg medium were obtained from scrapings of the skin of the upper arm.

It may be argued that the diplococcus under discussion is a streptococcus, but I have not seen it occur in chains in the urine, and its reactions do not correspond well with those of any of the better known streptococci except perhaps those of S. Salivarius.

To allow of comparison I have included in the table, the reactions of some of the more common varieties of streptococci.

From the pneumococcus it is easily distinguished by its sugar reactions and its inability to affect Hiss' medium.

There is apparently a close resemblance between this organism and the joint coccus described by Hale White (12), but the former differs in clotting milk and in its reaction to lactose.

Neither can it be said to be identical with the diplococcus described by Dudgeon (18) as occurring in Normal urine, for the organism which is being considered occurs only in arthritic cases, and here again the reactions of the two are not reconcilable.

No.	Medium	Diplococcus described in the text.	Staphylococcus epidermidis albus.	Pneumococcus.	Diplococcus of Dudgeon.	Streptococcus Salivarius.	Streptococcus Anginosus.	Streptococcus pyogenes.
1.	Litmus milk-acid.	+	+	+	+	+	..	+
2.	Litmus milk-decolourised	-	..	..	+	..	..	..
3.	Litmus milk-clot.	+	+	+	+	+	+	-
4.	N.R. Broth anaerobically	+	+	-	+	+	+	-
5.	Saccharose	+	+	+	+	+	+	+
6.	Lactose	+	+	+	+	+	+	+
7.	Raffinose	-	-	+	+	+	-	-
8.	Salicin	+	-	-	+	-	-	+
9.	Mannite	+	-	-	+	-	-	-
10.	Inulin	-	-	+	-	-	-	-
11.	Coniferin	..	-	-	..	-	-	-
12.	Glycerin	-	+	..	..	+	..	..
13.	Dextrin	+	-	..	+	..	..	..
14.	Glucose	+	+	..	..	..	..	..
15.	Galactose	+	+	..	..	..	..	..
16.	Maltose	+	+	..	+	+	..	..
17.	Dulcite	-	-	..	..	..	..	..
18.	Sorbite	-	-	..	..	..	..	..
19.	Laevulose	+	..	..	..	..	..	..
20.	Arabinose	-	..	..	..	..	..	..
21.	Nitrate	-	+	..	..	..	..	..
22.	Hiss' Medium	-	..	+	-	-	-	-
23.	Gelatin at 20°C	+	+	-	..	+	+	+
24.	Gelatin liquefied	-	+	+	..	..	-	-
25.	Haemolysis	+	..	-	..	-	+	+

C A S E S .

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Case 1.

Miss R. aet. 34.

Duration of the disease 8 months.

The patient was recommended to me by her medical adviser, the diagnosis being rheumatoid arthritis.

The various prescribed remedies, salicylates included, had been tried without any beneficial result.

Inquiry into the previous history elicited the fact that the patient had suffered from a severe influenzal attack about two years previously. There was no history of rheumatic fever and the heart sounds were normal. As far as could be gathered there was neither uterine nor gastro-intestinal disturbances, and a careful examination failed to reveal any focus of suppuration in the mouth or nasopharynx.

At various times previous to the onset of the disease the patient had noticed "cracking" in the region of the right temporo-maxillary articulation during mastication. An examination of the patient's condition showed swelling of the proximal interphalangeal joints of the two middle fingers of the left hand and of the middle finger of the right hand. The left wrist joint was also swollen.

Pain, worse on movement, was present in all

the affected articulations and the amount of mobility was limited.

Considering the duration of the disease the atrophy of the muscles surrounding the affected joints was particularly striking.

A blood examination showed a leucocyte count of 9760 whilst the reds worked out at 4,000,000. The Index to the diplococcus was .7.

Having satisfied myself that the case was indeed one of the atrophic variety of arthritis deformans in the acute stages, a sample of the urine was obtained, the usual precautions to avoid contamination being taken.

A film from the sediment of a centrifuged specimen revealed the presence of the diplococci in large numbers.

A further confirmatory specimen of urine was obtained in this, as in the remainder of the cases to be described.

Growth on neutral red egg medium showed the typical draughtsman-like colony, whilst the further culture and reactions corresponded with those described in the table.

From egg, subcultures on agar grew

sufficiently well in 36 hours to allow of the preparation of a vaccine.

A commencing dose of five million was considered to be quite safe and this was accordingly given.

On visiting the patient on the following day, however, I was rather alarmed at the severity of the reaction, which had apparently succeeded the injection. I found the patient in bed suffering from the usual effects of an over-dose of vaccine namely, rise of temperature, malaise and depression, but in addition to these the local symptoms were greatly aggravated, the affected joints being swollen tender and painful.

The Index taken two hours later, was .6.

As one of the joints appeared to show the presence of fluid I punctured it aseptically with a fine needle in the hope of obtaining a culture. In this, however, I was disappointed, as no fluid was obtained and streaking of egg media with the needle gave a negative result.

At the end of a week, as the symptoms had, to a large extent, subsided to their former condition, a further dose of 5 million was given, and the reaction on this occasion, although still marked,

was not so severe as was the case with the previous injection.

A blood culture taken about this time gave a negative result.

Seven days later, an injection of six million of the diplococci was given and thereafter this dose was increased weekly by one million.

Before this dose, the Index was taken, and was found to have jumped to 1.3. At the end of the following week however, it had fallen to .9.

At the end of six weeks, the patient noticed a marked improvement in the condition of the joints especially with regard to the amount of pain on movement.

She decided therefore to continue the treatment and the subsequent further improvement quite exceeded all expectations.

The tenderness of the joints almost entirely disappeared and the amount of mobility was slightly increased. By this time, what appeared to be the optimum dose 10 million had been reached and thereafter, although continued, it was not increased.

Only once did there appear a tendency to

relapse - during a menstrual period - but the joint condition improved again at the end of the fifth day.

An examination of the urine about this time showed a striking diminution in the numbers of the diplococci present. The Index had reached 1.2, which high level it now maintained almost throughout.

At the end of four months' treatment, the patient was well enough to regard the acute stage as cured. There was still some thickening to be felt around the articulations especially those of the left hand.

Massage and movements, subsequently carried out, did much to decrease the swelling and increase the range of movement.

The injections were now temporarily discontinued, and as the patient has never had a return of the symptoms it was not thought necessary to recommence routine treatment.

As a prophylactic measure, however, the patient continues to receive a dose of five million once a month.

Cultural examination of the urine gives a negative result and has continued to do so for the last five months.

I was at a loss in this, and in some of the subsequent cases, to explain the marked reaction that occurred on injection, as I naturally thought that there would be a fair immunity to germs eliminated by the urine, and which must I presume have been circulating in the blood-stream.

Case II. The doctor under whose care the former patient had previously been kindly recommended for vaccine treatment, the following case.

Mrs. P. aet. 37, wife of a medical man.

Duration of the disease two years.

There was here, as in the previous case, no history of rheumatic fever nor of septic absorption. Shock and worry appeared to have been important factors in determining the onset of the disease. At that time the doctor had under his care in the house a mental case, who suddenly developed acute symptoms and attempted to injure the patient. Following upon this, the death of one of her children caused a complete nervous prostration, on recovering from which the symptoms of arthritis commenced. Spa treatment, followed by a sojourn in Egypt, had, the patient thought, only tended to aggravate the condition.

The usual drugs had been tried, the most useful proving to be aspirin, which relieved the pain.

None of them appeared to have any effect in arresting the progress of the disease, and the patient was regarded as fast becoming a helpless invalid.

On examination the patient looked frail and cachectic. The interphalangeal joints of the left hand were deformed and there was present a certain amount of ulnar deviation at the wrist. There was creaking on attempting to move the latter joint.

The joints of the left hand, although at the time of examination free from pain, were still liable to recrudescence attacks. The right wrist and the left ankle were swollen and painful, and there was also some swelling of the finger joints of the right hand. Pain had occasionally been felt in the right elbow.

A blood count showed leucocytes 10,000 and reds 4,250,000. The Index was .9. Blood culture proved negative.

As previous joint puncture had been tried without success I did not investigate further in

this direction.

Two samples of the urine - one a catheter specimen - yielded the diplococcus which conformed to the various tests.

From subcultivations on agar a vaccine was prepared and injections commenced. It was found that where in Case I. a dose of five million had caused a severe reaction, the reaction in the second case although marked was not nearly so severe. Hence slightly larger doses were given than in the previous case.

Here also, a distinct alleviation of the acute symptoms soon became evident.

The index never rose above normal, but the diplococci gradually diminished and disappeared from the urine.

At the end of six months, the patient, having been free from acute symptoms for seven weeks, decided to try hot air treatment, massage and electricity for the fixed joints.

Whether this caused any injury to the joint or not, I cannot say, but evidently it brought about a lowering of the vitality of the left wrist,

for this joint suddenly showed a return of the disease.

This attack stubbornly refused to yield to the vaccine for two months, but at last the symptoms again subsided.

During this time, however, the other joints remained free from trouble and the patient has not had a return of the disease for 4 months.

It was curious to note that during the second attack in the left wrist the urine showed a positive result by culture. Later, however, attempts at cultivation were unsuccessful.

During the treatment, I had not the opportunity of taking the blood count regularly, as the patient lived at a distance, and her husband regulated the vaccine treatment.

So encouraging were the results, and so interesting was it to find the diplococcus present in the urine of both patients, that I looked up a patient, who had been under my care two years previously. My intention was to examine the urine and if the result was positive try the effect of vaccine treatment on her condition.

Case III.

The patient Mrs. D. aet 39. had now been

suffering from the disease three years. I found her in much the same condition as she had been when I had last treated her with guaiacol and Iodides.

That the disease was progressing however, was evidenced by the fact that she had had occasional attacks affecting the elbows and left shoulder.

The hands were greatly deformed and the patient complained of much pain in the ankles when walking.

A re-inquiry into the history confirmed my impression that here, as in the former cases, a history of rheumatism and sepsis was wanting. In this case however, "lumbago" and a feeling likened to trickling of cold water down the spine, had been noticeable features in the premonitory symptoms of the affection.

The patient had recently undergone an orthopaedic operation on the right knee, and neither her doctor nor myself were able to persuade her to undergo a trial of vaccine treatment.

This was all the more disappointing when a urine examination showed that the diplococcus was present.

Two weeks ago, however, the patient wrote to me saying that she had decided to undergo the

treatment, but as she has so far only had one injection I regret that I shall not be able to record the results until a later date.

Dr. P. whose wife (Case II) I had treated, kindly sent me a case of arthritis of doubtful etiology.

Case IV. The patient, Mrs. W. aet 31. had suffered from the disease 3 months.

The most noticeable feature in the history was the fact that there had been two abortions.

There were no children.

The malady had commenced acutely in this case, and had followed closely upon the second abortion.

I could not obtain a history of syphilis from the husband, and the patient had noticed no rash, and had only suffered from an "average number" of sore throats.

She had considered the condition of her joints due to an attack of rheumatism, and had, only a week before, consulted her doctor. Examination showed swellings of the left wrist, right

knee and right elbow. The wrist joint, however, did not present the typical appearance of the disease under consideration, nor was the distribution the usual one.

The leucocyte count was 8500 whilst the reds numbered 3,850,000.

A Wassermann test was twice done, but the result was doubtful in both cases. The urine showed the presence of Bacillus Coli alone. Vaccines of this organism given once weekly did not appear to have any effect, and the treatment was ultimately abandoned. In spite of the direct absence of specific trouble, Potassium Iodide and mercury were given a trial, and as improvement is resulting, I think that this case must be excluded from the class known as rheumatoid arthritis.

Syphilitic arthritis is, however, without doubt one of the infective forms of deforming arthritis.

Case V.

Mrs. S. aet 38, wife of a doctor had suffered from rheumatoid arthritis for  $4\frac{1}{2}$  years. In this case worry and shock seemed to have been important predisposing causes.

Here again, also, the premonitory spinal

symptom already described had been a noteworthy feature before the onset of the affection. The heart sounds were normal, but the pulse rate proved to be persistently high, namely, about 91, whilst the temperature was usually 98.3 in the morning. The index was .6, the leucocytes 9,500, and the red corpuscles 4,250,000.

I found both wrist joints fixed and the hands somewhat deflected to the ulnar side. The finger joints were also deformed. There was a certain amount of creaking on attempting to move the left wrist. Both ankles were somewhat stiff and very painful, especially in the mornings when the patient first began to walk. Acute attacks, accompanied by pain and swelling, occurred in one or other of these latter articulations on an average once a fortnight. The left elbow was showing signs of being the next joint affected, whilst clicking of both temporo-maxillary articulations had been present at various times throughout the course of the malady.

The patient had been through all the routine treatment from Guaiacol to massage and electricity. The latter form of treatment she had found of much temporary benefit in the case of the fixed joints. Subsequent attacks in these joints had, however, undone the good effects of the electricity.

The patient's physical condition was otherwise good and the depression, usually such a marked feature in these cases, was absent.

There was nothing in the history to note, apart from the fact that the disease had commenced with severe backaches.

One noteworthy point in this case was that two years after the onset of the disease a blood culture taken by a bacteriologist had shown a "streptococcus". A joint puncture performed at the same time had given no result.

Vaccine treatment was not then carried out as the patient had made arrangements to go to Buxton.

Acting on this hint, I obtained 5 c.c.'s of blood from the median basilic vein and inoculated egg tubes, agar tubes, and broth. I was somewhat surprised to find, at the end of 36 hours, a certain amount of turbidity in the latter. A small deposit was also later noticed and this on examination showed chains resembling those of streptococci.

Subcultures were made on egg, with the astonishing result that the typical colony of the diplococcus appeared. Passage through the sugars gave reactions similar to those of the organism under discussion, and similar to those of the diplococcus,

which by this time had been isolated and cultured from the patient's urine.

A second sample of blood gave a positive result, and in addition the colony appeared this time primarily on the egg as well as in the broth.

The agar smears were negative in both cases. I attempted to demonstrate directly the presence of the organism in the blood, but numerous smears failed to show its presence.

The efficacy of a vaccine in such a case was, of course, doubtful, but the patient was anxious to give it a trial.

Treatment was commenced with a dose of ten million and carried out on lines similar to those of the former cases described. At the end of two months some slight improvement was noted. This improvement did not continue, however, and frequent examination of the urine has shown no diminution in the numbers of the germs.

The Index has remained low so far. I am rather doubtful as to whether the ultimate progress will be any better, and in this case I have advised a continuance of treatment with Guaiacol.

Case VI.

Mr. T. aet. 36. Duration of the disease  
13 months.

The patient was sent by his doctor to see if anything could be done for him in the way of vaccine treatment.

In this case, the affection was spreading more rapidly than in any of the previous cases, in spite of vigorous drug treatment.

There was a history of prolonged gastric trouble and of a gastric ulcer. The joints of the fingers were swollen and painful, as were also the ankles, wrists and right elbow.

At first I was inclined to the opinion that this case would fall best into the osteo-arthritic group, but later I altered this view.

The leucocytes counted out at 8,500 and the reds at 5,000,000. The Index was .7. Examination of two samples of urine - one a catheter specimen - showed that the diplococcus was also present here. In addition, however, there appeared an organism which closely resembled, on culture, the streptobacillus described by Pfeiffer (19) as occurring in 42% of normal male urethrae. It was present in both of the specimens of urine examined, and in all later samples.

Blood culture was negative, as also was joint puncture, although a small amount of fluid was obtained. In this case I also performed a lumbar puncture later, but with a similar result, although 5 c.c.'s of fluid were planted out.

In the treatment of this case, the most interesting feature was the marked reaction after injection as evidenced by the increased pain and tenderness of the affected parts. Injections of the streptobacillus, however, caused no reaction even in doses of twenty million.

Recently it seemed as though an improvement in the condition of the patient was taking place, but the left shoulder has since shown signs of becoming affected.

The injections, after the first three weeks, were administered by the patient's doctor, who, in spite of the reactions, ran the dose up to fifty millions, and this, I am inclined to think, accounted for the tendency to spread to the shoulder joint.

The dose has now been reduced again to ten million, and the reactions are much less severe, and I hope that an improvement may result.

The germs show slight signs of diminishing in the urine, whilst the Index, which has varied

remarkably throughout, is now .7 again.

Case VII.

Mrs. J., aet. 39. Duration of the disease about one year.

The urine of this patient, whom the doctor says is suffering from rheumatoid arthritis, was sent to me three weeks ago. An examination of this and of two other samples - one taken in the prescribed manner, and one a catheter specimen - showed the diplococcus to be present.

The patient resided at a distance, and I have not yet seen her. As far as I could ascertain, the only point in the history is the alacrity with which the onset of the disease followed a "severe shock".

The patient has only recently left home for a course of treatment at Harrogate, and I have not had the opportunity of trying the effects of a vaccine.

#### SUMMARY AND CONCLUSIONS.

From the urine of each of six cases of rheumatoid arthritis a diplococcus was isolated and cultured.

The urine was obtained with all due precautions against accidental contamination.

In the systematic microscopical and cultural examination of the urine of 400 cases of persons of normal health (15%) and of persons suffering from diseases other than arthritis (75%) this diplococcus was not present.

The cultural characteristics and sugar reactions of this organism distinguish it from the known cocci, whilst the morphology of its colony on neutral red egg medium is diagnostic.

Vaccines of the diplococcus caused, in an early case of rheumatoid arthritis, so far, apparent arrest of the disease, and in two other cases some alleviation of the symptoms.

As a result of vaccine treatment the organisms disappeared completely from the urine in two of the cases and showed a remarkable diminution in numbers in one other.

In some of the cases the Opsonic Index varied in a rational manner, with the stage of the disease and with the injections.

In culture of the blood of four of the cases one was positive and showed an organism which exactly resembled in cultural characters and reactions the diplococcus isolated from the urine.

Puncture of the joints in three of the cases

yielded fluid in one instance only, and this on cultivation proved sterile.

Lumbar puncture in one case also gave a fluid which showed a negative result, on cultivation.

Careful examination of the blood by leucocyte count and enumeration of reds gave such inconstant results that no definite conclusions could be based on the observations.

The effects of the vaccines tended to prove the pathogenicity of the organism and that it is not merely a saprophyte in the body.

As to how far exactly the presence of this organism in the urine is actually concerned in the causation of the disease it is, at present, impossible to say, as a sufficiency of cases have not yet been examined.

In submitting this paper I fear that I am presenting a survey of investigations in progress, rather than a full and considered report on a completed piece of research.

(OVER)

REFERENCES TO LITERATURE.

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1. Adams, Rheumatic Gout, 1857.
2. Nathan, Am. Jour. Med. Sc. pp. 857-873 - 1906.
3. Hale White, Guy's Hosp. Rep. vol. lvii - 1902.
4. Schüller Verhandl. Deutsch Gesch.f.Chir - 1892.
5. Dor, Gazette Médicale de Paris, Series II vol. 8.
6. Bouchard & Charrin Sem. Méd. 1891 II p. 387.  
Assoc.de Sc.Caen I 1894, p.254.
7. Bannatyne, Lancet 1896 I p. 1,120.
8. Painter, Boston Med. Jour. Nov. 28, 1901.
9. Chauffard & Ramond, Revue de Méd.1896 XVI p. 345.
10. von Dungern & Schneider, Munch.Med.woch.Oct.25 1898
11. Poynton & Paine, Trans. Path. Soc. Lond. vol. 53,  
pp. 221-227 - 1902.
12. Hale White, Guy's Hosp. Rep. vol. LVII - 1902.
13. Fayerweather, Am Jour. Med. Sc. vol. CXXX p.1051  
1905.
14. Painter, Boston Surg. & Med. Jour. Nov. 7, 1907.
15. Crowe, Proc. Roy. Soc. Med. vol. V pp. 159-171,1912
16. Gordon, Jour. Path. XV pp. 323-32 - 1911.
17. Welch, Am. Jour. Med. Sc. p. 439 - 1891.
18. Dudgeon, Lancet II p. 1696 - 1911.
19. Pfeiffer, Arch.f.Derm u Syph Wien u. Leipz.  
LXIX pp. 379-410 - 1904.
20. Morton, Brit. Med. Jour. Aug. 31, 1912 p.481-2.