examination of the original skiagram demonstrated its presence in the antrum.

As to a sequestrum, we are probably familiar with cases, particularly of chronic antral suppuration, in which resolution is delayed after operation until the extraction or spontaneous expulsion of a fragment of dead bone.

The treatment of the cases in Group (b) is, I understand, the primary object of this discussion. We have to consider their treatment from two points of view—namely, local and constitutional. Possible methods of local treatment seem to be: repeated washing out of the sinus or sinuses; the use of suction to empty them; the application of antiseptic packs to prevent drying and to increase secretion; the use of oily applications for the same purpose; the employment of ionization with the idea of attacking the infection in the mucosa; and perhaps the use of radium.

Experience has led me to believe that washing out should be avoided as far as possible in both the immediate and late post-operative stages. It seems to me to introduce a risk of spreading infection both to previously uninvolved regions of the nose and throat and to the ears without producing any favourable effect on the condition for which it is used. I am of the opinion that the secretion should be got rid of by hawking or blowing and that an attempt should be made to keep an oily film over the surface of the mucosa to prevent drying and crusting. I have had no encouraging results from the use of antiseptic packs with silver preparations, etc., but my experience with them is not extensive. The technical difficulties in employing ionization in the paranasal sinuses are considerable; I have had no personal experience of the method, but, in view of the favourable results which have been obtained by its use in cases of infection of the mucosa of the middle ear, a thorough trial would seem to be worth while. I have found that by using a relatively large dose of radium, only lightly screened, for a short time, an improvement is produced in cases of resistant ethmoidal infection with polypi. A vigorous reaction occurs, and at the end of two or three months the local condition has been much improved. I do not know if it has been employed for purely suppurative cases; if not, I should think a cautious trial would be justifiable.

Treatment from the constitutional side is more difficult. You have probably been struck by the great variation in the degree of general constitutional disturbance accompanying chronic sinus suppuration. While some patients are more or less invalids, with muddy complexions and constant headaches, others, although their noses are constantly producing pus, are rosy-cheeked and never have a headache. I have been impressed by the slight degree to which infection and new growth of the nasal sinuses involve the lymphatic system. As long as infection remains within the nose, any evidence of involvement of the lymphatic glands is very unusual, while a spread to the skin, nasopharynx, or pharynx at once produces a lymphatic infection, as shown by enlargement of the glands. I wonder whether this lack of absorption into the lymphatics may not be one reason why the body does not develop an adequate resistance to the infection. If so, one would expect good results with vaccines. Personally, I have found them of little, if any, use in chronic cases. Anything which improves the general condition of the patient may be expected to have a favourable influence on the sinus suppuration, although, as I have already said, constitutional and local improvement do not, by any means, always go together.

There is one factor which I believe to be of the utmost importance and one which is frequently neglected—namely, time. I have lived long enough to have seen cases which I regarded as incurable clear up with the passage of years, and I strongly advise that a very ample margin of time should be allowed to elapse after operation in these cases before judging of the result, and particularly before deciding on any further operative treatment. Many a patient has become a mental wreck through repeated operations which have not even improved the nasal condition. In my opinion, provided reasonable drainage exists from the nasal sinuses, headaches, if present, are due to a general neurasthenia rather than to the secretion of pus in the nose. Repeated operations do not relieve such cases, but merely make them worse.

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¹ *Journal of Laryngology, Rhinology and Otolaryngology*, 1927, p. 192.

AVERTIN.*

BY

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THE production of general anaesthesia is almost invariably effected by the inhalation of volatile substances. This method has attained popularity for two reasons: first, on account of the wide therapeutic margin of the volatile drugs available, and secondly, on account of the facility of administration which permits the anaesthetist to control and regulate accurately the depth and duration of anaesthesia. Furthermore, absorption by this method is almost as rapid as by intravenous injection.

Non-volatile anaesthetics must be given either by the mouth, the rectum, or intravenously, the choice of method being governed by the properties of the individual anaesthetic. There are three groups: (1) liquids with too high a boiling point for administration by the lungs, paraldehyde being an example of this group; (2) alkaloids such as morphine and hyoscine; and (3) solid substances, often very insoluble in water, which act by virtue of lipid solubility. This last group includes chloral and its derivatives chlorotone, chloralose, and isopral; sulphonal and methylsulphonal; veronal with its derivatives sodium veronal, luminal, and pernocton; and urethane with its derivative hedonal.

All these drugs are excellent hypnotics, but as a general rule they are unsuitable as anaesthetics because the therapeutic margin is insufficient. A dose that will produce insensibility and render the patient free from pain does not necessarily produce a corresponding degree of immobility; in some instances the anaesthesia lasts so long that the use of the drug is impracticable. Unless a non-volatile anaesthetic can be administered by continuous intravenous infusion it must be given in a single dose, usually per rectum, and this has the disadvantage that when it has been absorbed it is impossible to control its action further. In addition, there is always the risk of local irritation upon the rectal mucosa. Such non-volatile drugs cannot be excreted rapidly, if at all, by the lungs; they are eliminated comparatively slowly by the urine, sweat, or faeces. For these reasons it is impossible to ensure a constant concentration of the anaesthetic in the blood and tissues, a condition easily attained when volatile anaesthetics are employed; with this group, therefore, it is impossible to maintain the patient at a constant level of anaesthesia without the risk of overdosage. The quantity to be administered must be calculated in proportion to the body weight of the patient; this method is the best at our disposal, and yet it is unscientific, because it takes no account of his age, temperament, or infirmity. Further, if we accept the view that anaesthetics act by virtue of lipid solubility, the obesity of the patient must be taken into consideration when estimating the correct dose. There is no need for accurate dosage with a volatile anaesthetic, because there is a close correlation between the amount administered and the depth of anaesthesia. With such difficulties to overcome the introduction of a new non-volatile anaesthetic may appear unnecessary, but it must be remembered that even volatile anaesthetics do not give entire satisfaction. If the ideal anaesthetic is considered as one which is absolutely safe for the patient, produces complete insensibility and immobility, and is simple in administration the defects of the volatile type are at once apparent, and therefore the properties of any new anaesthetic should be critically examined.

Avertin, or tribromomethylalcohol, is one of the latest non-volatile anaesthetics; it was first prepared by Willstätter and Duisberg²⁵ in 1926 by the reduction of bromal. It is an odourless white crystalline powder containing 85 per cent. of bromine, and soluble in water to the extent of 3 per cent. at 37° C.; but the powder dissolves very slowly, taking more than forty-five minutes, though aided by vigorous shaking to produce a clear solution. This was a serious disadvantage, but the drug is now issued already dissolved in amylene hydrate in the proportion of 1 gram

* A paper read in the Section of Anaesthesia at the Annual Meeting of the British Medical Association at Winnipeg, 1930.

of avertin in 1 c.cm. of the solvent. This solution is readily soluble in water; moreover, it presents the additional anaesthetic effect of amylene hydrate, which also stimulates the respiratory centre and tends to counteract the depressant action of avertin upon respiration. The drug is given in aqueous solution by the rectum; it is peculiarly suited to this form of administration because it is non-irritating to the mucosa, and it is absorbed therefrom within a very short time. Further, the therapeutic margin is greater when the drug is given in this manner.¹² Anaesthesia can also be produced by intravenous, subcutaneous, or oral administration, but although these methods have been used for animals they are not so convenient for man.

Solutions of avertin must be freshly prepared without the use of heat; heating above 40° C. and exposure to light and air cause decomposition of the drug into dibrom-acetaldehyde and hydrobromic acid. Both these substances are intensely irritant to the rectal mucosa, and many of the earlier difficulties in the use of avertin by rectal administration were due to their presence. If a solution of avertin is decomposed by heat and injected into a cat's rectum an acute haemorrhagic proctitis results in a very short time. It is therefore important to be quite sure that a stable solution is being used, and before administration it must be tested for its reaction by adding two drops of a 1 in 1,000 solution of Congo-red to 5 c.cm. of avertin solution. If the reaction is less than pH=4.5 (due to the presence of hydrobromic acid) the indicator gives a purplish or blue colour and the solution must not be used, but if the orange-red colour of the Congo-red is unchanged the solution is satisfactory. A 3 per cent. solution of avertin is commonly employed, because the required quantity of the drug can then be given in the smallest possible volume; it is probably better, however, to administer a 2.5 per cent. solution, because in this concentration the drug is more evenly absorbed by the rectal mucosa.²¹

DOSAGE.

Correct dosage is a matter of considerable importance, for avertin is no exception to the general rule that when once an anaesthetic is given by the rectum it is impossible to control its action. No variation in the degree of narcosis can be effected by withdrawing any free avertin from the rectum, for the drug is absorbed completely by the time surgical anaesthesia is reached. When avertin was first introduced doses of 0.15 gram and over per kilogram of body weight were commonly used in the mistaken belief that full surgical anaesthesia could be obtained with safety. It has since been realized that this dose is unsafe for general use; 0.1 gram per kilo is safer and, for general purposes, more satisfactory because, although it produces complete anaesthesia in only 30 per cent. of cases,⁵ the other 70 per cent. are in such a state of narcosis that a very little additional volatile anaesthetic serves to produce complete anaesthesia. This dose may now be taken as the standard for healthy patients, but for cachectic and exhausted patients, whose glycogen reserves are diminished and whose powers of detoxicating avertin are impaired, it is sufficient to administer 0.08 gram per kilo.

Although the smaller doses now given may be relied upon to produce deep narcosis they do not always produce full surgical anaesthesia. This may be achieved in one of two different ways: either by supplementing avertin by an inhalation anaesthetic, such as nitrous oxide or ether, or by utilizing Butzengeiger's method of giving small additional doses of the drug per rectum (for example, 0.025 gram per kilo) at fifteen-minute intervals.⁵ This intermittent method is not generally used, probably on account of the trouble and time required and the grave danger of administering an overdose. Avertin should therefore be regarded as a particular form of premedication which will produce deep narcosis upon which full surgical anaesthesia can be superimposed by other methods.

It is generally agreed that 10 grams should be the maximum quantity of avertin administered to each individual irrespective of weight, though in certain cases the usual dose may safely be exceeded. The most important of these is exophthalmic goitre, where doses of 0.2 gram per

kilo, and even more, can be given without ill effect; in tetanus it can be given in still larger doses, when it reduces the number and severity of the spasms without unduly depressing the respiration. A case of tetanus has been reported¹⁷ in which a total of 63.8 grams was given during a period of twelve days to a child weighing 20 kilos; this represents an average daily dose of 0.28 gram per kilo.

Many drugs have been employed as adjuvants previous to the administration of avertin in the attempt to produce full surgical anaesthesia. Veronal and its derivatives, morphine, and hyoscine have all been used extensively in this connexion. If morphine is first injected smaller quantities of avertin than would otherwise be necessary are required, but it has the grave disadvantage of accentuating the depressant action of avertin upon the respiratory centre. It is therefore inadvisable to use morphine as a premedicament unless the dose is restricted to 1/8 grain.

THE ANAESTHESIA.

The induction of anaesthesia by means of avertin is most pleasant for the patient and easy for the anaesthetist. The pressure of the mask upon the face and the odour of the anaesthetic are abolished, while the administration of an appropriate quantity of the warmed solution is associated with no inconvenience to the patient. The solution, which has been prepared and tested by Congo-red, is slowly run by gravity through a rubber catheter into the rectum. No obvious change occurs in the patient for ten or fifteen minutes after the administration is completed; after this interval he begins to feel drowsy, and gradually lapses into unconsciousness. There is usually no preliminary excitement or struggling. The respiration becomes slow and shallow, and a slight degree of cyanosis may be noticed. Anaesthesia deepens, and the operation may commence about half an hour after the administration was started.

At this stage it is necessary to consider whether an additional anaesthetic is required or not. The usual signs of anaesthesia are unreliable, for, although the corneal reflex may be absent, a painful stimulus may elicit reflex movement, and indicate that anaesthesia is not complete. According to Blomfield and Shipway⁴ the best test is to apply a mask well wetted with ether to the face; if the breathing remains quiet the operation can begin, but if there is any holding of the breath full surgical anaesthesia has not been obtained, and it is necessary to continue with ether or some other anaesthetic. In any circumstances, a much smaller quantity of inhalation anaesthetic will be used than otherwise would be the case.

The blood pressure in man falls 10 to 20 mm. Hg, and a comparable fall occurs in both cats and rabbits; Bender states¹ that this is due to loss of vasomotor tone, but my own experiments¹⁸ indicate that it is due to a central cardiac effect, and not to dilatation of the peripheral blood vessels. Avertin has a definite action upon the heart; it causes a slight increase, followed immediately by an appreciable diminution in the force of the beat, which is accompanied by a slowing of the rate. In the isolated rabbit's heart this effect is marked when it is perfused with a 1 in 2,500 solution. Continuous perfusion with a strength of 1 in 1,250 causes arrest of the heart in systole within five minutes, an effect which is produced by chloroform in a dilution of 1 in 20,000. It appears, therefore, that so far as its action upon the cardiac musculature is concerned, avertin is about sixteen times safer than chloroform.

Respiration is markedly affected; it is very shallow, and the rate may fall to 8 or 10 per minute. After the administration of a normal dose the centre still retains all its reflex effects and its response to drugs; in man the administration of ether by inhalation produces quickening of the respiration, while in animals inhalation of ammonia and the injection of hydrocyanic acid still produce quickening and deepening of respiration, while the stimulation of an afferent nerve, such as the vagus or sciatic, elicits the normal response. If, however, the limits of safe dosage have been exceeded the respiration, in animals, shows that type of breathing known as apnoeic. The animal first takes a normal inspiration, which is followed, not by a normal expiration, but by five or six extremely

short expirations and inspirations; a normal expiration then occurs, and the process is repeated. Toxic doses of avertin cause death from respiratory failure, and it is important, therefore, to keep respiratory stimulants at hand when administering this drug.

The anaesthesia is very satisfactory for the surgeon, because muscular relaxation is complete, and it is comparable with that observed in chloroform anaesthesia. The pupil in both man and animals occupies the midway position, but with toxic doses it is contracted. A cat dies with pin-point pupils, and this affords a strong contrast with the dilated pupils which result from the administration of toxic doses of other anaesthetics. This is due to a central effect, for there is no action upon the pupil when an aqueous solution of avertin is instilled into the conjunctival sac.

With a dose of 0.1 gram per kilo anaesthesia is said to persist for about one and a half hours;²¹ the patient subsequently passes into a deep sleep, from which he can be roused with difficulty, and which lasts for some hours. There are usually no undesirable after-effects, and vomiting or nausea seldom occurs. Avertin acts as an analgesic after operation; it is therefore of considerable value in diminishing post-operative pain and in abolishing the use of morphine for this purpose. Further, the patient has no recollection of being anaesthetized, because avertin causes amnesia.

THE FATE OF AVERTIN.

It has been shown by Straub²² that avertin is absorbed by the rectal mucosa quicker than the water in which it is dissolved; accordingly, anaesthesia is produced with great rapidity. The subsequent course of events is uncertain, but it is stated¹³ that the drug is detoxicated in the liver by combination with glycuronic acid. It has been observed²⁰ that the duration of narcosis is longer in fasting animals on account of the diminished glycogen reserves, and this explains why a smaller dose of avertin is efficient for cachectic patients. The converse, however, is not true, for the administration of glycuronic acid, glycogen, or cane sugar to a patient under avertin has no effect upon the duration of anaesthesia,²⁰ and consequently these substances are of no value for detoxication.

There is no doubt that avertin is excreted by the kidneys; a sufficient quantity of bromine can be recovered from the urine to account for 98 per cent. of the ingested avertin.^{24 18} Traces of bromine, however, can be found in the sweat and breath.²³ The drug is not excreted unchanged, or as inorganic bromide, for neither of these substances can be demonstrated in the urine. The constant presence of glycuronic acid in the urine suggests that avertin is excreted as urobromalic acid—a compound formed by the union of tribromethylalcohol with glycuronic acid—but tests for this substance fail to prove its presence. The assumption, therefore, is that the drug is excreted as a complex organic compound of bromine.

At one time it was thought that avertin circulated in the blood stream as sodium bromide and was excreted as such.⁷ The suggestion was therefore made that the rectal administration of a solution of sodium chloride to a subject anaesthetized with avertin would diminish the period of unconsciousness and lead to a more rapid recovery from anaesthesia. This depends upon the fact that bromides are excreted in the urine *pari passu* with chlorides, and if the rate of excretion of chloride is raised that of bromide will follow. It would be easy, therefore, if the drug circulated as inorganic bromide, to bring an anaesthetized patient to consciousness as required, a matter of considerable importance in view of the long period of narcosis following the injection. It is now certain that avertin does not circulate as sodium bromide, and hence the subsequent administration of sodium chloride has no effect upon either the duration of anaesthesia or the rate of excretion of bromine.¹⁸

The concurrent administration of certain inorganic salts with avertin, however, has an effect upon the anaesthesia; if potassium or magnesium salts are given with the drug less is required. Again, it has been shown² that the withdrawal of calcium and sodium salts from the body has a similar action.

It has been suggested that certain other drugs are useful in detoxicating avertin, and both thyroxine¹⁹ and caffeine sodium benzoate⁸ have been used for this purpose. Probably the former is the more encouraging, because patients suffering from exophthalmic goitre bear avertin anaesthesia extremely well, and can safely take far greater doses of the drug than can be tolerated by the normal individual. Carlton suggests that the bromine in avertin saturates the thyroxine.⁸ Caffeine sodium benzoate, also, has been found to interrupt avertin anaesthesia in animals, and to stimulate respiration when this function is profoundly depressed, but personally I regard this suggestion with some misgiving, because it is now well known that the administration of caffeine in alcoholic and other forms of coma accentuates the toxic effect.

Avertin is excreted at a comparatively slow rate; experiments show that between 50 and 70 per cent. is excreted in the first twenty-four hours following administration.¹⁸ Bromine is found in the urine in progressively diminishing quantities until about the seventh day (see chart), and therefore, since the drug is cumulative, great care should be observed in administering a second dose. In spite of this, several instances^{11 14 17} have been recorded in which large doses of avertin were given on successive days without ill effects to patients suffering from tetanus.

Graph showing the rate of excretion of bromine in a rabbit weighing 1.8 kilograms after the subcutaneous administration of 0.4 gram of avertin (=0.346 gram bromine).

THE PRESENT POSITION OF AVERTIN.

All rectal anaesthetics possess definite advantages over inhalation anaesthetics because, as already pointed out, the administration is more agreeable to the patient and simpler for the anaesthetist. Avertin is preferable to other rectal anaesthetics because it does not irritate the mucosa, and it is unnecessary to wash out the rectum before administration or after the operation. The preparation of solutions of avertin for injection is not difficult if the solution in amylene hydrate is used, but it requires some care. Preparation, testing, and administration should be carried out by the anaesthetist and not delegated to a nurse.

Induction is most pleasant for the patient because there is no excitement or struggling, and the only sensation appreciated is that of falling asleep. The anaesthesia is characterized by excellent muscular relaxation, which, for abdominal surgery, is accentuated by slow and shallow respiration. The usual undesirable post-anaesthetic effects seldom occur, but, on the other hand, the patient requires constant attention on account of the prolonged coma.

Serious drawbacks to the use of avertin as a routine anaesthetic are those concerned with detoxication and elimination. From a study of the literature Lundy¹⁵ has calculated that the death rate intrinsic to avertin, after making all allowances for the submission of bad risks to operation, is about 1 in 3,333. Hewitt's figures,⁹ published nearly forty years ago, for the intrinsic death rates of chloroform and ether are 1 in 3,162 and 1 in 16,302 respectively. Accordingly both avertin and chloroform anaesthesia have a similar risk to life which is much greater than that due to ether; it is evident that avertin is not an anaesthetic for general use when others at our disposal are much safer.

Unlike chloroform, avertin has little effect upon the heart; its danger depends upon the fact that it is so slowly destroyed and eliminated. It should therefore not be used when there is disease of the liver or kidneys, which hampers these processes. As avertin produces marked respiratory depression its use is inadvisable when there is extensive disease of the lungs; nor can it, of course, be given when local disease of the rectum or colon prevents satisfactory administration.

There are certain conditions, however, in which avertin has a definite advantage over other anaesthetics, and the

most important of these is exophthalmic goitre. In this disease anaesthesia can be produced with the least possible distress, and the excess of thyroxine present detoxicates the drug and minimizes the risk of toxic symptoms; the absence of any deleterious effect upon the heart is an additional advantage. Avertin is of value in operations about the nose and throat when the use of inhalation anaesthetics is inadmissible; in spite of prolonged coma and depression of respiration it is stated³ that it can be used in these cases without anxiety. Further, it is useful in certain abdominal conditions because of the absence of post-operative sickness.

It is possible that some persons are unduly sensitive to avertin, for, even when allowances have been made for the unsatisfactory method of calculation, administration of the usual dose of 0.1 gram per kilo does not necessarily produce the same degree of narcosis in different subjects; for example, in some cases unconsciousness is not obtained, while in others death has occurred for no apparent reason.^{10 16} This is a point which might well be investigated further.

My object in this paper is to indicate the relative advantages and disadvantages of solid as opposed to volatile anaesthetics. Avertin is perhaps the best of the solid anaesthetics which have been made available up to the present time, and, although it is not so satisfactory for routine use as the volatile inhalation anaesthetics commonly employed, it is of particular service in the conditions which I have mentioned.

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CONGENITAL RADIO-ULNAR SYNOSTOSIS.

BY

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CONGENITAL radio-ulnar synostosis, which consists in ankylosis of the upper end of the radius and ulna, is exceedingly rare. The condition is said to be due to a constitutional error—the result of the imperfect separation by the mesenchymatous tissue of the cartilaginous axials of the forearm, which take part in the formation of the bones.

The factor which controls the development of a synostosis is unknown, and various causes have been invoked to account for the condition. Certain records suggest an inherited condition with synostosis as a dominant Mendelian characteristic; a second possible factor is related to those which control the chondrification and ossification of the skeleton, many of the affected individuals being subject to exostoses. In our case, in spite of lengthy cross-examination of the patient and her relatives, we were unable to find a history of a tendency to loss of supination in any other member of the family, whereas the patient was of healthy appearance and of normal stature, without any disproportion in the size of the limbs, etc.; no exostoses were present.

The condition is described as having three types. (1) The radius is unaltered in shape, but the head is ossified to the region of lesser sigmoid fossa of ulna. (2) The upper part of the radius shaft shows no definitely moulded head (the headless type), and the upper end is moulded to the

outer aspect of the ulna. (3) In the "dislocated head" type the head of the radius is well developed, but it is displaced backwards or forwards. This condition is usually unilateral, and associated with syndactylism, supernumerary thumb, or even absence of thumb. The case here reported belongs to the third type, and it also presents the unusual occurrence of being bilateral.

A girl, aged 18, was referred to me on July 23rd, 1929, at the out-patient department, and I reproduce the doctor's letter verbatim: "The bearer, M. S., suffering from fractured left olecranon. It was done seven weeks ago; a stellate type of fracture was found. The arm, after extension, was flexed to give her the 'carry to mouth,' and she was put on early massage. Massage has not yet completely straightened the arm."

On examination it was found that the left elbow could not be fully extended, whereas flexion was normal. The hand was held

FIG. A.

FIG. B.

in semi-pronation, but no supination was possible. Pronation could be carried out to about 90 degrees. The olecranon process appeared to be deviated towards the medial side of the elbow, whereas the head of the radius was directed towards the posterior aspect of the external condyle of the humerus, and was palpable as a distinct projection on the outer side of the elbow. No trace of the olecranon fracture of the elbow could be made out. On examination of the right elbow it was found that a similar condition was present, the arm being held in semi-pronation with limitation of extension. Flexion at the elbow-joint was normal, whereas pronation could be carried out to about 90 degrees.

The muscular development was normal, and there were no exostoses present. There was no disproportion between the upper

FIG. C.

FIG. D.

arm and forearm. No history could be obtained of any familial difficulty or abnormality. The patient stated that she could not carry things "as other girls could," but she had not found any disability in doing her work. The blow on the elbow had caused much pain when incurred, and it was only after this that the mother thought that the patient could not extend the arm properly.

X-ray photographs were taken of the elbow-joint, radius, ulna, and humerus on both sides, and line drawings have been made. From these it is seen that the radius of the left side is more curved than normal (Fig. A). The head of the radius is somewhat expanded and displaced backwards with relation to the humerus, and does not articulate with the humerus. A clear definition cannot be seen between the radius and ulna, and ossification appears to be present between the radius and the ulnar region of the coronoid process. A similar condition is seen in Figs. D and C, which were taken of the right elbow region. Fig. A shows how it was possible in a bad radiogram to diagnose a fracture of the olecranon.