These recommendations are sometimes not acted upon by the authorities because the facilities do not at present exist, but I hope they may assist ultimately in the framing of schemes for administrative advance. The number of cases is large, and their continued supervision a matter of very considerable difficulty.

The serious figures I have given, showing that in 35 per cent. of the cases death or permanent cardiac crippling supervened, may be subjected to criticism from two aspects. In the first place, it can be urged that chiefly serious cases were sent to the clinics, and this is no doubt true to some extent. But it is not altogether so, because school medical officers were informed that it was *rheumatic* children with whom it was desired to deal, and they knew that the underlying effort was the prevention of heart disease. The other criticism that can be put forward is that these children were not efficiently cared for. This criticism I also, regretfully, accept in part, and shall deal with some details in a moment; but this must now be said—that exceptional care and attention have been paid to these children, no pains have been spared in their treatment, and in many instances the degree of their improvement has been remarkable. I am definitely of opinion that the development of specific rheumatic clinics with associated home visitation and regular supervision has improved the prognosis.

There are some cases in which we are forced, in spite of every conceivable form of treatment and all facilities, to watch the child passing from the early infected period to that of grave cardiac disease and ultimately death. But such cases should be rare, and are rare if the early signs of the first active infection are noted and dealt with. When these early signs are noted close care for a prolonged period is essential. But in a series of 52 consecutive cases of acute rheumatism recently admitted to the Children's Hospital, Liverpool, in only 18 instances was it possible for direct transference to another institution—country hospital or convalescent home—to be carried out, while of the total 52 cases 75 per cent. were retained in the City Hospital for only a month or less. Efficient therapeutic prophylaxis was here evidently not carried out; but, owing to the need for beds in town for acute cases, it is impossible to retain these children in city hospitals, and sufficient accommodation is not provided for them in country hospitals. Many patients have to wait months for admission to the Heswall Hospital, and frequently such waiting period leaves marks of serious damage.

The new Local Government Act will bring about many changes and open up many possibilities. I am sure that no more important development can occur than the setting aside of specific beds or wards for the prolonged care of rheumatic children.

As regards the active care of the children, I would lay great stress on the removal of infected tonsils. Of the 531 rheumatic children alluded to in this paper, 130 underwent tonsillectomy in hospital and 22 at a school clinic; in 4 cases parents refused permission for operation, and in 67 cases operation is desirable and probable. Thus in 213 out of 531 children—or about 40 per cent. of cases—I have considered tonsillectomy advisable.

Contrary to what some may think, I consider that in being responsible for these figures I have acted in a conservative manner. I have considered as indications for operation:

1. Obviously unhealthy tonsils—irrespective of size.
2. The presence of rheumatism with a history of tonsillitis as initial symptom.
3. The presence of rheumatism with recurring attacks of nasopharyngeal catarrh associated with exacerbations of active rheumatism.
4. Cases of active rheumatism running a prolonged course resistant to all medical measures, whatever the appearance of the tonsils.

In none of the cases operated on did unfavourable symptoms develop from the operation, however active the rheumatic symptoms at the time; while in most cases obvious and marked benefit accrued. It is, however, impossible to consider the operation as an isolated factor in treatment, as good results from it can only be justly

expected when enucleation is complete, when the immediate after-care of the child is as thorough as after a major operation—which this is—and when, after suitable institutional care, home supervision is so prolonged as to tend to prevent or at least deal early with subsequent intercurrent infections.

I cannot but feel that the term "acute rheumatism" in childhood has been stressed unduly in the effort to obtain accurate delimitation. Our foe is *active* rheumatism, and, perhaps unfortunately, its symptoms are not always acute. It is usually easy for the clinician to make a diagnosis between rheumatic infection and the varied rheumatoid conditions; and syphilitic cardiac conditions are rare at this age. It is the early diagnosis of active rheumatic infection which is so important, which is sometimes difficult, and which, I think, is sometimes delayed because of the common use of the term "acute" rather than "active."

The early diagnosis and suitable care of active rheumatism give good results. Fortunately for the children of the well-to-do, frequent medical supervision and constant educated home care serve to prevent acute ebullitions and disastrous end-results even without the need of accurate diagnosis. For, however, the children of the hospital class, once they show symptoms of active rheumatism, and whether they have been previously classed as "dyspeptic," "hypoglycaemic," "pre-acidotic," "intestinal," "toxic debilitated," or simply "pre-rheumatic," I consider the value has been fully demonstrated of specific hospital clinics and associated home visitation and prolonged supervision by private practitioner or through the clinic.

I also consider that tonsillectomy, efficiently carried out and succeeded by suitable and prolonged care, takes a very important place in treatment, and that the need of adequate institutional beds for prolonged care is clamant.

HYSTERO-SALPINGOGRAPHY IN THE DIAGNOSIS AND TREATMENT OF STERILITY AND PELVIC DISEASE.*

BY

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In a previous paper on the subject of sterility¹⁷ I emphasized the great importance, in all cases where no definite cause could be found for lack of conception, of ascertaining the patency of the Fallopian tubes before treatment was begun. At that time I was using the Provis-Rubin method of CO₂ insufflation, and I instanced two cases of pregnancy following on the clearing of the so-called "sticky tube"; since that date I have met with four further successful cases, in each of which the patient became pregnant within six weeks of the insufflation. The object of this paper is to further the claims of a method of diagnosis and treatment which is, in my opinion, far superior to the gas insufflation, good though that is. This procedure consists of injecting lipiodol into the uterus and tubes under the control of an x-ray screen, and then the taking of a series of skiagrams. It is equally valuable in diagnosis and treatment.

Before coming to the technical details it may be of interest to give a short history of this method of diagnosis. As far back as 1914 Carey⁸ in the United States attempted to pass collargol through the tubes, but got no practical negatives, while Dimier in Paris recorded a death while using the same procedure. These results caused the method to be abandoned. In 1915 Rubin¹⁵ published a paper on collargol injections. In 1923 Kennedy¹³ made use of sodium bromide, and in the same year we also tried it at the Bristol Royal Infirmary; but these methods gave poor and unreliable results, and a few cases of peritonitis were recorded.

The discovery of the suitability of lipiodol for the injection material was the means of establishing this technique on a sound basis. Carlos Hueser¹¹ and Carelli,⁵ during

* From a lecture with lantern slides delivered to the Bath and Bristol Branch, February 27th, 1929.

1924 and 1925, produced a series of beautiful photographs of the injected uterus and tubes, and soon afterwards this method of diagnosis was taken up enthusiastically on the Continent and in America. Gynaecologists in this country, with the notable exception of Forsdyke,¹⁰ have, for some reason, fought shy of this most useful help to diagnosis and treatment. A flood of literature has recently resulted, especially in France, where Bécclère^{2,3} has produced several papers and a most useful and indeed invaluable monograph⁴ on the subject. As a few typical papers I would mention those of Cotté,^{7,8} Sicard and Forestier,⁹ Randall,¹⁴ Rubin,^{15,16} and Jarcho.¹²

Complete details of technique and results, and a very full bibliography, can be found in Bécclère's book. He quotes 168 authorities, and I am much indebted to this very complete list of authors. It is of interest to note that I have been able to find only three cases of any ill results following lipiodol injections, one reported by Rubin, and two by Bécclère in the *Bulletin de la Société Obstétrique et de Gynécologie de Paris* for February, 1929.

Technique.

The patient requires no special preparation unless an anaesthetic is to be given, but it is most important to make the test at least a week from the beginning or end of a menstrual period. Pregnancy, purulent cervicitis, and active salpingitis are contraindications. Although the discomfort is not very great, and is a most useful check on the pressure used, I employ a general anaesthetic for nulliparae and for very nervous patients, for the reason that the whole test may be spoiled if the patient jumps and the lipiodol runs out from the vagina and up her back, thus making a dense shadow to the x-rays. In many cases I find a small dose of morphine and scopolamine a great assistance. I use a special syringe made for me by Messrs. Allen and Hanburys, modified from that of Dr. Bloch-Wormiser. It consists of a 25 c.cm. metal syringe, with a screw-in piston, which delivers 1 c.cm. of lipiodol to each complete rotation of the handle. The pressure

example, fibroids. The nozzle itself is strongly made of metal, and is quite short and blunt, with the hole at the side and not at the tip; the taper of the cone allows it to fit well in cases of laceration of the cervix, and the short tip gives rise to no trouble if the uterus is sharply anteverted. To perform the test the syringe and nozzle are filled with lipiodol at blood heat (warming it lets it run much more easily). The patient is then placed upon the x-ray screening couch, lying on her back. If an anaesthetic is now given it is essential that an experienced anaesthetist should be in charge, as the room is often in darkness for seven or eight minutes. The legs are now raised by a nurse, and the cervix is caught with a bullet-forceps vulsellum, and the cervix and os are swabbed with a Playfair probe dipped in tincture of iodine. The nozzle is inserted into the cervical canal, and kept firmly in place by combined pull on the vulsellum and pressure on the syringe; this causes very little, if any, discomfort to the conscious patient. The legs are now placed flat again.

It is an advantage if the observer can adjust his eyes, by closing them, or wearing special spectacles for three minutes before the actual test, as the filling of the tubes will then be seen easily on the screen.

The lights are now turned out, the screen is placed on the patient's abdomen, and the current switched on. The nozzle and vulsellum will now be plainly seen. The piston is then screwed in so as to deliver 5 c.cm. of lipiodol, and the uterine cavity will at once become obvious as a triangle, apex downwards. This triangle is roughly equilateral if the uterus is in normal position, but becomes almost crescentic from foreshortening if the fundus is retroverted or anteverted. The injection is now slowly continued, while the pressure is watched carefully. There is usually a short delay before the tubes begin to fill; this is caused by the presence of the sphincters at the cornual ends of the tubes, described by Hueser and Bakke.¹ Then, in a normal case, the tubes will suddenly fill, and the lipiodol can easily be seen running out along them, and forming a small collection in the peritoneal cavity. If the tubes are obstructed this process may be seen to a greater or less degree on either side, or no lipiodol at all may enter the tubes. When it is

FIG. 1.—Normal uterus and tubes, at 120 mm.

FIG. 2.—The same two minutes later at 150 mm. Lipiodol passing into peritoneal cavity.

is registered on a manometer, which has a luminous dial, so that it can be read in the dark of the x-ray room. There is an oil lock with sliding piston between the lipiodol and the anaeroid, thus preventing the latter being injured by the lipiodol. The oil lock is kept full of liquid paraffin, and this occasionally needs refilling owing to seepage. A swinging side tube with a three-way tap action permits the syringe to be refilled without removing the nozzle from the cervix, which is most useful in dealing with enlarged uterine cavities—for

FIG. 3.—The same twenty-four hours later. Lipiodol well diffused; tubes empty.

suspected that the tubes are blocked the manometer must be watched with care. A conscious patient will complain of pain when the pressure is between 180 and 250 mm. Hg, and I do not think it safe to let the pressure rise above 250 mm. when the patient is anaesthetized.

In any case, as soon as the tubes are filled up, or as soon as the pressure reaches 250 mm., a radiogram is taken, and a second one when the maximum pressure has been reached. The patient is now turned on to her side (the nozzle still *in situ*),

and a lateral-view film is exposed. This last one is most important.

The procedure is now finished, and the patient rests for a short time, and can then go home. In no case have I heard any

FIG. 4.—Obstruction at the fimbriated ends of both tubes. Lipiodol did not pass at 250 mm.

complaint of the typical pain caused by the CO₂ method when the patient stands up. After twenty-four hours another radiogram should be taken. It is surprising how, in some cases where the lipiodol did not seem to pass through the ends of the tube into the peritoneal cavity, it will be found there next day, and this "twenty-four-hour film" is a valuable check on negative results.

The radiographer needs considerable experience to produce the best results, and Dr. Mayes, the radiologist to the Bristol Royal Infirmary, tells me that high amperages are needed, the average exposure being about 1 to 2 seconds for front views and 3 to 5 seconds for lateral. A Potter-Bucky apparatus produces most beautiful x-ray films, but renders screening very difficult, unless specially made for this purpose, and I have found that the ordinary screening couch apparatus produces films quite good enough for ordinary diagnosis. The whole procedure does not take more than ten or twelve minutes, and is no great tax on

FIG. 5.—Fibroid; typical distortion of uterine cavity; obliteration of both tubes, stump of left tube showing.

the radiologist or gynaecologist, but I must extend my sympathy to the anaesthetist, if one is employed.

The advantages derived from this simple operation fall into two groups—diagnostic and curative. Although the injection of CO₂ is of the greatest value, I think anyone who has tried the lipiodol method will agree that it is very greatly superior, for the following reasons.

1. It will demonstrate the exact position of any tubal block, even if only one tube is obstructed, and in conditions of obstruction of both tubes the prognosis is entirely dependent on the site of the obstruction. Any operation for freeing the tubes is almost useless unless the obstruction lies at the

FIG. 6.—Uterus bicornis-unicollis; severe chronic salpingitis both sides, but lipiodol passed on the right. (Verified at operation.)

- fimbrial ends, in which case the prognosis as to pregnancy is fairly good after operation.

2. It will demonstrate the fact that a uterus is not pregnant, a difficult question in the early months.

3. It will show the presence of interuterine growths, such as myomata or carcinomata, in cases of metrorrhagia with a big uterus, and so distinguish them from "fibrosis uteri."

4. It gives a very good idea as to the ease or otherwise of an intended myomectomy.

5. It will decide whether a pelvic tumour is of a gynaecological nature or not—for example, in a case of carcinoma of the colon which had become adherent to the fundus both tubes were normal.

With regard to its use in treatment, I feel sure that the heavy oily lipiodol is a better clearer of the so-called "sticky tubes" than is gas. In many of my cases the lipiodol did not pass until 180 or 200 mm. were registered, but the

FIG. 7.—Normal pregnancy showing the lipiodol lying round the sac and in the lower segment.

twenty-four-hour film showed complete emptying into the peritoneal cavity. In two cases gas insufflation had previously failed, but the tubes opened up to lipiodol. Jarcho¹² claims that the iodized oil is a most useful therapeutic agent, and quotes several authors to this effect; I have had no personal experience of this.

It would seem that in the lipiodol injection, when

properly controlled by x ray, we are possessed of an invaluable method of diagnosis in cases of sterility, far superior to any previous technique. Its only contraindications are septic cervicitis or pregnancy, and the latter is quite disregarded by Hueser,¹¹ but Bécère⁴ advises against using this method of diagnosis owing to the bad effects of the x rays (not the lipiodol) on the pregnancy.

Apart from sterility, I think it is a useful, but by no means necessary, adjunct to diagnosis, for the reason that a pelvic tumour usually calls for operation, and the mistaken diagnosis of a fibroid for a parovarian cyst is of small moment to the patient, however annoying it may be to the surgeon concerned.

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THE PRODUCTION OF IMMUNITY TO TUBERCULOSIS IN MAN AND ANIMALS.*

BY

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BEFORE discussing the problem of immunity to tuberculosis it will be necessary to consider very briefly some of the outstanding facts about this disease. Tuberculosis, unlike other infectious diseases, advances slowly and progressively, and though it may be arrested in its march at the lymph glands—the first natural barrier—only to become active again later, its progress, as in pulmonary tuberculosis, is more often continuous. It is probable that in addition to the human, bovine, and avian tubercle bacilli there are certain intermediate types, and that the human body may be attacked by a mixture of types. Each type of tubercle bacillus is selective and can live only in the host to which it has become accustomed for centuries.

From twenty-five years' experience of subculturing and growing tubercle bacilli, I am inclined to the opinion that the bovine bacillus is the original and true tubercle bacillus, and that the other types have evolved from long residence in different hosts. This view cannot be proved by investigations on animals, as they are generally not susceptible to infection by human bacilli. The human body is readily infected by both human and bovine bacilli; avian bacilli, which infect chicken and birds, do not infect the human subject. In the light of our present knowledge we cannot determine with certainty the exact origin of every infection of the human body by tubercle bacilli. Cytological differentiation between human and bovine bacilli is not possible; mankind, from its consumption of milk, butter, and cheese, has become so accustomed for centuries to infection from cattle that the bovine bacilli have adapted themselves to their new environment and grow well in human tissues; yet the human bacilli will not grow in the tissues of cattle.

In studying tuberculosis it is necessary to consider what may happen to an invading organism in a foreign host. Bovine bacilli introduced into the body of a child may, after a few years, undergo a modification of type; their virulence may be reduced and they may assume the characteristic properties of the human bacilli. Should such modification occur it would obviously be difficult by ordinary laboratory methods to determine with accuracy whether or not the bacilli belonged to the human or the bovine type.

* Summary of paper read before the Liverpool Medical Institution, March 21st, 1929.

A child infected with bovine bacilli in infancy might possibly be certified ten or fifteen years later as suffering from a human infection, owing to the transmutation of the organism in human tissues.

In 1901 I published a paper in the *British Medical Journal* stating the following views. (1) That human and bovine infections produce separate and distinct diseases in the human body, and that they are antagonistic to each other. (2) That human bacilli cause primary pulmonary tuberculosis, while the bovine type cause enlarged glands, mesenteric disease, bone and joint lesions, etc. (3) That patients suffering from pulmonary tuberculosis rarely develop bone, joint, or gland lesions, and vice versa; in fact, that the human subject is protected by one infection against the other. (4) That cattle and pigs are immune against infection by the human bacilli, but that the human subject is susceptible to both. It was evident to me at that time that it would only be possible to immunize animals by using human bacilli. A series of animals were tested in this way, but the bacilli used were too virulent and every animal was killed.

In 1906 I decided to attempt attenuation of bacilli by repeated subculturing and thus reduce their virulence and lower their toxicity. The only certain method of permanently attenuating virulent cultures of tubercle bacilli is by long-continued and systematic subculturing spread over a number of years. For this purpose I used a pure culture on glycerin agar of human bacilli from a virulent case of pulmonary tuberculosis, a virulent bovine culture from the mesenteric glands of a cow, and a culture of avian bacilli from the liver of a chicken. These cultures have been grown on glycerin potato and transferred to glycerin agar every month for twenty-two years, the present growths representing the two hundred and sixtieth generation. The growths are still profuse and true to type, but they are now completely non-pathogenic to animals. Every year since 1906 I injected these bacilli into animals, and until the year 1913—that is, until the eighty-fourth generation of subcultures—I observed no change in their virulence. After that time attenuation became marked, and in a series of animal inoculations carried out in 1914 the subcultures were observed to be avirulent.

A further series of animals was inoculated a year ago with a protective vaccine prepared from attenuated cultures of human bacilli, and these animals, together with unprotected controls, were given each half a milligram of virulent bovine bacilli. All the unprotected animals rapidly developed general tuberculosis and died within four months, while the protected animals showed only local and non-progressive lesions. An animal which can resist the laboratory dose of virulent bacilli can certainly resist the comparatively mild infection it may meet in everyday life. If, then, we can produce artificial immunity in man and in animals sufficient to enable them to resist ordinary infection we shall have gone a long way towards stamping out tuberculous infection.

Calves that are to undergo immunization should be separated from the mother at birth, and having been fed on healthy milk or on the pasteurized milk of the mother for a week should be given the first dose of vaccine, the second dose following a week later. They should then associate with the other animals. This method of immunization is applicable only to non-infected animals. During the past three years it has been applied to over 2,000 calves in valuable pedigree herds, and careful records have been kept. These calves have been tested at the end of a year, and in many cases again at the end of a second year, with Pasteur's tuberculin, and in practically all cases the result has been negative.

The production of immunity in the human subject is complicated by the fact that children are susceptible both to human and to bovine infection. A year ago, at the request of their parents, I inoculated all the children—about one hundred—living in a large tuberculosis colony, where all the male parents were suffering from pulmonary tuberculosis, with two doses of protective vaccine prepared from bovine bacilli. So far these children appear to be quite healthy, and though it will require years of observation before we can form any opinion as to the efficiency of the vaccine, I believe that in time it will be possible to