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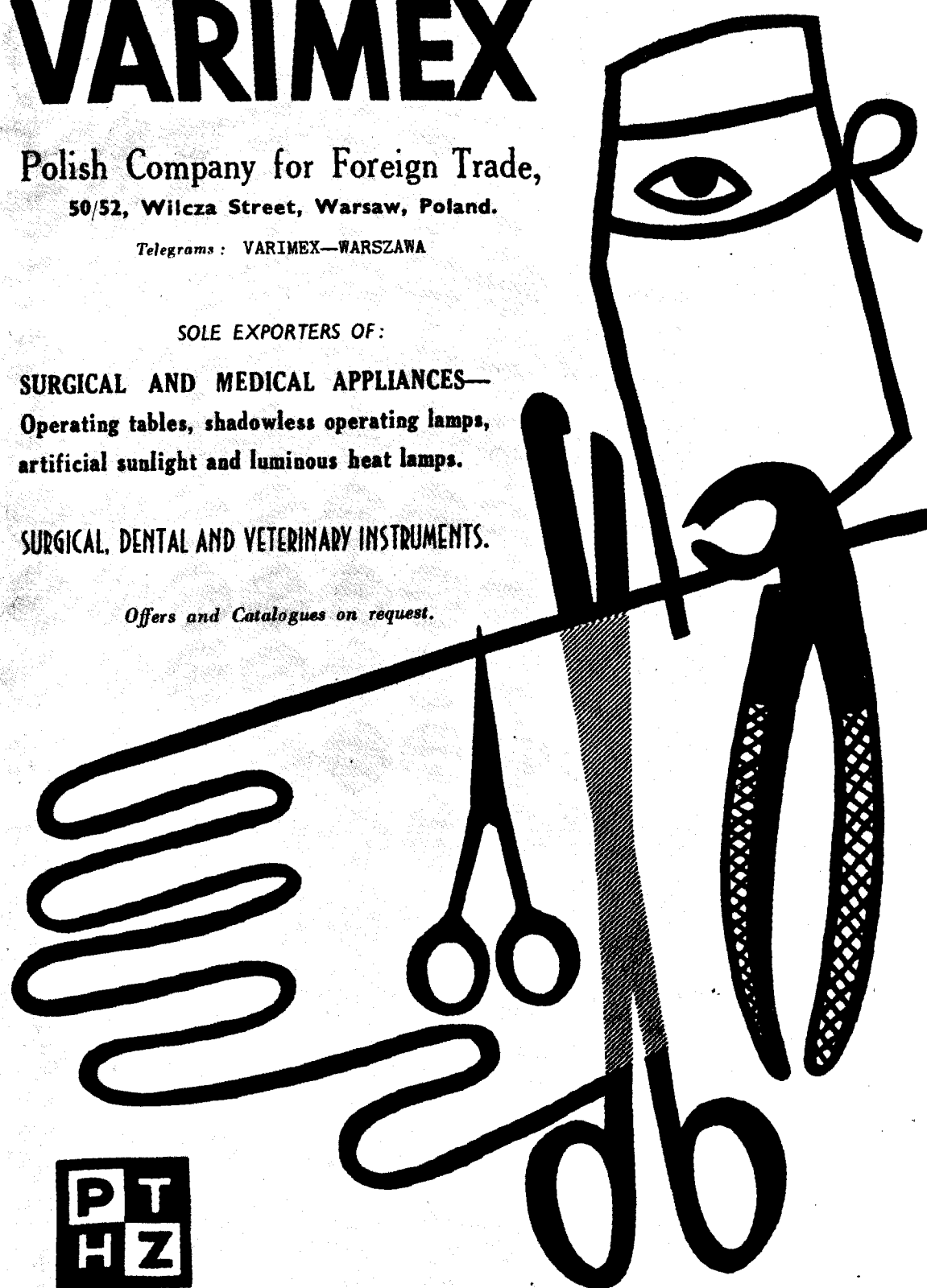
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"PASSING OUT" AND "GOING TO FOREIGN"

FULL of youthful energy and ambition the newly qualified doctor stood in front of the college canteen, gaily chatting with his friends. "Now that I have passed out I want to go foreign" he said reflecting in his remarks the ambition of almost all medical students throughout the country as soon as they qualify. "Passing out" was his way of saying that he had successfully completed his examinations and had qualified to practise as a Registered Medical Practitioner. "To go foreign" meant that it was his desire to travel abroad in the pursuit of further knowledge and enlightenment and to profit by travel in distant lands.

Why is it that almost every student who qualifies turns to foreign lands for the pursuit of higher studies as devoutly as the Muslim turns to Mecca? Who succeeds in going abroad? Is it merely the glamour of Western countries that attracts them or do they have any specific object in mind? What stands in the way of the fulfilment of their dreams? When they do go which countries do they go to? Do they go for under-graduate or post-graduate study? Do they profit by their stay abroad? Do they come back? When they do come back, with what ideas do they come? What happens to them? Is the exodus of large numbers of medical men spending Indian currency welcomed by the country? Can they obtain the study and practical experience in our country itself? These are some pertinent questions we may try to find the answers for.

The newly qualified doctor turns abroad for two main reasons. The first is the natural instinct of wanderlust which is not uncommon in most people although there may be material or other reasons why it does not get fulfilled. It is always interesting to see how other people live and conduct their affairs. Foreign films have a considerable effect on glamourizing life in the West. The second is a feeling that there is great enlightenment to be received from the leaders of medicine in the West. After all every textbook which is followed is written by a Western author. Our generation of senior teachers were taught Western medicine by doctors from the West. In spite of attempts to decry the value of medical education in the West, everyone is convinced that there is something worthwhile to be learnt abroad. While these are not very powerful motives there is one far more violent and for that reason more sinister. It is that the newly qualified doctor goes through a process by which many of his ideals are shattered. Brought up on a feeling that the country needs doctors, he suddenly finds as he looks around for a suitable employment that doctors are not so vitally required; or at least they are required at such a low price that it comes to him as a rude jolt. The newly qualified man becomes somewhat cynical and hopes that by a visit abroad he may acquire a certain glamour, and obtain a post-graduate qualification of some sort, and that on his return his material prospects will be brighter.

Between ambition and its fulfilment there lies a great ocean of practical difficulties. The first is finance. To go abroad and stay at one's own expense is no mean undertaking



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and unless one is sufficiently well off it is not practicable. Scholarships and fellowships can be had but most of these go to senior people in the services and that too usually in the evening of their professional lives when they are already at the head of a department of medicine. Stay abroad, however easy the Western films may make it appear is not that easy. Considerable acclimatization is necessary before getting used to great changes in climate, food, and environment. Of course these things are only appreciated when one actually gets abroad. Lastly apart from these difficulties there are the domestic ties and other responsibilities which stand in the way of going abroad. Yet in spite of all these difficulties a number of doctors do get abroad for a course in post-graduate medical education.

Almost always it is the English speaking countries which they select. That means generally the United Kingdom and the United States. The continental countries like Austria (Vienna) which were popular at one time do not enjoy the same status, partly as a result of language difficulty but more because they have been disturbed by recent wars of no small magnitude. Undoubtedly the United Kingdom is more popular for the reason that most of the textbooks which are used are written by Englishmen and our contact with them is far more intimate. The impression (probably quite a sound one) is that there is something substantial about English education and of course the fact that Sterling is more easy to get than Dollars. Life in the United States is terribly expensive.

The exceptional student may go for under-graduate study but almost all go abroad in search of post-graduate medical education. Yet in England it is not uncommon to hear the doctor who has come for post-graduate study say "I have had to forget everything I was taught and start learning afresh the fundamental principles of medicine". I think there is much in that because I believe that an Indian benefits more by under-graduate study than by going there for post-graduate study. I believe this to be so in spite of the majority view to the contrary. There are several reasons for this.

The Englishman is the first to admit that facilities for post-graduate study in the U. K. as it stands today is far from satisfactory. Most of the post-graduates from abroad are birds of passage and the teachers do not have an opportunity to get to know them or to take a personal interest in them as he would if they studied under him at his hospital. This applies to the different courses the Post-Graduate Federation conducts in Surgery, Medicine, Obstetrics, Gynæcology and other subjects. However, this can be offset by taking up a hospital appointment when the doctor comes under the direct influence of a consultant. Provided his consultant is interested in him, the value of such appointments are enormous although this aspect is not generally appreciated and many doctors simply attend a course of lectures, watch some complicated operations in big teaching hospitals (sometime on these occasions, the theatre is so crowded that he may never find out what is happening except for occasional glimpses!) take their post-graduate diplomas and come away.

Even if hospital appointments are valuable to hold, the Indian post-graduate is more keen to get his diploma (F.R.C.S., M.R.C.P., M.R.C.O.G. or other diplomas) than to

learn techniques and acquire practical experience because getting diplomas and degrees is what is going to get weightage when he returns to India. The authorities are going naturally to prefer the man who went and actually got his MS or FRCS in a year than a man who worked under able thoracic surgeons say at a chest Unit for five years and acquired practical knowledge but still returned without a diploma or a degree. We tend to go by what degrees or diplomas a chap has after his name rather than what he can do but today we are fast moving towards a pattern of society which does not even care for that and the criterion is, whom does the chap know and how much influence does he wield and how important and influential are his relatives or sponsors.

No one can go to a foreign country and come back without having profited in some way. Yet it is desirable that the advantages he has obtained is commensurate with the time and money which he has spent. Of course this is a very difficult matter to judge but we would certainly do well to find out hereafter what a chap is qualified to do and what he is fit for than simply go by other considerations.

After some time spent abroad it is natural under an environment which, if not certainly strange is at least one that does not offer all the home comforts he is used to, the Indian feels the call to return to his own country. If he returned without any expectations there is little room for disappointment but that is not usually the case. His imagination is fired by reports of the great advances his country is making. He hears about the rapid progress which is being made as the result of bold five year plans executed with determination by the people. No year passes without at least one visit from the Prime Minister who talks to Indian nationals and makes a vigorous plea that they should return and contribute their share to the reconstruction of their country. The Health Minister visits more frequently and no week passes without some delegation (trade, goodwill, cultural and of other types which evade precise definition) and all are unanimous in their full throated appeal "We need more doctors... We need more nurses..." So the Indian doctor having completed his course or his work and having acquired the hall mark of a diploma returns full of confidence and hope that his people need him; that the moment he returns he will be taken up in the service of his nation. Great thoughts are good. He is wanted, but as he drifts from one public service commission to another, from one employment exchange (by this I mean those organizations who can give doctors a job) true enlightenment slowly dawns on him. He is wanted, yes. But he is wanted at a price which he did not expect. There are always jobs open to him and no dispensary would dare to refuse to pay him the minimum of Rs. 100/- per month in view of his "high" qualifications. If he gets into a service he can get his Rs. 200/- He is wanted at a salary which he can barely afford to live on. He becomes disillusioned and depressed. He finds the big wigs whom he met at India House receptions abroad and rubbed shoulders with and who were so informal and friendly are quite different people now. They have no time to see him. He must apply through proper channels if he wants a job. He should appear before a public service commission. Yes—he should accept the posting to go to the village if that was where he was wanted. No. He could not be paid a better wage. India was a poor country. May be he was worth £980/- a year in England. In that case he was a fool to return and he could go back.

Completely disillusioned he has to think of the next step. Should he stay or return? After all he was not a complete nit-wit. The country may not want him at his price or at a price which most people would agree was reasonable for a trained member of the medical profession. There was nothing to stop him putting up his board and starting a general practice in the city. He could make a comfortable living. So forgetting all he learnt of special methods and special operations whether it be at the Thoracic Unit at Boston or at the Plastic Unit at Basingstoke he settles to the comfortable life of a general practitioner, prescribing for coughs and colds, undertaking safe risk operations and sending the difficult cases to hospitals. What of his special training abroad? What of the special techniques he picked up?

There was no recognition of all that. He knew nobody. There was no one to sponsor him. On his skill and knowledge alone he had tried to find a place but alas his country did not want him, because India was a poor country. India could only afford to send out almost every other senior official almost every other month with his complete entourage on every type of mission (trade, goodwill, cultural, or other) but it could not afford to employ a skilled scientist who had spent hard-earned money out of his own pocket to acquire special skill and knowledge which he believed would be of ultimate benefit to his people.

Is there nothing we can do to put a stop to this sad state of affairs? Is fitness for a job not going to find a place at all? Are not our scientists of more value to us than half a dozen long haired musical members of a cultural delegation?

Those who are at the helm and who guide the nation in its technical advances would do well to consider this aspect of the problem and do something before it is too late.

Yet what is the view of those up at the top? A very great man, a distinguished educationist of India has deprecated the idea of sending medical graduates to foreign countries when we could now secure the best post-graduate training in all branches of the medical profession in the teaching institutions now existing in India. Yet soon after this noble pronouncement he complained of the great dearth of trained teachers which stood in the way of opening more new medical colleges and bewailed the rapid and continuing fall in standards. Noble and high-sounding words are often born on the tongues of those who rise to such lofty positions that they gradually lose touch with the earthy things in life. Noble words may please many people but it will not carry much conviction with those who fought for and followed an ideal and achieved a goal only to be caste aside by their own people.

An actress is supposed to have asked a hotel clerk. "Can you give me a room and a bath?" The sarcastic clerk replied, "I can give you a room, sister, but you'll have to take your own bath!"

A much married Hollywood character complained to a Hollywood cynic that his wife had run off with his best friend. "Your best friend?" echoed the cynic, "Who's that?" "I dunno his name" was the reply, "but whoever he is — he's NOW my best friend".

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ACTION OF FLUORINE ON THE TEETH IN RATS

By DR. S. C. PILLAI and T. K. WADHWANI

Department of Biochemistry, Indian Institute of Science, Bangalore.

IN a recent communication the results of the present authors' studies on the influence of diet on fluorosis in rats were given (Pillai and Wadhwani, 1956). It was of interest to continue the studies, more particularly on the behaviour of the teeth under the influence of fluorine. The further observations made are briefly described in this paper.

Smith (1934) estimated the normal growth of the incisors in rats to be at the rate of 3.17 mm. per week. Such rapid rate of growth of the incisors would explain the disappearance of the external symptoms of mottling of teeth on stopping the administration of fluoride to the experimental rats (Pillai, 1942; Pillai *et al.*, 1944).

The incisors in rats are known to wear away steadily by functional attrition which may be defined as the normal wearing away of the teeth due to functional activity. The alternate backward and forward movement of the jaws in gnawing produces a much more rapid wearing of the relatively softer cementum and dentin on the lingual side than of the very hard enamel on the labial surface, and results in a sharp chisel-shaped edge (Schour and Massler, 1942). When by reason of accident one of the incisors is broken or when a mal-occlusion occurs, the non-attrition of the opposing incisor and its continuous growth results in an elongation or so-called overgrowth. This overgrowth is the result of the lack of wear, just as long hair can be the result not of overgrowth but of lack of trimming. The unworn teeth assume the shape of a typical 'logarithmic spiral.' They may perforate the palate or the lip and in wild life will cause the death of the animal through starvation.

The growing tooth is the first organ to react to fluorides and the growing enamel and enamel-forming cells give the most delicate response (Schour and Massler, *loc. cit.*). But the rapid rate of growth of the rat incisor would very considerably influence the action of fluorine on it. The nature of this influence was studied to some extent.

EXPERIMENTAL

Effect of oral administration of fluorine on the teeth in rats. Four weeks old albino rats (as far as possible from

the same litter) were used for the experiments. The rats were placed on a normal stock diet. To the experimental rats 5 mg. of sodium fluoride per rat per day were administered orally (along with diet and water), and the effect of fluorine on the teeth was observed.

In the experimental rats the incisors did not grow normally and in two weeks, particularly the lower incisors, put on a dull opaque white colour and lacked the natural polish of the well-formed teeth. In the early stages the teeth were corrugated transversely, indicating intermittent interference with their development. In some cases the lower incisors were loosely spaced. The lower incisors further underwent changes in the structure and hardness, wore away easily and were chipped off badly in some cases (Figs. 1, 2 and 3). Sometimes the lower incisors were so badly eroded that the erupted portion of the teeth was reduced to a level with the gum line. In such cases, the upper incisors grew abnormally, tending in every case, to grow backwards into a circle and finally to penetrate the roof of the mouth (Figs. 4 and 5). At this stage, to a few of the rats the administration of sodium fluoride was stopped for a week and then continued intermittently. It was then observed that more number of teeth erupted out from the position of the two upper incisors (Fig. 6).

The overgrowth of the upper incisors was presumably not caused by any stimulative action of fluorine on the tooth formative organ. It was caused probably by the lack of natural wear which the incisors, under normal conditions, would exert on each other in occlusion. The incisal attrition and consequent reduction by wear did not take place as the upper and lower incisors did not occlude. The incisors were chipped off because of their inferior quality. The fluorine apparently interfered with the tooth development.

Effect of varying concentration of fluorine on the rat incisors and on stopping its administration. In a further series of experiments the amount of sodium fluoride in the drinking water was steadily increased up to 7 mg. (per rat per day) in course of two months. The teeth of these animals were found very considerably mottled and pitted. At this stage the animals were changed



Fig. 1



Fig. 2



Fig. 3



Fig. 4



Fig. 5



Fig. 6

Figs. 1 to 6. Photographs showing the effect of fluorine on the teeth in the experimental rats.

over to ordinary fluoride-free water, and the condition of their teeth was closely observed. It was of interest to note that by the end of three months all the experimental rats developed normal teeth, the mottled condition having completely disappeared. This is understandable in the light of the observation of Smith (1935) who recorded that the lower incisors of the rat completely renewed themselves every 30 days. The replacement of the defective incisors by normal ones was delayed in the experimental rats probably because of the cumulative effect of fluorine in the system.

In another series of experiments the water used for the animals (about six weeks old) contained 10 parts per million of sodium fluoride. Although symptoms of

mottling of teeth were seen in the case of the experimental rats, their growth rate, as observed during a period of three months, differed only slightly from that of the control animals (Fig. 7). On changing over the experimental animals to fluoride-free water, the external symptoms of mottled enamel gradually disappeared in the course of two months. During this period also the rate of growth of the animals was not very different from that of the control animals.

Effect of intraperitoneal injection of fluorine on the teeth in rats. When 1 cc. of sodium fluoride solution containing 1 mg. per cc. was injected every day intraperitoneally, the characteristic effect of fluoride on the teeth was observed after two to three weeks. Abnormal areas

appeared at the gum line. Later, after two weeks, particularly the lower incisors exhibited a transversely corrugated pattern. Both the enamel and the dentine of the incisors showed a pair of light and relatively dark incremental layers for each injection of sodium fluoride. The light layers represented the immediate response to the injections and were imperfect in formation and calcification. The dark layers represented a recovery response and were normal in formation. This incremental pattern was always noticed unless the dose was greater or was given even more frequently.

When the fluoride was administered to the rats orally, the bleaching of the teeth was caused in a shorter period than that it took when the fluoride was injected intraperitoneally; moreover, in the first case, the bleached areas were found spread over the whole surface of the tooth and were not confined to the gum line.

DISCUSSION AND SUMMARY

The above experimental observations indicate that fluorine has a local as well as a systemic action on the rat incisors. The disappearance of the symptoms of mottled enamel in rats, on changing over to fluoride-free diet and water, was apparently brought about by the continuous growth of the incisors. The continuous eruption and wear of the rat incisor would soon obliterate the mottling process that might take place in the exposed portion of the tooth.

The local or direct action of fluorine may be explained by assuming that during the process of drinking fluoride-containing water or eating of fluoride-containing foods, fluoride is absorbed selectively on the enamel of the teeth and acts upon it. Volker *et al.* (1940) exposed samples of powdered enamel, dentine, bone and hydroxyapatite to solutions of sodium fluoride. The amount of fluorine picked up by these substances was found to follow the absorption isotherm, thus demonstrating that fluorine does absorb on dental tissues. The fluorine thus absorbed on the dental tissue might act upon it.

Pandit and Narayan Rao (1940) observed that when fluoride solution was administered by means of stomach-tube, mottling of teeth did not occur in monkeys whose permanent teeth had erupted prior to starting the experiment. During the period of observation, one monkey gradually dropped some of its deciduous teeth and developed two lower permanent central incisors and later two upper central incisors. Mottling of the enamel of these teeth was observed. This has a bearing on the

general observation that the teeth of children or adults, who do not begin drinking water containing fluoride until after their second sets of teeth have erupted, do not later show mottled enamel. The exact reason for this is not yet known, but it was explained by Smith (1935, *loc. cit.*) by assuming that in humans, the enamel organ disappears as soon as the enamel of the permanent teeth is completely formed and calcified. The enamel does not feel to regenerate itself and behaves like a dead tissue. This explanation, however, does not permit of fluorine having any local or systemic action on teeth in humans after a particular period.

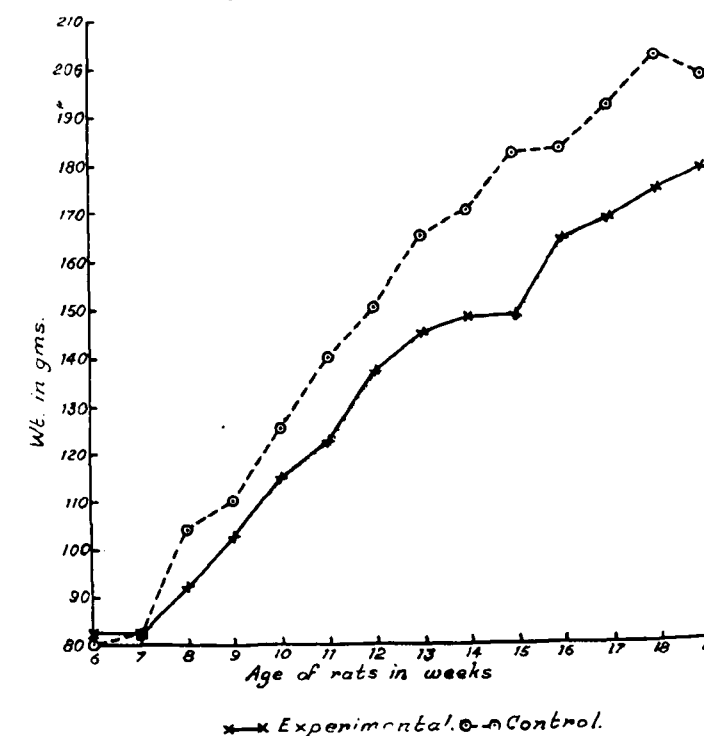


Fig. 7. The rate of growth of the rats in the experimental (receiving fluorine) and in the control series.

Irving (1944) reported that a variety of substances (oxalate, manganese, calcium, phosphorus, magnesium, molybdenum and beryllium) besides fluorine were capable of producing altered incremental lines in the dentine of the rat incisors. Measurement showed that the effects were as with fluorine at the time of injection. However, in no case any effect on the organic enamel was found. Irving further observed that the action of fluorine on the enamel was independent of the Ca: P ratio of the diet, but that on dentine depended upon the Ca: P ratio and that the first action was a direct one on the enamel organ and the second was indirect by altering the concentration of blood constituents. He concluded that the other substances also acted by altering the composition of blood but had no direct action on the

(Continued on page 12)

ACUTE OTITIS MEDIA

By DR. WALTER D. CHASE, M.D., F.A.C.S.

Bethlehem, Pa.

There are two types of acute inflammation of the middle ear:

1. Acute suppurative otitis media
2. Acute "catarrhal" otitis media, or serous otitis media

The acute suppurative type is the familiar involvement of the tympanum which occurs during acute inflammation of the nose or throat. This occurrence may be when the inflammation is localized to the nasal, nasopharyngeal, or oropharyngeal areas, or it may accompany infections of the whole respiratory tract, such as influenza and pneumonia. Scarlet fever, measles, and diphtheria frequently are complicated by acute suppurative otitis media. Of course, the middle ear mucosa is the victim of infection when water enters the Eustachian tube while swimming and from damaging syringing of the ear canal when the tympanic membrane has a perforation.

The "catarrhal" or serous otitis media, or "transudate," as it is sometimes called, is believed to be so mild a type of inflammation as to create fluid accumulation in the middle ear, *without* the evidence of bacterial damage with the production of necrosis and pus. There is no doubt that this milder type of middle ear involvement has become much more common since the universal use of the antibiotics, these bacteriostatic substances reducing the virulence of the organisms common to the upper respiratory region to such an extent as to make the

damage to the tympanic mucosa so much less than occurs in the suppurative type that it has been taken too lightly by physicians. Since there is no *pain* in the serous type, the family doctor, the pediatricist, and also some otologists take the condition very lightly, and usually damage to the hearing results in these cases, whereas skilled treatment can remove the cause and correct the tympanic state.

Treatment: In acute suppurative otitis media, unless the pain ceases within 24 hours, immediate incision of drumhead is mandatory. Also, even if there be little discomfort, if the drum-membrane *bulges*, incision must be done. Undrained pus anywhere in the body is dangerous; in the ear, extension to the meninges, the sigmoid sinus, or into the depths of the brain itself is a constant threat. Antibiotics should be immediately begun, using the one that is type-specific if it can be determined. Dosage must be *large enough* and it must be continued *long enough*. Almost always, the drug is given for too short a time. Unless given for about five days after all discharge has stopped, the inflammation slumbers on in the deep tissues, and intracranial complications may occur, weeks later; also, almost certain damage to hearing results if not continued long enough. With correct therapy, mastoid surgery is nowadays almost never required. Inflation of the middle ear is neglected by most otologists. Any otologist not familiar with Politzer's teachings is an ill-prepared otologist. Every case who has had any middle ear inflammation needs inflation by Politzer's method, both during the time

(Continued from page 11)

tooth and that in any event it would be unlikely that such diverse substances would directly act on the tooth but they might affect calcium and phosphorus metabolism. But Schour and Smith (1934) observed that fluorine exerted a direct local action on the enamel-forming cells and that the changes observed in the enamel and dentine were not produced by changes in blood calcium and phosphorus.

REFERENCES

- | | | | |
|-----------------------------------|---|---|---|
| Irving, J. T. | (1944), <i>Nature</i> , 154, 149. | Pillai, S. C., Rajagopalan, R. and De, N. N. | (1944), <i>Ibid.</i> , 79, 261. |
| Pandit, C. G. and Narayan Rao, D. | (1940), <i>Indian J. Med. Res.</i> , 28, 559. | Pillai, S. C. and Wadhvani, T. K. | (1956), <i>Surgical & Med. News</i> , 2, 28. |
| Pillai, S. C. | (1942), <i>Indian Med. Gaz.</i> , 77, 19. | Schour, I. and Massler, M. | (1942), <i>The Rat in Laboratory Investigation</i> (by a staff of thirty contributors, edited by J. Q. Griffith and E. J. Farris), J. B. Lippincott Company, pp. 102-163. |
| | | Schour, I. and Smith, M.C. | (1934), <i>Arizona Agric. Expt. Sta. Tech. Bull.</i> , No. 52, p. 69. |
| | | Smith, M.C. | (1934), <i>J. Dental Res.</i> , 14, 139. |
| | | <i>Idem.</i> | (1935), <i>Amer. J. Pub. Health</i> , 25, 696. |
| | | Volker, J. F., Hodge, H.C., Wilson, H. J. and Voorhis, S.N. | (1940), <i>J. Biol. Chem.</i> , 134, 543. |

immediately after the early drainage stage and especially from that time on until normal hearing has been restored. I most always instruct the family in Politzer's method of inflation by use of an 8-oz. or 12-oz. rectal syringe. It may be necessary to enlarge the tip of syringe by putting a short section of rubber tubing on the vulcanite tip, so that it fills the one nostril. I have the inflation performed several times daily. It is also very important to make a thorough investigation to be sure as to whether or not a sinus may be infected, this keeping up the ear involvement unless corrected. It is a very common experience for me to discover a complicating sinus, especially an antrum, as the cause of continuing middle ear disease. In children, of course, adenoids should usually be removed, together with the tonsils. I frequently do the "T. & A." before the patient leaves the hospital, if he was hospitalized for the treatment of the ear condition.

Predisposition and prevention of otitis media should be emphasized. Those predisposed are children with unhealthy tonsil and adenoid states, with the tendency for recurring attacks of inflammation of this lymphoid tissue, those with allergy and the exposure which swimming causes. Nose clamps are not uncommonly seen nowadays and the swimmer need not feel unduly conspicuous by appearing with them attached to nose. Besides being the direct cause of involvement through the Eustachian tube, the ear may be secondarily damaged, due to the sinus disease which swimming and diving frequently cause. Gross nasal conditions, such as polyps, must be completely eradicated. Chronic sinus disease is very frequently accompanied by middle ear disease and must be corrected before one can expect the middle ear to clear up. Closing perforations in the drumhead will protect the middle ear from re-infection from showerbaths, swimming, etc., but this must not be attempted until existing infection in the tympanum is eradicated.

Attention of the physician is directed to serous otitis media condition by the patient's having a feeling of "stuffiness" in the ear; the hearing is decreased and sometimes there is noted a sensation as of fluid moving in the middle ear, as when the position of the head is altered from one side to the other, or while swallowing or blowing nose. The degree of decreased hearing may be temporarily lessened on blowing nose, especially if the nose is held so tightly as to cause air to be forced into the middle ear through the Eustachian tube. On inspecting the drumhead, one does not find the normal grey

drumhead, but a change characterized by a faint yellowish tint with increased sheen, and a fluid-line is frequently seen, this sometimes being seen in only the anterior or the posterior half of the drumhead. Sometimes there is retraction of the drum membrane at Shrapnel's area. If the ear is inflated, air bubbles usually appear in the tympanum. Fork tests reveal Weber referred to the involved side, with negative Rinne on that side.

Treatment of serous otitis media consists in removing the cause, such as unhealthy adenoid states, enlarged turbinates, polyps, sinusitis, allergy, etc. The fluid should be removed by incision of drumhead and forceful Politzerization, the Politzerization then being carried out at home by use of the rectal syringe previously described. I often place a wick of gauze, saturated with 10% phenol in glycerine, into canal in contact with the drumhead; this keeps up hygroscopic pull on the fluid and helps prevent closure of incision too soon. It is surprising how soon the incision heals. Re-opening for further drainage is sometimes necessary. I also sometimes employ atropin sulfate during the early days of treatment. It is probable that use of antihistamine should be more commonly followed, as obscure allergy is no doubt present in a big percentage of cases. In addition to these well-known treatment methods, I look for the development of new discoveries which may bring about dramatic improvement in the treatment of this troublesome middle ear condition.

I find a great many patients who have hypertrophy of the inferior turbinates, and I employ galvanocautery on the lower borders of these structures, applying it particularly thoroughly at the posterior ends, which so often are found as a prominent, rounded mass. Correcting this condition can afford marked improvement in some ear conditions, as well as in patients with nasal complaints alone.

Since the advent of the antibiotics, physicians show an unmistakable tendency to hold on to their patients with ear and sinus infections, avoiding a consultation if possible. The earache may continue two or more days, indicating dangerous pus-retention, with the danger of extension intracranially, yet the patient is often denied skilled drainage procedure, the attending doctor administering some antibiotic (usually prescribing "Auralgan," with its spurious claims that it *enters* the *middle ear* and counteracts its inflammation, though we know that the 3-layered drum membrane is impermeable), and trying

(Continued on page 14)

VITAMIN 'C' AND ITS ROLE IN TUBERCULOSIS

BY DR. B. B. RAI, M.B., B.S., O.B., St.J., R.S.,

Medical Officer Incharge, Govt. T.B. Clinic, Bareilly, U. P.

HISTORY

THE discovery of Vitamin C was due to the development of scurvy in people, when they were given a diet excluding fresh fruits and vegetables. Thus scurvy has been a menace to seafarers, explorers and armies since classical times. Vasco-da-Gama who in 1498 sailed round the Cape of Good Hope describes how he lost hundred of his crew out of hundred and sixty. Jacques Cartier (1535) during his exploration of Canada found that the native Indians prevented the disease by drinking a decoction of pine needles, which we now know contains ascorbic acid. Lind in his book "A Treatise on the Scurvy" (1757) mentions the value of Citrus fruits and green vegetables in the treatment of Scurvy. He gave patients suffering from this disease several treatments including two oranges and one lemon a day. The patients receiving the oranges and lemons showed improvement. But all this was not appreciated until Holst & Frolich in 1907 produced experimental scurvy in guinea pigs.

The vitamin, whose absence is responsible for the scurvy, was first isolated by Szent-Gyorgyi in 1928 from suprarenal glands and subsequently from orange juice and cabbage. In 1932 Waugh & King isolated it in crystalline form from lemon juice and showed its powerful antiscorbutic activity and in 1933 it was named Ascorbic acid.

CHEMISTRY

Ascorbic Acid, which forms colourless crystals, is freely soluble in water and slightly soluble in acetone and lower alcohols. If kept dry and not exposed to light ascorbic acid is stable for considerable time. It is readily inactivated by oxidation.

NATURAL SOURCES

Fresh fruits and vegetables are the best sources of the vitamin. Generally speaking the ascorbic acid content

of the fruits and vegetables increases to a maximum just before ripening and then decreases steadily. Thus dried legumes and cereals are poor sources of the vitamin. However, the following is the list of fruits and vegetables which contain high amounts of the vitamin :—

Fresh Fruits: Rose hips and haws, black & red currants, straw berries, Orange, Lemon, grape fruit, goose berry, guavas, Myrobalan (Aonla) and West Indian Cherry. There is a small amount present in pear plum, grapes and apples.

Fresh Vegetables: Brussels, Sprouts, Cauliflower, Cabbage, Tomato and new potato.

Ascorbic acid is also formed during the germination of the seeds.

The ascorbic content of cow's milk is very variable depending upon the fodder. The value also drops as soon as it leaves the cow and cools down. There is a loss of 20 to 30% in the vitamin content within 24 hours even when the milk is raw.

Cooking in iron, copper or badly tinned vessels causes destruction of the ascorbic acid content of the vegetables and fruits. Stainless steel, aluminium or pyrexglass vessels have no deleterious effect. Restaurant and cafeteria meals contain very small amounts of the ascorbic acid because of the long time taken from the peeling and preparation of the vegetables to their being served on the table.

ABSORPTION

Ascorbic acid is absorbed from the small intestine by a simple diffusion mechanism and the rate of absorption varies with the amount ingested. It has been observed by some workers that in rat about 60% of the total ingested ascorbic acid is absorbed and the rest is lost somewhere in the gastro-intestinal tract. Now after absorption from the small intestine it is deposited in

(Continued from page 13)

to quiet the patient's outcries with analgesics. Though the patient may be fortunate enough to have spontaneous rupture, and escape intracranial complication, his hearing is very frequently damaged permanently. This is not immediately evident to the family doctor, who does not employ refined hearing tests, but examination at a later date discloses the hearing-loss, and by that time it is

probably too late to bring about correction of the condition. I appeal to all physicians to help preserve the hearing of their patients, especially the child-patients, by applying needed consultant skills. Complete medical service presupposes this co-operation between family doctor and his otological colleague, as well as the employment of our new, "myrical drugs".

tissues generally to the greater extent in glandular tissues and least in muscular tissues, spleen and fat. Ascorbic acid is also present in the blood, saliva, gastric juice, milk and sweat. The major part of the ascorbic acid is in the cells and not the plasma. Farmer and co-workers believe that in man the absorption of the vitamin from the intestine is almost complete in health, because in normal intakes the faecal excretion is negligible.

Regarding the utilization of synthetic ascorbic acid and natural ascorbic acid much investigation has been carried out and it appears that synthetic ascorbic acid is utilized just as well as the natural one occurring in vegetables and fruits.

FUNCTIONS

It has been considered that ascorbic acid acts as a hydrogen transporter in the living cells functioning as a component of a reversible oxidation-reduction system. Ascorbic acid is fundamentally concerned in the formation of intercellular substances including the collagen of fibrous tissue structures, the matrices of bone, cartilage and dentin. In the absence of the protection afforded by this vitamin the condition known as scurvy develops. The vitamin is synthesised in the body of most animals, but man, monkeys and guinea pigs are the only exceptions, so these are dependent upon a supply in foods.

ASCORBIC ACID IN DISEASES

Ascorbic Acid has been suggested for the treatment of numerous and diverse diseases unrelated to a deficiency of this substance like acute infections wherein clinically it has been found that toxic symptoms show definite abatement and the general sense of well being of the patient is improved; principally because it is strong reducing agent and is alleged to have potent detoxifying properties. Clinically its efficacy has also been established in the treatment of hay fever and asthma. It has also been found that the ascorbic acid assists the body to resist infection, particularly in the diseases which show an elevated body temperature.

ASCORBIC ACID & TUBERCULOSIS

Since Hojer (1924) and Bieling (1925) showed that the ascorbutic state increases susceptibility to tuberculosis more attention has been directed to the role of Vitamin C in this disease. Thus Perla and Marmorston (1937) observed the favourable effect of vitamin C on increasing resistance to Tuberculosis.

Getz and co-workers' (1951) extensive studies have revealed that a marked vitamin A & C deficiency occurred in man who developed pulmonary Tuberculosis.

Poor housing and living conditions exposure to infections, protein intake and occupation may have been contributory to the disease.

Now as healing in Tuberculosis is characterised largely by the formation of connective tissues for which vitamin C is essential it is possible that the vitamin deficiency may delay the process of healing and thus create an unfavourable effect on the course of the disease.

A diminished excretion of vitamin C and low plasma levels have also been reported in tubercular patients and on the basis of excretion studies it has been found that requirement of the vitamin increases in such patients.

Rai & Kehar (1941) have also observed that the average daily excretion of ascorbic acid in tubercular subjects is lower than in normal persons. These workers have further observed that if the diet of tubercular patients is supplemented with an optimal intake of vitamin C from citrus fruit juice or a single massive dose of ascorbic acid, the excretion of vitamin C increases though there is still an indication of considerably more destruction than in normal subjects.

Animal experiments suggest that the vitamin C deficiency predisposes to tuberculosis infection. Birkhaug (1939) reported that the large doses of the vitamin caused a significant increase in body weight and reduction in the tuberculosis lesions of guinea pigs infected with tuberculosis. He also records that the vitamin C inhibits the tuberculin reaction in tuberculosis guinea pigs.

Sweany and his colleagues (1941) thought that ascorbic acid was of some benefit and prolonged life in advanced cases. The McConkey (1943) thought that Cod Liver Oil and tomato juice were helpful in preventing laryngeal tuberculosis as a complication of pulmonary tuberculosis.

REFERENCES

1. Bieling, R. Zischr. F. Hyg. 1925, 104, 518.
2. Birkhaug, K.E. Acta Tubercul. Scand., 1939, 13, 45.
3. Getz, H. R., Long E. R. & Henderson, H. J., Am. Rev. Tuberc. 1951, 64, 381.
4. Hojer, J. A. Acta Paediat. 1924, 3. (Exptl.), 8.
5. McConkey, M., Amer. Rev. Tuberc. 1943, 47, 284.
6. Perla, D. and Marmorston, J. Arch. Path. 1937, 23, 543.
7. Rai, B. B., & Kehar, N. D., Antiseptic, 1945, 42, 414.
8. Sweany, H. C., Clancy, C. L., Radford, M. H. and Hunter, V.; J. Amer. Med. Ass. 1941, 116, 469.

ACKNOWLEDGEMENT

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STRUMA LYMPHOMATOSA

(Chronic Lymphatic Thyroiditis, Hashimoto's Disease, Hashimoto's Thyroiditis Lymphadenitis—Joll)

A Report of 133 cases *

BY DR. NOLIE MUMEY, A.B., M.A., M.Sc. (Surg.), F.A.C.S., F.I.C.S.
Denver, Colorado, U. S. A.

ANY disease becomes known by many names when it is not clearly understood. The literature, in its complex and voluminous accumulation, becomes confusing to the reader when various terms are applied to the same disease by different writers. Hashimoto's Disease has added to the confusion because of terminology.

The condition was first described by Hashimoto¹ in 1912, when he reported four cases of "lymphoid goitre". He described the disease as being different from Riedel's² thyroiditis, which was described in 1896.

In 1922, Ewing³ came to the conclusion that Riedel's and Hashimoto's were the same disease. It was not until 1931, that Graham⁴ described the two as being separate entities.

In 1925 and 1929, Williamson and Pearse⁵ described the same condition by the name of "lymphadenoid goitre." In 1939, Joll⁶ used the term "lymphadenitis," which does not seem to apply to the disease, for the evidence of inflammation is rarely, if ever, found.

Hashimoto's Disease involves the thyroid gland, and is characterized by finding lymph cells that have invaded the interacinal connective tissue. The disease confines itself to the gland without involving the capsule, while Riedel's struma not only involves the capsule but areas

beyond the gland. It is slow in onset, occurs mostly in women around the menopause, and is most frequently associated with myxedema. The most noticeable characteristic of the disease is the absence of the symptoms of hyperthyroidism, although the patient will present a picture which will resemble this condition. A physical examination will reveal a hard, uniformly enlarged gland without the usual evidence of toxicity.

ETIOLOGY

The etiology of the disease is somewhat obscure. It may be the end results of thyrotoxicosis. Skillern⁷ believes the disease is due to a primary failure of the thyroid cells, which results in a compensatory hyperplasia and a secondary lymphocytic infiltration. Others have attributed a faulty diet, vitamin a deficiency, metallic poisoning, virus and bacterial infection, or an inflammatory process, as being the cause of Hashimoto's Disease.

DIAGNOSIS

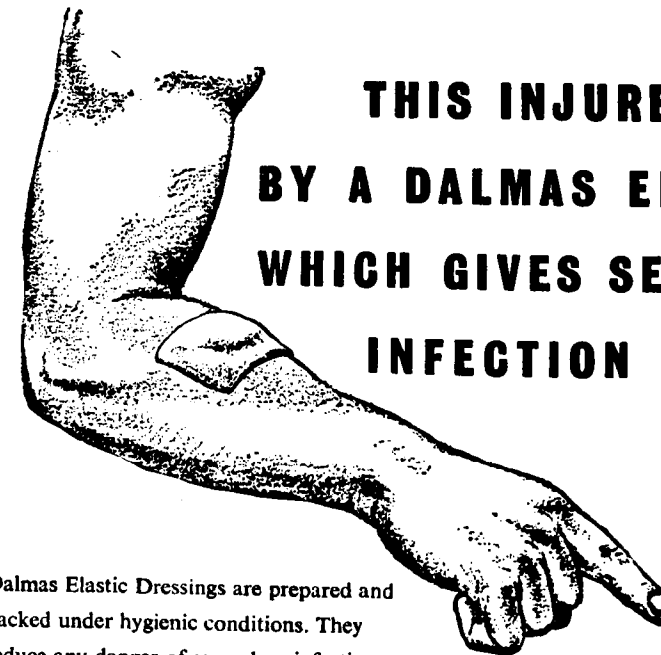
The diagnosis of Hashimoto's Disease can be confusing. The basal metabolic rate is usually minus; the radio active iodine uptake is from high to low, but usually normal.

* From the surgical service of Presbyterian Hospital, Denver, Colorado, U.S.A.

- 1 Hashimoto, L. A., "Zur Kenntnis der Lymphomatosen Veränderungen der Schilddrüse," Virchows. Arch. of Path. Anat., 97: 219-248, 1912.
- 2 Riedel, B. M., "Die Chronische zur Biedung eisenharten Tumoren führende Entzündung der Schilddrüse," Verhandlt D. Dent. Gesellsch. F. Chir., 25: 101-105, 1896.
- 3 Ewing, J., Neoplastic Diseases, (2nd ed. 1922; 3rd ed. 1928), Phila., W. P. Sanders & Co.
- 4 Graham, Allen, "Riedel's Struma in Contrast to Struma Lymphomatosa (Hashimoto)," West. Jour. Surg., 39: 681-689, 1931.
- 5 Williamson, G. S., and Pearse, I. H., "Lymphadenoid Goitre and its Clinical Significance," Brit. Med. J., 14:5, 1929.
- 6 Joll, C. A., "Pathology, Diagnosis and Treatment of Hashimoto's Disease (Struma Lymphomatosa)," Brit. Jour., 27: 351, 1939.
- 7 Skillern, P. G., et. al., "Struma Lymphomatosa: Primary Thyroid Failure With Compensatory Thyroid Enlargement," Jour. Clinical Endocrinology and Metabolism, Vol. 16, No. 1, Jan. 1956, pp. 35-54.

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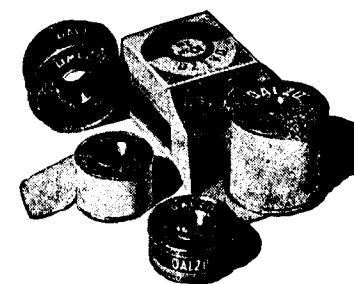


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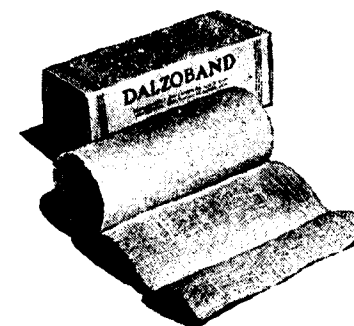
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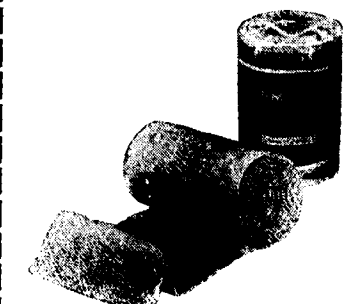
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Hashimoto's disease (lymphomatous struma) showing hyperplastic lymphocytic follicles and atrophic thyroid parenchyma.

The thyroid stimulating hormone (thyrotropin) test (T. S. H.) will sometimes aid in the diagnosis. There may be an elevation of the serum gamma globulin. The

ingestion of iodine might cause the gland to enlarge rapidly. Thirty-six such cases have been described by Skillern⁸.

The serum colloidal gold was described by Skirpan,⁹ et. al. The gland is diffusely enlarged and is very firm in consistency.

TREATMENT

The treatment is surgical, however 2 to 3 grains of desiccated thyroid has been advocated. The rationale being that the thyroid would depress the excess of T. S. H. which is believed to cause the process to take place in the gland.

OCCURRENCE

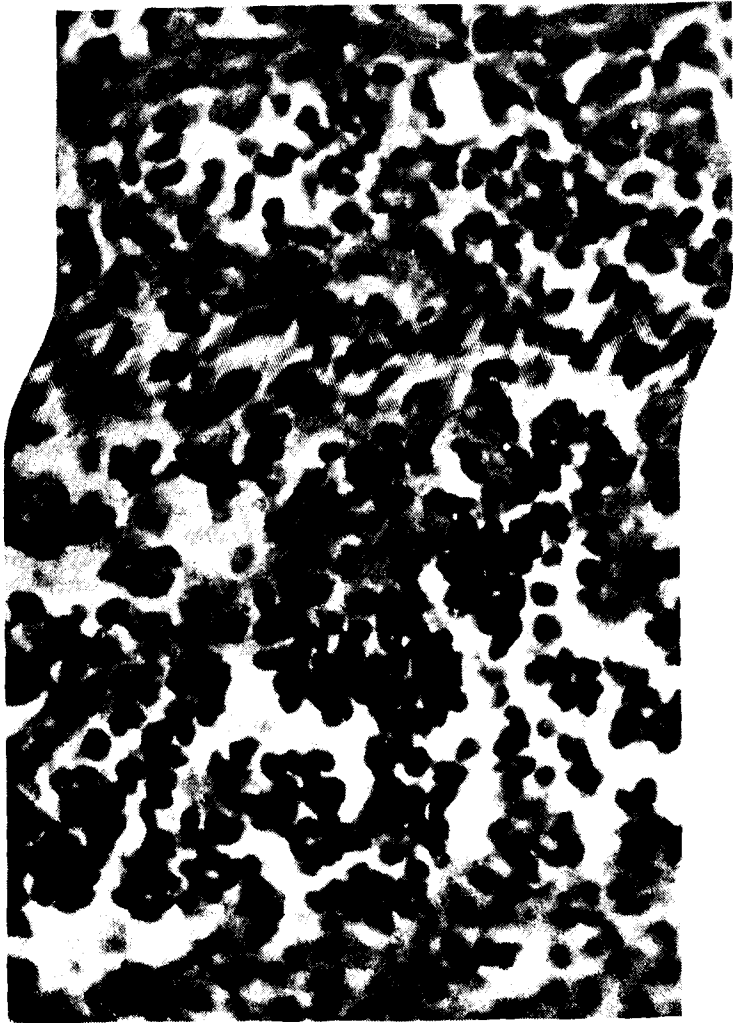
Hashimoto's Disease has been reputed to occur in 1% or less of all thyroidectomies. The number of cases reported in literature has been rather confusing. Up to 1939 there was a total of 85 cases, which were reported as follows:

Hashimoto	4 cases	1912
Graham	24 cases	1931
McClintock & Wright ¹⁰	50 cases	1937
Renton, Charteris & Heggie ¹¹	7 cases	1938
Total 85 cases		

From 1939 to 1956, inclusive, there were 55 cases reported:

Karhausen & Zylverszoc ¹²	17 cases	1955
Skillern, et. al.	36 cases	1956
Fisher & Creed ¹³	2 cases	1956
Total 55 cases		

8 Skillern, *ibid*.
9 Skirpan, Philip; Reich, Alfred and Crile, George, "The Serum Colloidal Gold Test—an Aid to Diagnosis of Struma Lymphomatosa," *Am. Jour. Clinical Path.*, 25: 1274-78, 1955.
10 McClintock, J. C. and Wright, A. W., "Riedel's Struma and Struma Lymphomatosa, (Hashimoto) a Comparative Study," *Annals of Surgery*, 106: 11-32, 1937.
11 Renton, J. M., Charteris, A. A., and Heggie, J. F., "Riedel's Thyroiditis and its Treatment by Radium," *Brit. Jour. Surg.*, 26: 54-70, 1938.
12 Karhausen, L., and Zylverszoc, S., "Myxedema in a Patient with Hashimoto's Struma," *Brit. Med. Jour.*, Sept. 24, 1955, pp. 766-768.
13 Fisher, Edwin R., and Creed, Donald L., "Struma Lymphomatosa (Hashimoto's Disease) in the Male," *Am. Jour. of Surgery*, 21: 60-65.



High power of thyroid showing atrophic acini and lymphocytes.

This makes a grand total of 140 cases reported in the literature up to 1956, as compared with 133 cases from the surgical service of Presbyterian Hospital in Denver, Colorado, U. S. A., covering a ten-year period from July,

1946 to July, 1956, in a total of 1535 thyroidectomies. In the Hashimoto's group there were:

132 females
1 male

The age groups of the 133 cases were as follows:

15-19	20-29	30-39	40-49	50-59	60-69	70-79
YRS	YRS	YRS	YRS	YRS	YRS	YRS
3 fm	22 fm	26 fm	35 fm	31 fm	8 fm	1 fm
1 m						

(ages of 6 patients could not be ascertained)

The frequency in this group represents 8.6%, which might seem high in comparison with other writers.

CONCLUSIONS

1. Hashimoto's Disease is a separate entity.
2. It has been confused with Riedel's struma, which explains why so few cases have been reported in the literature.
3. Occurs mostly in women around the age of menopause, and is usually associated with myxedema.
4. The disease does not extend beyond the capsule.
5. The gland is hard, firm and diffusely enlarged.
6. 140 cases have been reported in the literature of the past 44 years.
7. 133 cases are reported from one hospital covering a period of 10 years.
8. Hashimoto's Disease occurs more frequently than has been suspected.

A Reno hotel guest was indignant when the clerk handed him a bill for 35 dollars. "But that includes the meals" explained the clerk. "But I didn't eat here" said the guest.

"That's not my fault", assured the clerk. "They were here for you"

"In that case," declared the guest, "you owe me 35 dollars for kissing my wife"

"What do you mean?" flared the clerk "I didn't kiss your wife"

"It's your own fault," said the guest. "She was here for you."

Dramatic Decline of Mortality from Pneumonia

But Pneumonia still ranks among 10 greatest killers

W. H. O. SURVEY

A dramatic decline in the number of deaths from pneumonia has occurred since penicillin and other antibiotics have become available, according to a statistical report of the World Health Organization (WHO). Expressed in percentages, this decline ranges from 14.1% in Portugal to 62.1% in New Zealand.

Nevertheless pneumonia still ranks among the 10 diseases causing the greatest number of deaths in the economically-developed countries. Despite great improvement in the past few years, pneumonia remains one of the three leading causes of death among infants, and is even more serious among the aged.

The report compares figures for pneumonia deaths in 1936-1938 and at the present time in 20 countries, and show that the decrease has been moderate among infants under one year of age, extremely important among children and adults, and much less marked among the aged.

Most lives have been saved from pneumonia in New Zealand, Switzerland, Italy, the Netherlands, the USA and Sweden. In these countries the decrease ranges from 62.1% to 53.1%. Next come Norway, Denmark, Canada, Finland, Austria, Scotland, Ireland, Germany and Japan, with a drop of 46.3% to 32.6%. The figures for South Africa, Northern Ireland, England and Wales, and Portugal go from 26.2% to 14.1%. The only exceptions in this general and strongly marked trend are to be found among people over 80 in a few countries such as France, Finland, the UK and Portugal, where an increase in pneumonia deaths is recorded for certain years.

Of the three forms of pneumonia (lobar pneumonia, bronchopneumonia and primary atypical pneumonia) the one responsible today for the greatest mortality is bronchopneumonia in the majority of countries, among them Canada, Finland, Denmark, USA, Ireland, Italy, Norway, Netherlands, the UK, Sweden, Switzerland, Australia and New Zealand. In Japan, however, lobar pneumonia leads, and in Germany and France primary atypical pneumonia (or virus pneumonia) causes most deaths.

A detailed analysis of statistics for 1951, 1952, 1953 and from a few countries, 1954, reveals little variation in the death rate for this disease from one year to the next, and it can be assumed that mortality from pneumonia will remain at the same stable level for some years to come.

MORTALITY FROM PNEUMONIA IN '36-'38 AND AT PRESENT TIME, AND DECREASE IN %

Rates per 100,000 population				
Country		Male	Female	
Union of South Africa	'36-'38	102.8	69.8	
European population	* '51-'53	57.0	43.2	
	-%	** (-45)	** (-38)	
Canada	'36-'38	72.9	62.6	
	'51-'53	37.2	29.7	
	-%	(-49)	(-53)	
United States	'36-'38	93.9	70.2	
All races	'51-'53	33.2	24.1	
	-%	(-65)	(-66)	
White	'37-'38	85.4	65.3	
	'51-'53	29.5	21.4	
	-%	(-65)	(-67)	
Non-white	'36-'38	169.9	112.3	
	'51-'53	65.3	45.9	
	-%	(-62)	(-59)	
Japan	1936	170.4	148.9	
	* '51-'53	52.0	45.4	
	-%	** (-69)	** (-69)	
Germany:				
Territory at the time	1938	96.1	73.8	
Federal Republic	'52-'54	46.5	39.6	
	-%	(-52)	(-46)	
Denmark	'36-'38	95.4	85.9	
	'52-'54	23.3	24.0	
	-%	(-76)	(-72)	

Country		Male	Female	
Finland	'36-'38	99.7	83.6	
	* '51-'53	42.0	48.0	
	-%	** (-58)	** (-43)	
France	1936	75.9	61.9	
	'52-'54	57.9	59.1	
	-%	(-24)	(-5)	
Ireland	'36-'38	91.1	76.1	
	'51-'53	39.7	37.0	
	-%	(-59)	(-51)	
Italy	'36-'38	227.1	187.8	
	'51-'53	69.3	61.6	
	-%	(-69)	(-67)	
Norway	'36-'38	98.7	102.6	
	'51-'53	37.9	47.0	
	-%	** (-62)	** (-54)	
Netherlands	'36-'38	65.6	56.0	
	'52-'54	23.3	22.4	
	-%	(-64)	(-60)	
Portugal	1937	132.7	110.8	
	* '52-'54	81.2	67.3	
	-%	** (-39)	** (-39)	
United Kingdom:				
England and Wales	'36-'38	83.0	54.1	
	'52-'54	49.2	41.8	
	-%	(-41)	(-23)	
Scotland	'36-'38	110.2	71.9	
	'52-'54	40.7	33.0	
	-%	(-63)	(-54)	
Northern Ireland	'36-'38	93.0	72.1	
	* '52-'54	44.1	37.6	
	-%	** (-53)	** (-48)	
Sweden	'36-'38	100.2	96.1	
	* '51-'53	36.0	39.0	
	-%	** (-64)	** (-59)	
Switzerland	'36-'38	74.0	66.8	
	* '51-'53	24.5	25.7	
	-%	** (-67)	** (-61)	

Country		Male	Female	
Australia	'36-'38	72.8	54.0	
	'51-'53	37.7	31.8	
	-%	(-48)	(-41)	
New Zealand:				
Excluding Maoris	'36-'38	67.1	37.7	
	'51-'53	24.5	20.6	
	-%	(-63)	(-45)	
Maoris	'36-'38	455.9	405.8	
	'50-'52	158.5	144.4	
	-%	(-65)	(-64)	

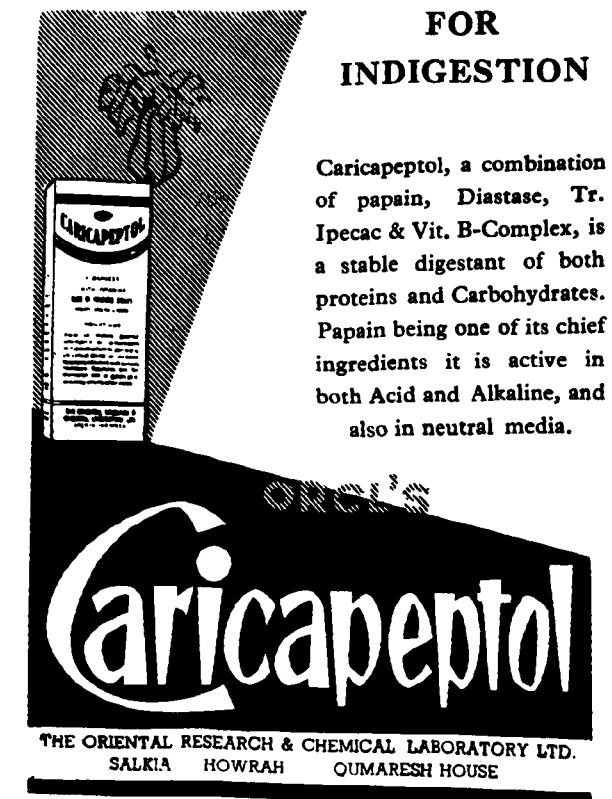
* Excluding pneumonia of the newborn

** These percentages show an exaggerated drop in mortality as the second series of rates did not include pneumonia of the newborn.

N. B. For detailed statistical tables, see WHO *Epidemiological and Vital Statistics Report*, Vol. 9, No. 9, 1956.

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The Psychological Aspects of Family Planning

BY DR. L. C. BHANDARI, M.A. Ph.D. (Lond.)

Associate Member, British Psycho-analytical Society; Associate British Psychological Society, New Delhi.

ALL major social projects which affect the economic, social and cultural aspects of the community life necessarily evoke from the general mass of people emotional responses of far-reaching character.

Notwithstanding the fact that large-scale plans of population control and family planning have been recently worked out in our country under the official patronage, intensive studies of motivation and social attitudes affecting general family-planning work have hardly been undertaken by trained social scientists.

Repeated applications of the techniques of the modern Dynamic Psychology to the study of social issues frequently reveal the fact that the individuals come to bear only those attitudes and reactions in regard to the various schemes aiming at widespread social change, which they have already formed, concerning issues of vital importance to them, in their everyday lives. Thus group reaction to such outstanding topics as marriage, divorce, sexual habits, family planning, sterilization, private property, religious and moral ethics etc., are to be understood not only in relation to the specific group factors, but also in terms of a unique constellation of emotional attitudes and habits which each individual comes to form in the long span of his personality growth and maturation. Thus each individual member of the group in terms of his personality dynamics makes an important contribution in determining the total group attitudes to the various salient problems of communal living.

In view of the above, clinical data yielded by the intensive psychodynamic studies of the emotional problems of the individual patients throw abundant light on the factors which either provide for or mitigate against general family planning activities.

In his psycho-therapeutic treatment of the patients, suffering from different types of emotional disorders, it has often been observed by the writer that occasionally the patient's attitudes to such problems as sexual relations, contraception, abortion and sterilization are not determined alone by the factors of ignorance, lack of adequate sexual knowledge, or religious prejudices, but also by deep-rooted unconscious emotional conflicts

responsible for their nervous symptoms and frequent disturbances in their inter-personal relationships. Psychodynamic investigations usually reveal that unconscious anxiety concerning sexual functions, guilt and need for self-punishment for past sexual practices, hostile trends towards the marital partner, omnipotent attitudes to procreativity and hypochondriacal and puritanical notions regarding sex relations are some of the important factors which make the use of any effective contraceptive methods particularly difficult by the married couples.

Amongst men a conscious wish to undergo sterilization, for example, may be based on an unconscious need to punish the spouse—motivated by repressed promiscuous wishes to atone for a deep-rooted sense of sexual guilt. The patient may try to convince the physician that he is guided to undertake this step on realistic basis to limit the size of his family and thus provide for the general prosperity and well-being of the family. In certain cases he may succeed in convincing the doctor of the validity of his argument and thus have himself sterilized, whereas the deeper motivation for this act may not be known by both the doctor and his patient. An illustrative case may be cited here of a patient who had strongly resolved to undergo sterilization when he came in to psychological treatment for some of his other emotional problems and was averse to use any of the reliable methods of contraception. Penetrating psychological investigations into his motives for resorting to this drastic course of birth-control showed that his decision to undergo sterilization was motivated by deep-rooted sense of guilt concerning his repressed hostile trends directed against his wife and two children. In other words sterilization for him would not only allay his sense of guilt but also provide for his unconscious hostile wishes, although unacceptable to the moral part of his personality. Unconsciously this step would also satisfy his aggressive wishes in relation to his wife by depriving her of the pleasure of having another child whenever she may desire it.

Similarly, other neurotic motives may enter into either adoption of a rigid plan of birth control or attempt to prove excessively fertile in marital life. This emotional trend may be further buttressed by the time-old cultural belief that the main biological role of women is to



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perpetuate the progeny and tend to the young ones. Again, the study of unconscious motivation of this type would reveal that such a conceptional framework is built up to mask feelings of personal inferiority and manifest disguised feelings of hostility against the wife. It is pertinent to mention here the example of a patient who because of his irrational and unfounded suspicions regarding the fidelity of his wife compulsively burdened her with almost yearly pregnancies.

A good deal of clinical evidence supports the view that a compulsive desire on the part of the husband to impregnate the wife frequently may reveal a strong defence against the anxiety connected with his repressed feelings of sexual inadequacy; since in the mind of an average man procreativity is equated with male sexual potency. It is often very difficult to remove the emotional resistances of a patient to have the understanding that fertility and potency are determined by entirely different biological and psychological processes.

The role of unconscious emotional factors in the wife's attitude to contraceptive measures is no less significant.

In our culture—it may be also true of many other cultures in the world—a "barren" woman usually is looked down upon with an attitude of disdain and social opprobrium in different strata of the society. In order to provide for the "perpetuation of the family line", multiple marriages have not been infrequent. Thus infertility, or biological capacity to bear a large number of children, are most likely to reflect upon the woman's conception of her self-image and self-esteem, as an important member of the family. Emotional stress created by these psychological problems connected with infertility may create neurotic disturbances in a number of cases. The issue of the inability to bear children alone in such cases may not explain the nature of psycho-pathology of these patients, rather it is the emotional significance which they attach to procreative function as such which may throw enough light on the nature of their fundamental disturbances. The psychological reaction in each case may be determined by the specific personality trends of the patient and the attitudes of the key persons in her environment that she has to adjust to. In some of these cases, the actualization of the much coveted for pregnancy may show a striking change in the clinical picture presented by the patient.

In regard to other psychological factors which may determine the woman's attitude to the issue of family planning, special mention may be made of the factors of sexual repression rigid puritanical attitudes in regard to sex relation in married life. Because of the social premium which is put in this culture on feminine virtues of modesty and purity of ideals of womanhood, conscious sex interest on the part of the woman both inside and outside the fold of wedlock may remain tabooed in all forms. Hence, both in regard to the initiative in the sex relations and the use of contraceptives it usually devolves upon the husband to assume the entire responsibility. Because of her rigid and prudish moral attitudes and abhorrence for anything connected with "sex" any attempt on the part of the woman to show keenness and intelligent interest in the use of birth control methods would amount to an implicit interest in her anatomy and the coital act. Such a behaviour-pattern in all probability would be condemned by the operation of an extremely rigid and punitive conscience which woman comes to develop on account of overly moralistic upbringing in the parental home and general cultural censure of the biological aspect of the sexual functions.

In the case of a few highly sophisticated and modernised women hypochondriacal fears may become attached to the practice of contraception. The whole procedure may appear too massy to them which would not allow them to have normal sexual satisfaction. In some of the cases faulty attitudes to sex life, and even presence of frigidity, may be responsible for the aversion to the use of contraceptives in any form; and then expressed reasons may only be rationalizations covering deeper psychological motives.

Because of the complexity of the problem and interplay of various psychodynamic factors affecting the emotional attitudes to family planning, it is not possible to deal with all the facets of the subject within the narrow compass of a single article. But it would have become abundantly clear from the foregoing that any comprehensive Family Planning Research programme would fall

short of deeper scientific evaluation and understanding of the basic factors operating against and for this scheme of wide social importance, unless an intensive study is carried out of the psychological aspects of planned parenthood. In the establishment of the family planning clinics, training of the clinical personnel and plans of community propaganda of family planning basic psychological orientation is the essential pre-requisite for the success of any measures undertaken in this connection. The study of personality factors should form an integral part of routine diagnostic case studies and formulation of the techniques of family planning counselling at both the governmental and voluntary family guidance institutions. In view of this, lectures and seminars on the psychological aspects of family-planning should be provided in the general curriculum of the training courses prescribed for the workers in this field.

The aims and objects of community planned parenthood are not fulfilled by mere disbursement of contraceptive goods on mass and social emphasis on the urgent need for population control. On the contrary, in the last analysis the success or failure of any measures of national magnitude undertaken in this connection, would depend upon the total individual emotional response—whether of acceptance or rejection—of the people affected by such projects aiming at widespread social amelioration, and consequent cultural change.

REFERENCES

1. Rao, B. K. Why Don't People use Contraceptives. Surgical & Medical News, Bombay, April, 1956.
2. Weiss & English Psycho-somatic Medicine. Saunders, W. B., Philadelphia, 2nd edition, 1949.
3. Stone, Hannah & Abraham A Marriage Manual, Gollancz, London, 1940.
4. Kahn F. Our Sex Life: Heineman (Medical Books) 1941.

A cincinnati doctor was importuned by an excited son of his patient "Doctor, my father's at Death's door," the doctor replied "Don't worry, my boy, I'll be there at once. I'll pull him through."

*

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*

An errant actor arrived home late frequently and was finally bawled out by his wife. When reprimanded he asked her to swallow some Scotch he had with him. She coughed and coughed and sputtered. "See," he said victoriously, "and you think I enjoy myself Saturday nights."

Lockheed Electronic Brains Working to Solve Problems of Human Heart Disease

BY A SPECIAL CORRESPONDENT

HIGH-SPEED electronic computers normally used by Lockheed scientists to solve guided missile problems now are helping battle man's Number One killer—heart disease.

The study promises to reveal extensive new knowledge of heart diseases, their earlier detection, and relief.

With electronic aids scientists now can "see" a fleeting heartbeat and analyze its characteristics with precision, it was reported today.

The heart studies are a co-operative effort of Lockheed's Missile Systems Division, Van Nuys, California, and Dr. Travis Winsor, eminent American cardiologist and director of the Nash Cardiovascular Foundation at Good Samaritan hospital in Los Angeles. The company is making available its IBM computers, largest battery of such "electronic brain" outside IBM itself, for cardiac computations during spare minutes between missile problems.

"The use of such electronic equipment constitutes the first major advancement in the accurate compilation of heart data in 50 years," a Nash Foundation spokesman said. "The program is one of the few co-operative industry/medical heart studies in the United States."

Heart studies at the Nash Foundation presently center primarily around hardening of the arteries and high blood pressure, and their effects on the circulatory system.

For the first time the electronic computers make possible the rapid and accurate analysis of the human heartbeat in terms of "harmonic content."

Specialists in the program explained that the heart's total activity is made up of many contractions, flutters, valve actions, and other motions. Harmonic contents, they said, is the combined frequencies (rates of occurrence), and amplitudes (high and low points of each occurrence cycle) of these many heart motions.

Computers are used in this new harmonic analysis method to describe and record in precise mathematical terms all the heart's activities. With this information, researchers can distinguish more accurately between normal and abnormal cardiac conditions.

To obtain most accurate heartbeat readings from patients, the heart researchers adapted the oscilloscope, an instrument used widely in the missile and electronics industry. Electrodes attached to the patient's body carry minute electrical impulses to the instrument which presents them visually as a wavy line. The scope—much like a television picture tube—allows researchers literally to "see" the fleeting heartbeat.

Doctors take carefully timed photographs of the heartbeat wave as it sweeps across the face of the scope. Enlarged photographs of a portion of the heart pulsation—covering only one-tenth of a second—are segmented into approximately 80 points from which the harmonic content is determined.

This step replaces the usual electrocardiogram, whose tracings are not sufficiently detailed for such highly refined studies.

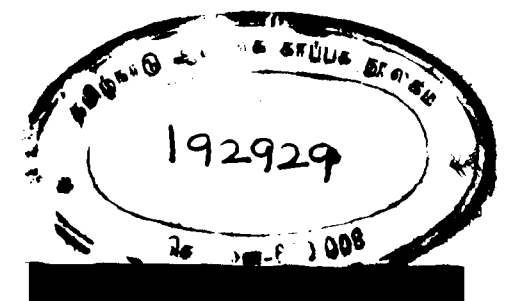
Heart data is then swiftly compiled on punched cards and fed into Lockheed's high-speed IBM 650 computers.

The computers produce in a few minutes results that a team of technicians working by hand would take weeks to obtain. The Lockheed 650s have magnetic drum "memories" from which data can be plucked in three-thousandths of a second.

Tabulations produced by other Lockheed equipment quickly show any deviation in the patient's heartbeat when compared with former records.

Applications of Dr. Winsor's technique are being made to determine success or failure of certain cardiovascular operations, to follow results of corrective treatment, to measure the success of artery grafting operations, and to show when blood clots are completely removed from arteries.

What's next in Dr. Winsor's combined medical-electronic research program? He and his staff are preparing to "listen" to the heart electronically as yet another step in the team effort between the medical profession and mathematical/electronic engineers.



Effect of Nuclear Radiation on Human Beings Examined

British Medical Research Council's Report Published

(FROM OUR MEDICAL CORRESPONDENT)

A reassurance as to the medical—including the genetic—aspects of nuclear radiation is contained in a report published in London recently by the Medical Research Council. The dangers from external radiation due to the "fall-out" from nuclear bombs at the existing rate of explosion are described as "negligible".

The report, entitled *The Hazards to Man of Nuclear and Allied Radiations*, represents the independent findings of the committee which was set up last spring to report on this subject. The committee had as its chairman Sir Harold Himsworth, Secretary of the Medical Research Council, and included such eminent authorities on the subject as Sir Ernest Carling, chairman of the International Commission on Radiological Protection, and Sir John Cockcroft, director of the Atomic Energy Research Establishment, Harwell.

At a press conference at which the report was released, Sir Harold made the point that the object of his committee had been to define the limits of nuclear experiment, with the purpose of seeing that these limits were such as society could accept. He made the point that the new power was "neither mysterious nor uncontrolled." There had, he went on, been much exaggeration.

The committee's report deals first with the acute and delayed effects which may be produced on the health of an individual who has been exposed. These, it is made clear, vary not only with the dose received and the time over which it is spread, but also with other factors such as the part of the body exposed. For instance, after exposure to a heavy dose or radiation, all may develop acute effects, but only a small proportion of the survivors will develop delayed effects.

As to the genetic effects, the committee emphasizes that no new categories of disease or abnormality are likely to be induced. Such effects are, in any case, cumulative, and depend only upon the total amount of radiation received during the whole of the reproductive life.

NO CAUSE FOR UNDUE CONCERN

The conclusion of the committee is that with proper safeguards, exposure in peace-time can be maintained at

levels which can be accepted by an individual without undue concern either for himself or his offspring.

As the report makes plain, men and women have been exposed to ionizing radiation in the course of their occupations for over half-a-century. The Atomic Energy Authority is now the main employer in the United Kingdom of persons occupationally exposed, having about 7,000 potentially-exposed employees.

The results of monitoring these persons show that in all recent years no employee has had an average weekly dose exceeding the maximum permissible level laid down by the International Commission on Radiological Protection, and that about 90 per cent. of those exposed average less than one-tenth of this dose. The excellent record of the Atomic Energy Authority shows the standard that is attainable and the practicability of being satisfied with nothing less.

The committee points out that it is, of course, impossible to explode a nuclear weapon without liberating radio-active matter into the atmosphere. Measurements, however, show that the inhabitants of the United Kingdom may receive, in the next 50 years, from the weapons already exploded, about 0.02 to 0.04 per cent. of the radiation that they will receive during the same period from natural sources.

EFFECTS INSIGNIFICANT

The point is made that if the firing of both atomic and thermo-nuclear bombs were to continue indefinitely at the same rate as over the past few years, there would be a build up of activity, gradually reaching a plateau, in about 100 years' time which would give an average individual a dose, over a period of 30 years, of about one per cent. of what he would receive in the same period from natural sources. It will be readily appreciated that the individual and genetic effects of such a dose of external radiation would be insignificant, the report adds.

Account must, however, be taken of certain constituents of the fall-out which retain their radio-activity for long periods, and which are deposited on the ground, where they may contaminate drinking water or agricultural crops.

The most important of these is strontium-90, which, if ingested, is concentrated in the bone where, if present in sufficient quantities, it may give rise to destructive changes, including cancer. In relation to strontium-90, the committee concludes that "at its present level no detectable increase in the incidence of ill-effects is to be expected". The maximum permissible concentration in the bone allowed for those who might have to deal with this substance is 1,000 units. At present, measurements in the United Kingdom show that the highest concentration in the bone is about one per cent., and calculation of the fall-out likely to come, if the present rate of firing continues, suggests that this level may be increased not more than tenfold in the course of several decades.

EDEN'S STATEMENT

The British Prime Minister said in the House of Commons recently that "this report is an important document which deals with complicated matters which will require careful study by all concerned. For this reason, it is obviously not possible at this stage to make detailed comments on its contents."

"The committee's findings about radiation from such sources as the diagnostic use of X-rays will require much detailed consideration with appropriate scientific and industrial bodies. To the extent Government departments are concerned, we are arranging for the necessary studies to be made as soon as possible".

It will be recalled that the Prime Minister, in a statement in the House of Commons on June 7 on the United Kingdom's forthcoming thermo-nuclear weapons test, pointed out that previously (December 6) he had emphasized to the House that the British Government was prepared to discuss methods of regulating and limiting test explosions which took account of the United Kingdom's position and that of the other Powers. He added: "This remains the policy of Her Majesty's Government, and we shall seek every opportunity to put it into effect".

"REASSURING" ON THE WHOLE

The Times comments: "The report by the committee of the Medical Research Council on the hazards to man of nuclear and allied radiations is, on the whole, reassuring."

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BENGAL CHEMICAL CALCUTTA BOMBAY KANPUR

Pointing out that the forces released by artificial dissolution of the atom are of a kind that is universally present in the order of nature, the newspaper says: "From the beginning of time, life on the earth has been exposed to these radiations... Now we are deliberately adding to the amount of radiation in the world; and since the energy released does not necessarily disappear, in the course of time we are bound to inquire whether it is accumulating in our environment to a degree that brings us into serious danger".

"The answer of the committee is, in general terms, 'No: provided we know what we are doing and take reasonable care'. The use of radiation for therapeutic and industrial purposes may be expected to increase; but the persons exposed to it by occupation are known, and with proper precautions the amount can be kept small enough to be reasonably safe. The possible genetic effects upon the progeny of exposed persons are a little more doubtful, because the relevant factors are imperfectly understood; but the committee does not see any cause for alarm.

"So far, at worst, the possible risks have to be measured against the benefits, to health as well as to other amenities of life, that the use of the newly discovered forces promises."

The Times adds: "Appropriate precautions can be defined by the medical profession; and it is for users of atomic power in peace to follow skilled advice.

"There remains the possible threat to mankind in general—as distinct from those whose calling exposes them to special risk—from the use of nuclear and thermo-nuclear power in war and preparation for war. Here the medical profession can only issue its warnings and leave statesmen and strategists to apply them."

U. K. MEDICAL RESEARCH COUNCIL REPORT EXAMINED

With the prospect that atomic energy will be developed on a large scale before the end of this century, it has become important to know in advance what standards of safety should be observed. The advent of thermo-nuclear test explosions has made it important to obtain the same information earlier.

The problem is the same in essentials, although it differs in detail in the two cases. It is that caused by

the penetrating radiations emitted by radio-active materials. Such materials are formed whenever fission, by which energy is released from the atom, takes place.

The process is a new one in the sense that its application on a large scale is new. But the radiations emitted by its products are of the same kind as those to which we are naturally exposed—both from cosmic radiation, which enters the earth's atmosphere from outer space, and from radio-active materials present in the earth's crust. In addition, there are other man-made sources of penetrating radiation—now widely used both in medicine and industry.

Hence the decision of the British Government to ask the Medical Research Council to appoint a committee, which has lately reported on the hazards to man of nuclear and allied radiations—that is, to cover the subject as a whole and not merely one part of it. It was a large and authoritative committee, and had as its chairman Sir Harold Himsworth, Secretary of the Medical Research Council.

TWO TYPES OF EFFECTS

Apart from the immediate effects of exposure to heavy doses of radiation—which, barring accidents, should happen only in a nuclear war—there are two main types of effects to be considered. One is damage to the individual during his lifetime. The other—about which more has been heard—is the possibility of long-term genetic damage which would affect future generations, i. e., the population as a whole.

Of these, the second is by far the more difficult to investigate and is also the more difficult to make rules about. Damage to the individual demands certain degrees of dosage above that naturally received, and if the dosage is less than this prescribed value it can be said that no detectable damage will result.

In the case of genetic damage there exists no such clear-cut limit. Any increase in natural exposure to radiation must be expected to bring about an increase, however small in the rate at which mutations—otherwise hereditary changes, usually for the worse—make their appearance in the population.

In any case, there must be variations according to the altitude and the part of the world in which different human populations live. And the practical questions

are, therefore, these: first, how much will the mutation rate be increased by a given increase in radiation; secondly, how large an increase in the mutation rate can be accepted as tolerable?

RADIO-STRONTIUM

These questions will have to be answered in the long run. But for the immediate purpose of the safety or otherwise of thermo-nuclear test explosions, it turns out that there is another criterion which will operate first. It arises from the fact that there is one particular fission product, radio-strontium, which tends to accumulate in bone where it takes the place of calcium. The amounts involved are very small.

But small as they are, there have been detectable increases—about sixfold—in the amount of radio-strontium in rain water since the beginning of nuclear explosions. Thence, through grass and cow's milk, it

finds its way into human bone. The amount found in human bone in Britain is now of the order of only 1/1,000 as much as would be accepted as permissible in the case of the worker in industry exposed to a regular hazard from radio-active materials.

The committee's view is that if the amount of radio-strontium in bone were to rise by a further factor of 10—that is, to 1/100 of the occupational limit—this position should be immediately reconsidered.

There will be some further increase, in any case, from the "fall out" of radio-strontium, now circulating high in the upper atmosphere. But the figures can be watched, estimates of future quantities made, and opinion formed. And this criterion will operate at a lower rate of thermo-nuclear tests than would any reasonable criterion based on long-term genetic effects, which it is, therefore, less urgent to establish.

A young starlet asked a studio still photographer for one of her pictures. "Would you like it mounted?" asked the photographer. "Oh that would be wonderful," replied the starlet, "I look so much better on a horse".

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Experimental and Clinical Data on the INH-resistance of Mycobacterium Tuberculosis

By DR. M. LANYI, J. ROKA, DR. L. EIDUS

Department of Phthisiology, University Medical School, Budapest, Hungary.

(Exclusive to SURGICAL & MEDICAL NEWS, Bombay)

ISONICOTINIC acid hydrazide (I. N. H.) is a very effective chemotherapeutic agent against tuberculosis. The effect is due to two factors. Quite low concentrations of the drug are capable of inhibiting the growth of tuberculosis bacilli, and, being without toxicity to the organism, relatively high concentrations may be attained both in the blood and the tissue fluids. While with streptomycin the average blood level, 20 microgrammes per ml., is about twenty times as high as the lowest concentration required for bacteriostatic action, 1 microgramme per ml., the average concentration attained in the blood during treatment with I. N. H. amounts to 5 microgrammes per ml., i. e., about one hundred times as high as the lowest inhibitory level, 0.05 microgrammes per ml. The high concentration obtainable in the organism led some authors to think that I. N. H. would be capable not only of controlling the growth of tuberculosis bacilli but also of exerting a bactericidal effect and consequently the pathogenic agent would develop no resistance to the drug.

However, further observations have failed to corroborate any of these assumptions. Experiments showed in vitro resistance to I. N. H. per ml., i. e., twenty times the lowest concentration required for inhibition, naturally no growth could be observed within 3 weeks. If, however, the tubes were incubated for 8 weeks, significant growth occurred. The resistance to I. N. H. of the bacteria thus cultured was tested in subcultures and was found to be 20 fold. Thus in vitro the simple prolongation of the incubation time sufficed for inducing resistance to I. N. H. The resistance thus developed by the bacteria has remained unchanged over the present examination period of 8 months.

In order to study the bactericidal effect of I. N. H. assumed and reported by various authors, a suspension of Mycobact. tuberculosis was mixed to solutions of I. N. H. ranging in concentration from 0.1 per cent to 1 per cent. Every day a drop of each suspension was removed, examined under a microscope and after careful, repeated centrifugating inoculated on a medium. Microscopic examination revealed no morphological or staining change whatever in such tuberculosis bacilli as had been kept for 10 days in a 1 per cent solution of

I. N. H., i. e., one containing 200,000 times the minimum bacteriostatic amount. The bacilli, after being dyed with Alexander Hauduroys triple stain, proved no less acid or alcohol resistant than untreated ones. Evaluable changes in shape and staining were recorded only after 20 days' incubation in the highly concentrated solution. Acid-resistance had almost completely disappeared, the lipid structure had undergone fundamental changes and the bacilli were no longer viable when inoculated on fresh media.

In animal experiments, I. N. H. was found to be more effective. In guinea pigs inoculated with a strain of the human type and treated with daily 20 mg doses of I. N. H. per kg of body weight from the 20th day following infection to the 60th day, the progress of the process was not only controlled and its generalization prevented but, apart from local and mostly regressive alterations, no organic lesions occurred. Cultures made with material obtained from different organs of the treated animals remained sterile. (4). The only exception was a guinea pig that died from intercurrent disease on the 44th day of treatment. Though on macroscopic examination of its organs the cultures prepared from the regional lymph nodes were found negative, the microscope showed well developed cords in the centrifugated sediment of the medium.

Certain conclusions may be drawn from the comparison of the experiments performed in vitro and on animals. It has been mentioned that in vitro the growth of Koch's bacilli depended on the time of incubation in culture media containing several times the minimum amount of I. N. H. required for bacterial inhibition. In vivo, thanks to certain favourable conditions, the bacteriostatic effect of the highest concentration of I. N. H. attainable in the blood, 5 to 10 microgrammes per ml., seemed to be more effective than in vitro. This was also shown by a relatively slower development of the resistance and the severe impairment of the bacteria observed in sputum examinations. The bacteria affected appear in the form of thin pale, feebly staining rods. They may even resist staining with Ziehl Neelsen's dye and, when inoculated on media, become incapable of forming macrocultures.

These findings drew attention to the possible clinical consequences of resistance to I. N. H. Our investigations were hampered in a number of cases by sputum negativity setting in during treatment. Resistance tests were carried out on Sula's medium by two different methods. By the 60 days' method Koch's bacilli, after rearing for 6 weeks, were transferred into a series of test tubes containing different concentrations of I. N. H.; the resistance of the strain was estimated after incubating the subcultures for another three weeks. The quantity of the inocula was in each case equal. By the other method, rapid rearing was effected in primocultures, and the microcultures checked after 12 days.

The results obtained with the two methods were similar. The only difference was that in about one third of the cases where the quick method had been adopted, Koch's bacilli remained viable and capable of producing microcultures while rearing for 6 weeks brought negative results. The centrifuged sediment of these negative cultures often yielded a considerable number of bacteria and even smaller cords which, in spite of the favourable conditions, had been unable to develop into macroclones in 6 weeks. As has been repeatedly stated, presumably

I. N. H.-medication deprives tuberculosis bacilli of their capacity to form macrocolonies whereas they may still be able to develop microcolonies.

Up to now, a total of 170 resistance tests have been carried out with I. N. H. This substance was administered to the patients in daily doses of 5 mg per kg of body weight. A negative result was obtained, i. e., no tuberculosis bacilli could be cultured by either method in 64 cases which leaves, for evaluation, 106 resistance tests performed on 95 patients.

Resistance to I. N. H., i. e., a bacterial growth up to a concentration of 3 microgrammes per ml. could be demonstrated in 40 patients out of the 94.

A detailed analysis of the results revealed the following:- in all cases (8 patients) in which the clinical picture showed marked deterioration during treatment the bacteria were found to be resistant to I. N. H. On the other hand, there were 3 cases where, despite of manifest resistance, treatment with I. N. H. was continued in consideration of the desperate state of the patients. In two of these patients further regression resulted though resistance had repeatedly been

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established. These observations support our conclusions drawn from the above experiments, namely that the effect of I. N. H. within the organism must be due to several concurrent factors, and its spectrum is much broader than the chemotherapeutical effect of the drug alone.

On analysis of the clinical picture of I. N. H. resistant cases it will be found that most of them suffered from extensive destructive processes.

	Non-Resis- Resis- Resis- tant No. tant to tant to per I.N.H. I.N.H. cent.				Grammes of I.N.H. adminis- tered before development of resistant.
Phthisis	53	35	18	66%	18.0
Fibronodous form	22	5	17	23%	24.4
Recent infil- tration	18	—	18	—	—
Extrapul- monary tb.	1	—	1	—	—
	94	40	54	—	—

After a certain symptomatic improvement at the early stage of treatment, stagnation or gradual deterioration of the clinical state signified in some cases only that I. N. H. had become ineffective. As shown in the table, an average amount of 18 g. of I. N. H. was administered in the 25 cases of phthisis in which resistance had developed. The smallest quantity of I. N. H. to give rise to resistance was 8.1 g. Such a low amount has in no case provoked resistance in subjects with less extensive lesions. It must be mentioned that most of these patients has already undergone medication with alternative anti-tuberculous drugs and there were several in whom I. N. H. was the third drug to develop resistance.

In the 5 cases showing localized chronic fibronodous tuberculous changes, resistance developed after an average total dose of 24.4 g. In the whole material under observation the smallest quantity of I. N. H. to elicit resistance was 17g.

A friend of mine patted me on the back one day at a bar and said, "You're a good egg, let's have a drink. You see my doctor is permitting me to drink sherry with an egg".

In patients with recent and infiltrative forms of tuberculosis the process sometimes showed very rapid regression on treatment with I. N. H. and in no such case could resistance to the drug be demonstrated even after prolonged administration.

It thus emerges that the dangers of I. N. H. treatment are the same as those associated with streptomycin therapy; in case of incorrect indication or incorrect dosage resistance to the drug is soon developed. We therefore made it our task to study from the outset the combination of I. N. H. with other antituberculous agents and the effect of such combinations on the development of resistance. The final results of our in vitro cross-experiments show that the effect of streptomycin and I. N. H. is not increased by their combination and streptomycin exerts no retarding action on the development of resistance to I. N. H. On the other hand, the combination of P. A. S. and I. N. H. displayed favourable aspects also in respect of antibacterial action, and the development of in vitro resistance to I. N. H. was considerably retarded by P. A. S. (2, 3)

We think that by combining the antituberculous drugs and by establishing the most suitable methods of treatment for each form of tuberculosis, the danger of resistance may be considerably reduced.

SUMMARY

In vitro resistance to I. N. H. appears rapidly. Due to adjunct conditions, the situation is more favourable in the organism where resistance is slower to develop. On clinical material, resistance to I. N. H. was established chiefly in prolonged treatment of inveterate forms of tb. or chronic fibrocavernous cases. No resistance was encountered in the promptly responsive alterations of recent cases. In cross experiments with I. N. H. and PAS, the latter prevented the rapid development of resistance to I. N. H.

NOTE

Since the above paper was written we have investigated resistance to I. N. H. in 300 cases. The total results are the same as those reported.

Granuloma Inguinale and the Gynaecologist

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INTRODUCTION

GRANULOMA inguinale (Granuloma venereum; Ulcerating granuloma of the pudenda; Granuloma contagiosum; Sclerosum granuloma) is an ulcerative disease of the pudenda and surrounding tissues. It is a mildly contagious, chronic, progressively auto-inoculable disease involving skin and corium and occasionally the lymphatics. It is generally considered to belong to the province of the specialist in venereology although its venereal origin has not yet been convincingly established. Nevertheless the disease is one which may confront the gynaecologist in the Department for Women's diseases. Also sometimes the lesion may be found in the pregnant woman and occasionally the sequelae of the disease may complicate child birth and the puerperium. Poor hygienic conditions and sexual promiscuity predispose to this disease.

ÆTIOLOGY

Although in 1905 Donovan of Madras described certain intracellular bodies "gigantic bacilli with rounded ends", the exact ætiology is in doubt. It is now generally agreed that the organism is probably a bacillus and has been christened "callymato bacterium granulomatosis".

The disease has been reproduced in human beings by inoculation of pus taken from pseudobubos of granuloma inguinale which contained no organism other than Donovan bodies.

The incubation period is believed to vary between 8 days and 12 weeks. As the lesions are not painful to begin with patients very often tend to put off consulting a doctor. Starting as a papule or vesicle usually on the labia minora the lesion increases in size. The surface epithelium becomes excoriated or eroded and ulceration occurs. The base has a red beefy granular appearance. Daughter lesions frequently develop near the larger lesions and by coalescence the ulcerative process becomes quite extensive. (Figure 1.) The advancing border of the ulcer has a characteristic rolled edge, the granulation tissue spreading over on to the epithelial surface. The lesion may have a peculiar odour but unless it becomes



Fig. 1. The genitalia in granuloma inguinale.

secondarily infected it does not give rise to constitutional disturbances. The labia, fourchette, vagina and the inguinal folds become gradually involved if the disease is not checked and warm moist areas are a favourite site and in such areas the extension of the disease process tends to be more rapid (Figure 2.). The ulcer tends to produce a scanty mucoid discharge and when this is wiped off and the soft granulation tissue brushed away, the base presents a red healthy looking velvety appearance and tends to bleed easily.

PATHOLOGY, CLINICAL FEATURES AND COMPLICATIONS

When the disease is fully developed it takes one of four forms:

1. *Hypertrophic verrucose type*: The lesion is extensive and involves the genitalia and the surrounding areas and the spread is very slow. The base of the ulcer is elevated above the level of the surrounding skin. It consists of coarse pale-red warty granulation tissue. The edge is often thickened and greyish white in colour. There is no exudate. Donovan bodies are not usually found in the surface exudate but typical capsulated intracellular organisms are easily demonstrated from the deeper parts of the granulation tissue.



Fig. 2. Granuloma inguinale has a predilection for warm moist areas. In such sites the spread is relatively rapid.

2. *The sclerotic or cicatricial type:* This lesion which is common in women is characterized by the formation of fibrous tissue. Islands of active disease become encircled by the rapid formation of fibrous tissue. Breakdown of scars is not infrequent. Cicatrization strangles lymphatic channels. When drainage of lymph is blocked pseudoelephantiasis of the vulva may occur. The fibrous tissue is hard and unyielding papillomatous tumours may sometimes result (Figure 3.). Stenosis of the urethral, vaginal and anal orifices may result and cause difficulty in micturition defaecation and parturition. These lesions may be traumatized during parturition especially if vaginal stenosis makes for difficult labour. The presence of genital infection predisposes to puerperal sepsis.
3. *The fleshy exuberant type:* Exuberant growth of bright red velvety glazed looking moist granulation tissue covering multiple or a large single ulcer characterizes this type of lesion. The edge is thin and undermined and the hypertrophic granulation tissue gives the appearance of overflowing over the edges. There is odema and infiltration of the skin surrounding the ulcerative lesion. The surface exudate is abundant and has a peculiar odour and it tends to have an offensive smell when it gets secondarily infected. Young non-capsulated forms of Donovan organisms may be isolated from the surface exudate and may be

found both inside and outside the mononuclear cells, polymorphs and eosinophils are found in large numbers. The patient often complains of intolerable itching in this type of lesion.

4. *The destructive necrotic type:* An acute rapidly spreading inflammatory exacerbation sometimes occurs in patients with chronic Donovanosis. Necrosis results in the production of greyish brown tissue with thick chocolate coloured exudate. There is considerable destruction. Secondary pathogenic invaders are easily isolated especially the fusospirillary organisms. The vulva, perineum and peri-anal regions may be completely destroyed. The destruction of the recto-vaginal septum converts the rectum and vagina into a single large pus filled cloacal cavity. Severe infections are accompanied by constitutional disturbances and toxæmia. Often the condition is fatal.

Involvement of the uterus tubes and ovaries is exceedingly rare in this disease but a case has been reported (Pund and Gotcher 1938).

Clinical picture: A papule or vesicle is the initial lesion and it is generally located on the external genitalia (labia minora) within about a week after sexual contact. It is insidious and there are few premonitory symptoms or constitutional upset. The lesion spreads centrifugally and by auto-infection of opposing surfaces. The labia fourchette and vagina in the female and the inguinal folds, perianal and perineal regions are all warm and moist and therefore favourite sites. The disease may take any of the pathological forms already described. Donovanosis may be a cause for vaginal discharge pruritus and pain.

Diagnosis and differential diagnosis: The diagnosis depends on the clinical appearance, the demonstration of Donovan bodies in the spreads, as well as on the histological study of biopsy. A chronic superficial granulomatous condition occurring in the genito-ingui-no-anal region without corresponding enlargement of the lymphatic nodes in the groin is suggestive of granuloma venereum. Spreads are made by scraping off a small piece of clean granulation tissue from the lesion and smearing the clean undersurface of this tissue along a glass slide. Spreads are dried and then suitably stained and examined under the microscope for the presence of Donovan bodies. The capsules of the Donovan bodies stain a purplish-



Fig. 3. This papillomatous mass in granuloma inguinale was excised after the disease was treated. The patient was 22 years old.

(Courtesy, The Govt. R.S.R.M. Lying-in Hospital, Madras)

pink and the nuclei a dark blue. More frequently pathognomonic cells (large monocytes with cytoplasmic cysts filled with Donovan bodies) are found. These cells may be seen sometimes in tissue sections also when they are stained with Delafield's hæmatoxylin. Granuloma inguinale should be considered in the differential diagnosis of all ulcerations of the female genitalia and has to be differentiated from syphilis, chancroid, lymphogranuloma venereum, and epithelioma.

Treatment: Although various aromatic pentavalent antimonial compound and the organic trivalent antimonial (Fouadin) were popular at one time, the advent of the antibiotic drugs have made a great advance in the treatment of this disease. Streptomycin, Aureomycin, Chloramphenicol (Chloromycetin) and Terramycin may

all be successfully employed. The dosage of the drugs depends on the extent of the lesion and on the sensitivity of the organism. Usually 4 grams of streptomycin daily in divided doses may be continued for 5 days. In case of recurrence a second course may be given. Aureomycin seems even more effective and is given in a dose of 500 mg. every six hours for about 12½ days. Larger doses may be exhibited for the resistant cases and nausea may be a side effect. Chloromycetin is as effective as aureomycin. So far Terramycin has been found to be the most effective antibiotic for the disease. This antibiotic does not cause nausea and recurrences are rare. Greenblatt and Barfield (1952) having tried out oxytetracycline came to the conclusion that this drug was the treatment of choice and advised a dosage of 2 Grams daily for 10—20 days.

REFERENCES

1. Adams A. R. D., and Magraith B. G. Clinical Tropical diseases, Blackwell Scientific Publications, Oxford 1953.
2. Crossen, R. J., Diseases of Women, The C. V. Mosby Co., St. Louis 1953.
3. Kosmak George W. Transactions of the Fifth American Congress on Obstetrics and Gynaecology, The C. V. Mosby Co., St. Louis 1952.
4. Rajam R. V. & Rangiah P. N., Donovanosis (Granuloma Inguinale, Granuloma Venereum) World Health Organization: Monographs series 1954.
5. Rubin I. C., and Novak J., Integrated Gynaecology, Principles and Practice, Volume I. The Blakiston Division, McGraw Hill Book Company Inc., New York, Toronto, London, 1956.
6. Sarma, Vishnu, Tropical disease in Obstetrics and Gynaecology Medical Digest, Vol. 23. No. 12 P. 995.

(The attention of the reader is specially called to a most valuable, detailed and authoritative account of Donovanosis in the attractively got up monograph by Drs. Rajam & Rangiah, quoted in the reference. V. S.)

Father called in his daughter for a chat. "Your young man was at my Office today," he told her, "and asked me for your hand. I consented."

"But, Father," faltered the girl, "I hate to leave Mother"

"That's perfectly all right, my dear, perfectly all right. Just take her with you".

Studies of Adrenal Cortical Activity in Patients

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INTRODUCTION

ALTHOUGH the pituitary is the co-ordinator of the endocrine glands, the adrenal cortex, despite its small size, is a vital organ; the survival period in animals is very short following adrenalectomy compared to the survival period following hypophysectomy. We do not know much about the activity of the adrenal cortex in various diseases although we do know certain aspects of the diseases of the adrenal gland itself. It has become evident in recent years, through the work of many investigators, that the adrenal cortex has a variety of functions and for this reason it is rather difficult to evaluate its functional condition by any one single test, though there are a variety of methods (chemical and biological) of estimating its function in clinical disorders. Selye¹ in 1937, in his classical work with animals has shown that a number of different types of stress cause a stimulation of the adrenal cortex which secretes more substances of steroid nature. The measurement of some of the compounds secreted by the adrenal cortex or of their metabolic products which are excreted in the urine, *e. g.*, neutral 17-ketosteroids has been used as one of the indices of adrenal cortical activity in recent years in addition to other tests.

Pincus and Hoagland² have shown an increased output of 17-ketosteroids in aviators under stress of flying, and Forbes et al³ have shown a similar increase in trauma (surgery). Pincus⁴ has shown that the night values of 17-ketosteroids are lower than the day values. All of these observations indicate that the adrenal cortex is dynamic and reacts to any insult or stress confirming Selye's observations.

Selye⁵ in his concept of the alarm reaction and the diseases of adaptation proposes that, as a result of continued exposure to any stress of non-specific nature, there is a continued secretion of adrenal cortical hormones leading to endogenous corticoid intoxication, finally resulting in diseases like hypertension, nephrosclerosis, rheumatic diseases and eclampsia which he groups under the heading of the "diseases of adaptation". In view of the findings of Fuller Albright et al⁶, Talbot et al⁷, Bruger et al⁸, and Mason et al⁹, that urinary 17-ketosteroids are considerably reduced in various diseases, *e. g.*, malnutrition, anemia, cirrhosis of the liver, infections, hypertension, hyperthyroidism and hypo-

thyroidism, this study was undertaken to estimate adrenal cortical activity in two "diseases of adaptation", namely hypertension and rheumatic disease and also other endocrine and non-endocrine diseases by means of both the urinary 17-ketosteroids and "cortin" determinations.

PHYSIOLOGY OF THE ADRENAL GLANDS

Though the identification of the adrenal gland was described by Eustachius about 300 years ago, its real history dates from 1855 when Addison¹⁰ gave the classical clinical description pertaining to the effects of destructive diseases of adrenal glands. Brown and Sequard¹¹ in 1856, confirmed experimentally by extirpation of the adrenal gland, that these were indispensable to life. In 1902, Abel¹² isolated a crystalline compound, epinephrine, from adrenal glands. In 1917, Wheeler¹³ demonstrated that adrenal cortex and not the medulla is essential to life. In 1933-34, Houssay¹⁴ and Shumacker¹⁵ et al, established that hypophysectomy resulted in rapid atrophy of adrenal cortex and that atrophic adrenals could be brought back to their normal histology by the use of suitable pituitary extract.

In 1932, Loeb¹⁶ first observed low concentration of sodium chloride in the serum of patients with Addison's disease, and the same was confirmed by Harrop^{17,18} et al, in bilateral adrenalectomized animals and also in patients with Addison's disease. Loeb¹⁹ in 1933, Harrop²⁰ in 1935, and Kendall²¹ in 1937, showed that patients with Addison's disease and adrenalectomized dogs could be maintained for a considerable time by giving a diet high in sodium and low in potassium. In 1937 Anderson²² et al noticed, in hyperadrenocorticism, changes in serum sodium, chloride, and potassium, diametrically opposite to that seen in Addison's disease.

Amelioration of diabetes produced by pancreatectomy, phlorhizin, or alloxan following adrenalectomy as shown by Long²³, Wells and Kendall²⁴ and Janes²⁵, and the reproducing of the severe diabetic state by giving adrenal cortical extract or crystalline steroid compounds²⁶, suggested the possible role of adrenal cortex in carbohydrate metabolism. Evans²⁷ and Long²⁸ by their work have shown that the adrenal cortex mobilizes protein and converts it into glucose. Long²⁹ and Ingie²⁹ et al, showed that administration of CII or CII-17 oxy-steroids is diabetogenic torats. Conn et al³⁰, in 1948,

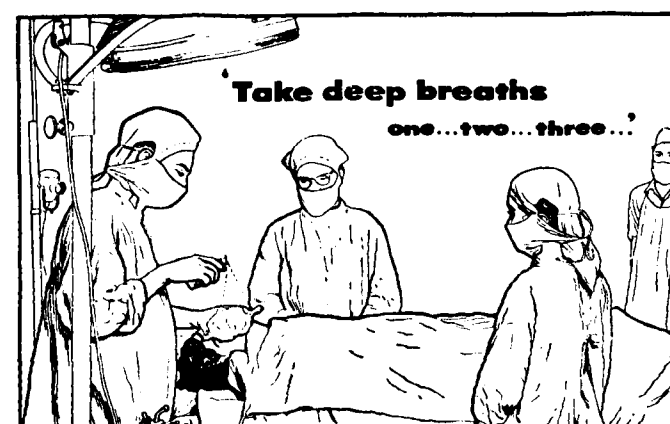
produced temporary diabetes in humans, by giving 120-150 mgm. of A. C. T. H.* daily for 8-10 days.

Jaffe³¹ in 1924, showed thymic enlargement in all rats surviving bilateral adrenalectomy for 3-5 weeks. Ingle³² found a decrease in the weight of the thymus by administering 2 mgms of 11-hydroxy-corticosterone. A similar amount of DOCA (desoxycorticosterone) produced no such change. Dougherty and White^{33,34,35}, showed a decrease in circulating lymphocytes, tissue lypolysis and an increase in circulating leukocytes following administration of A. C. T. H. In addition an increase in the antibody titre is seen after an injection of adrenal cortical extract or adrenotrophic hormone. Selye⁶ has included changes in circulating lymphocytes and eosinophils among the manifestations of "general adaptation syndrome". Gorman Hills³⁶ administering 25 mgms. of A. C. T. H. to normal human subjects noticed a characteristic alteration of the leukocyte pattern, *i. e.*, an increase in neutrophils, with decrease in eosinophils and lymphocytes and this does not occur in the

* Adreno-cortico-trophic hormone

absence of adrenal cortex. By giving 17-hydroxy-corticosterone in 20 mgm. doses a similar change is induced in patients with Addison's Disease and that DOCA, even 30 mgm. doses, has no such influence. So it is reasonable to assume that lymphatic tissue, lymphocytes and eosinophils seem to be under the influence of adrenal cortical hormones, particularly the sugar hormone (gluco corticoids).

Active chemical work dates from 1930 when Swingle and Pfiffner³⁷ and Hartman and Blomwell³⁸ announced the preparation of extracts capable of maintaining life in adrenalectomized animals. Main work has been carried on by three groups, *i. e.*, Reichstein and his associates at Zurich, Kendall and Mason at Mayo Foundation and Wintersteiner and Pfiffner at Columbia. In 1936-37, Mason and Kendall et al³⁹, Defermery et al⁴⁰, isolated corticosterone and dehydrocorticosterone in crystalline form from the extracts of adrenal cortex. Reichstein^{41,42}, in 1937, announced the synthetic preparation of desoxycorticosterone acetate and later he also succeeded in recovering this compound from an extract of



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adrenal cortex. In 1936, Wintersteiner⁴³ isolated 17-hydroxy-11-dehydrocorticosterone. In 1936, Reichstein⁴⁴ isolated an androgenic hormone adrenosterone from adrenal cortex and showed that it has only 1/5 the potency of male hormone androsterone. In 1940, Pfiffner et al⁴⁵, isolated 17 B-hydroxyprogesterone from adrenal cortex. The number of steroids isolated from the adrenal cortex at present is 25 but only desoxycorticosterone (Na-hormone), corticosterone, dehydrocorticosterone, 17 hydroxycorticosterone (gluco-corticoids), adrenosterone, androstane-3, 11-diol-17-one androstenedione (androgens N hormone), progesterone, estrone have been shown to have physiological activity. Kendall⁴⁷ has shown that the amorphous fraction of the adrenal cortical extract possessed by far greater physiological activity than any other compound isolated. Ingle⁴⁸ has shown that there is a qualitative difference in the biological effects of these physiologically active corticoids.

TABLE A⁴⁹

Relative Quantitative Effects of Compounds which have been proven to replace the Functional Activity of the Adrenal Cortex in one Respect or Another.

COMPOUND ¹	Life Maintenance	Electro-lyte Metabolism	Work	Carbohydrate Metabolism
Corticosterone	2	2	3-4	3-4
11-Dehydrocorticosterone	2	2	3-4	3-4
17-Hydroxycorticosterone	1	Na excretion?	4	4
17-Hydroxy-11-dehydro-corticosterone	1	Na excretion?	4	4
11-Desoxy-17-hydroxycorticosterone	1-2	?	0	0
11-Desoxy-6-hydroxycorticosterone	1-2	?	0	0
11-Desoxycorticosterone	4	4	1	1
Pregnene (5:6)-dial (3, 21)-one (20)	2	?	0	?
Progesterone	1	1?	0	0
Amorphous fraction	+4?	?	2	?

1. Efficacy gauged as 1, slight activity, to 4, marked activity.

Desoxycorticosterone by virtue of its affecting retention of sodium, chloride and water, and increasing excretion of potassium has been used with considerable success in the treatment of Addison's disease.

In 1937, Selye¹ described under the term of 'alarm reaction' the role of adrenal cortex in rats subjected to non-specific stress. In 1943, Sayers et al⁵⁰, and Li⁵¹ et al, prepared purified pituitary adrenocorticotrophic hormone. In 1943, Albright⁵² marshalled evidence indicating over production of S hormone in Cushing's syndrome, and his explanation for these symptoms is by far the best that has been proposed. In 1945, Selye et al⁵³, produced experimental nephrosclerosis in rats and later in 1946, he suggested that intoxication with excessive amounts of endogenous cortical hormone resulted in "diseases of adaptation"⁵⁴. In 1946, Sayers et al⁵⁴, showed in rats, that after an injection of A. C. T. H. there is a fall in the ascorbic acid and cholesterol content of adrenal cortex. Long⁵⁵ has shown that various noxious stimuli such as cold, burns and injection of epinephrine, rapidly reduced the adrenal ascorbic acid content, and the adrenal cholesterol more slowly. Sayers et al⁵⁴, in 1948, have used this estimation of ascorbic acid of the adrenal cortex for the assay of A. C. T. H.

17-KETOSTEROIDS

The term 17-keto-steroid was first introduced by Callow and co-workers⁵⁶ to designate those steroids with a ketone group on the 17th carbon atom of the cyclopentenophenanthrene nucleus.

A color reaction was introduced by Zimmermann^{57, 58} which was based on the fact that substances containing the group CH₂CO in the presence of alkali *m*-dinitrobenzene produce a red color. This reaction, further modified by Wu and Chow⁵⁹, and by Callow et al⁵⁶, has been used as a quantitative estimation of 17-ketosteroids. Callow et al⁵⁶, showed that only 17-ketosteroids develop an intense absorption band with a maximum in the green, thus differentiating them from 3-, 6-, and 20-ketosteroids. This chemical test roughly parallels the biological assay method for urinary androgens, but it is not a test for androgens as such. The most important limitations are: (1) some androgens, *e. g.*, testosterone, fail to give the reaction since they are not 17-ketosteroids, (2) other compounds, *e. g.*, estrone, while 17-ketosteroids, do not react, because being phenols, they are removed by the alkaline wash purification step, and (3) other compounds

such as etiocholanone, while not androgens, are 17-ketosteroids and react with *m*-dinitrobenzene, thus contributing to the color development. The advantage of this estimation lies in the fact that there is more facility to perform than the biological assay.

From the study of 17-ketosteroid excretion in the urine of eunuchs⁶⁰, of normal⁶¹ and castrated women^{62, 63}, of patients with adrenal cortical tumors and cortical hyperplasia^{64, 65}, of male and female Addisonian patients⁶, of a patient with an interstitial cell tumor of the testis⁶⁶, of hypogonadal patients receiving testosterone^{67, 68}, it is evident that urinary 17-ketosteroids are excretory products of dual origin in the male, *i. e.*, from the adrenal cortex and from the testes, while in women their sole origin is the adrenal cortex. To elaborate a little on this matter, female Addisonian patients do not secrete any 17-ketosteroids in their urine while male Addisonians continue to secrete small amounts. Thus it seems likely that, in the male, about two-thirds of the urinary 17-ketosteroids are derived from the adrenal cortex and about one-third from the testes. Albright⁶⁹ thinks that in women the axillary and pubic hair is due to this androgen activity of the adrenal cortex.

The principal neutral 17-ketosteroids that have been isolated from human urine are androsterone (an alpha ketosteroid) and its two isomers isoandrosterone and dehydro-isoandrosterone (beta ketosteroids). The beta ketosteroids can be precipitated by digitonin and in this manner separated from the alpha ketosteroids which do not give a precipitate with digitonin. High levels of 17-beta-ketosteroids are found in patients with adrenal cortical carcinoma and this finding has assumed diagnostic significance. Further, this finding indicates that the 17-beta-ketosteroids originate from the adrenal cortex.

The data from different laboratories vary due to variations in methods^{70, 71, 72}. Pincus⁷³ has developed a new color reaction using a concentrated solution of antimony trichloride.

Nathanson et al⁷⁴ and Talbot et al⁷⁵, have shown that boys and girls from three to seven years of age excrete small amounts of 17-ketosteroids and estrogens. From 10 to eleven years of age there is an increased excretion of 17-ketosteroids and sex hormones, the 17-ketosteroids excretion increasing more rapidly in boys, while the estrogen excretion increases more rapidly in girls. The fact that boys do not excrete significantly

greater amounts of 17-ketosteroids than girls do suggests that the adrenal cortex is the chief site of origin of urinary 17-ketosteroids during childhood. However, boys excrete considerably more 17-ketosteroids after eleven years of age when the secondary sexual characteristics begin to appear.

Buchman⁷⁶, Werner⁷⁷, Forbes et al⁷⁷, have shown that the output of 17 ketosteroids in a twenty-four hour period is not an absolute constant from day to day in a given subject, but Talbot et al⁷⁹, have shown that the fluctuation which occurs under normal conditions is not very great. It is probable that a single specimen will fall within 15% of the average obtained from thirty to forty specimens from a given patient and accordingly one or two accurately determined values will suffice for clinical diagnosis.

Dorfman⁸⁰ et al, have shown that 3.2-13.8% of desoxycorticosterone acetate and 2.8-12% of adrenal cortical extract are converted to 17-ketosteroids. Deakin⁸¹ has shown that the administration of testosterone causes an increase of urinary 17-ketosteroids while methyltestosterone does not. The 17-ketosteroids excretion is increased in adrenal cortical tumors⁸², adrenal cortical hyperplasia⁶⁵, adrenogenital syndrome, and decreased in Addison's disease, malnutrition, panhypopituitarism, cirrhosis of the liver⁶, myxedema⁸, hyperthyroidism⁹, starvation⁸³, leukemia⁸⁴, hypertension⁸, diabetes⁸⁵ and cancerous patients⁸⁶.

AVAILABLE METHODS OF STUDY

- I. Salt deprivation test of Harrop et al⁸, introduced in 1933. In adrenal insufficiency salt restriction results in an increased excretion of urinary sodium above the intake with a simultaneous fall in blood sodium.
- II. Cutler, Power, and Wilder's test⁸⁷, introduced in 1938. When given a standard amount of sodium and potassium chlorides, patients with adrenal cortical insufficiency excrete urine with a high concentration of chlorides. Both of these test, I and II, are not without hazard.
- III. Robinson, Power, and Kepler's test⁸⁸ introduced in 1941. The test is based on the fact that patients with adrenal insufficiency do not develop normal diuresis after ingestion of large amounts of water.

The above three estimations are of limited value in the evaluation of adrenal cortical function for it is only in well advanced cases of adrenal cortical insufficiency that these tests are positive. They are of much less value in hyperadrenocorticism since in these conditions there is not always excessive secretion of hormones which regulate electrolyte metabolism. Wilson et al.^{8,9}, have noticed characteristic electrolyte changes in blood and urine in only a small percentage of patients with Cushing's disease.

- IV. Venning et al.¹⁰, introduced a biological assay of urinary adrenal corticoids in 1946 which depends upon the deposition of glycogen in the livers of adrenalectomized mice.
- V. Chemical assay—the colorimetric estimation of 11-oxysteroids of Talbot et al.¹¹. The neutral extract is purified and its ability to reduce copper reagents is measured.

The tests IV and V give a measure only of the compounds which affect carbohydrate metabolism and does not give any idea of the androgenic and electrolyte functions of the adrenal cortex.

- VI. Chemical assays of "cortin" in urine.
 - a. Heard et al.¹². An acid extract is used in rather crude form and its ability to reduce phosphomolybdic acid is measured.
 - b. Daughaday et al.¹³. An acid extract is purified and its ability to liberate formals dehyde on treatment with periodic acid is measured.

All of these tests measure the adrenal cortical hormones which have electrolyte and carbohydrate regulating activity with varying degrees of specificity. None of them is specific in that other substances present in the extract affect the net result.

- VII. Estimation of urinary neutral 17-ketosteroids¹⁴. This test gives an index only of the androgenic function of the adrenal cortex.
- VIII. Pituitary adrenocorticotrophic hormone test of Thorn et al.¹⁵ introduced in 1948. Following the injection of ACTH in normal individuals there is an immediate fall in circulating eosinophils and an increase in uric acid excretion.
- IX. Epinephrine test of Recant¹⁶ and Thorn introduced in 1948. Following an injection of

1.5 mg. of epinephrine there is a fall in the circulating eosinophils of 70–80% in normal persons. Since pituitary and adrenal cortex must be normal to obtain this response, primary adrenal and pituitary adrenal insufficiency can be differentiated, using the test in combination with A. C. T. H. test.

The tests VIII and IX are of value only in cases of adrenal cortical insufficiency but do not give much aid in cases of hyperadrenocorticism.

- X. Ascorbic acid estimation of Sayers et al.¹⁷. This test can be employed only in animals and is chiefly used for the assay of A. C. T. H.

METHODS AND PROCEDURES

Most of the patients were selected from Research & Educational Hospitals and a few from Cook County Hospital. The clinical diagnosis was established after careful study in all the cases. Twenty-four hour urine specimens were collected in a clean bottle (no antiseptic to be used) and the estimation of urinary 17-ketosteroids and cortin was determined.

1. Method for Determination of Urinary 17-Ketosteroids.¹

The method of Robbie and Gibson¹⁸ was used without modification. Essentially it involved the hydrochloric acid (25 cc of concentrated) hydrolysis of the 250cc aliquot from the 24 hour specimen preserved with 10cc of concentrated hydrochloric acid per liter, for ten minutes, followed by refluxing the hydrolyzed specimen ten minutes with 75cc of carbon tetrachloride. The carbon tetrachloride layer was drawn off through a separatory funnel, washed with 20cc of distilled water, 20cc of 10% sodium hydroxide, and twice more with 20cc portions of distilled water. The purified extract was filtered and transferred to a 125cc Erlenmeyer flask and evaporated to dryness on a steam bath. The residue was taken up in 10cc of 95% ethanol. One cc was treated with 1cc of 2% *m*-dinitrobenzene in the presence of 1cc of 2.5M potassium hydroxide. A standard for comparison was prepared by treating 1cc of 0.2 mg./cc dehydroisoandrosterone solution in exactly the same fashion. An unknown solution blank and reagent blank were also prepared. The tubes were set in a dark place for 45 minutes to allow the color to develop. Each time 25cc of 70% ethanol was added to each tube, the contents mixed and read on a photoelectric colorimeter.

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Natural Hæmatinic principles, Vitamin B Complex factors and Digestive Enzymes of the freshly Proteolysed Liver Yeast Extracts fortified by Synthetic Vitamin B Complex factors Folic Acid, Vitamin B₁₂ and Lipotropic factors Choline and Methionine.

COMPOSITION

Each fl. oz. contains

Proteolysed Liver Extract Equivalent to
(1 oz. fresh liver)

Proteolysed Yeast Extract 60 gr.

Stomach Extract Equivalent to
(5 gr. fresh stomach)

Folic Acid	3 mg.
Vitamin B ₁₂	12 mcg.
Vitamin B ₁	40 mg.
Vitamin B ₂	3 mg.
Vitamin B ₆	2 mg.
Calcium Pantothenate	5 mg.
Nicotinic Acid amide	60 mg.
Choline Chloride	300 mg.
Methionine	300 mg.
Copper Sulphate	0.05 mg.
Calcium Glycerophos.	3 gr.
Pot. Glycerophosphate	2.5 gr.
Manganese Glycerophosphate	0.25 gr.
P. B. A.	10 mg.

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II. Chemical assay of Urinary "Cortin"

The method of Heard and Sobel¹², and Heard, Sobel, and Venning¹³, was slightly modified and adapted to the equipment available in this laboratory. This colorimetric chemical method for the estimation of the urinary reducing steroids, sometimes called "cortin", was used as an index of adrenal cortical function. It is based on the supposition that the reducing power of the lipid soluble, water insoluble components of urine is due, at least in part, to adrenal cortical steroids containing an alpha-beta unsaturated 3-ketone and a primary a-ketol side chain at C₁₇. Both of these groups were shown to be strongly reducing¹².

The principle of the test is an oxidation-reduction reaction in which the urinary extract is oxidized by phosphomolybdic acid which is reduced to molybdenum blue, the intensity of which is an indication of the urinary "cortin". The test is only roughly quantitative, as some biologically inactive compounds in the urinary extract contribute to the color development. The test does measure corticoids, a group of substances of unknown structure but containing the following among others, *e. g.*, 11-dehydro-17-hydroxycorticosterone, dehydrocorticosterone, and desoxycorticosterone and its acetate, together with some androgens.

The test, based on the reducing power of the urinary steroid extract, gives results which are in the same range as those obtained in the formaldehyde liberation estimation of Daughaday, Jaffe, and Williams¹³. The latter test is undoubtedly more specific in view of its partition of the extract between benzene and water, the water phase containing some of the more highly oxygenated corticosteroids. However, the present adaptation of the test of Heard, Sobel, and Venning gave very useful information with far less effort.

Reagents

1. Phosphomolybdic acid solution, Folin and Wu¹⁹.
2. Glacial acetic acid, analytical reagent grade.
3. Phosphomolybdic acid reagent, a solution made up of equal volumes of the above phosphomolybdic acid solution and glacial acetic acid (the precipitate formed on addition dissolved on mixing).

4. Ether, U. S. P. grade was distilled through a 90 cm. vertical column packed with glass chips and washed twice with concentrated sulfuric acid (25 ml. to each liter of ether). The supernatant ether is removed and again distilled. Stored in the refrigerator, the ether remains stable for at least two weeks.
5. Chloroform, U. S. P. grade was distilled through the same 90 cm. packed column described above.
6. Ether-Chloroform solvent; a 4:1 mixture of the two solvents was prepared immediately before the extraction was carried out.

Procedure

A 24 hour specimen was collected in a carefully cleaned bottle (no antiseptics were used) without preservatives, kept in the refrigerator and worked up immediately. The specimen should not be stored more than 24 hours. A 100 ml. aliquot was acidified with 12 N sulfuric acid to pH 1.0 as determined by the glass electrode. The acidified sample was extracted four times in a 250 ml. separatory funnel with 40, 20, 20, and 20 ml. of the ether chloroform solvent. The combined extracts were placed in a 250 ml. centrifuge bottle and centrifuged at about 1500 r. p. m. for 20 minutes or more if necessary to break the emulsion. The aqueous phase was removed with a large pipette and the ether-chloroform phase was again transferred to the 250 ml. separatory funnel where it was washed 5 times with 10 ml. portions of 0.1 N sodium hydroxide and then 5 times with approximately 10 ml. portions of distilled water. The ether-chloroform solvent phase was then shaken with 1-1.5 gm. of anhydrous sodium sulfate to absorb dissolved and adhering water. The solution was filtered through a pledget or ether washed glass wool into a 125 ml. Erlenmeyer flask fitted with a ground joint. To effect a quantitative transfer, the separatory funnel was rinsed and shaken three times with 10 ml. portions of ether and there washings were likewise filtered into the 125 ml. Erlenmeyer, the laboratory vacuum line was connected to the flask and when the flask became well chilled due to evaporation of the solvent, it was immersed in a water bath at room temperature. After the solvent was evaporating smoothly, the water bath was gradually warmed up to about 50° C by changing the water. When the solvent was completely removed, 10.0 ml. of phosphomolybdic acid reagent was pipetted into the Erlenmeyer flask

which was then immersed in boiling water for exactly 60 minutes, then removed and chilled in a basin of cold water for 30 seconds. The samples were then transferred to Corex absorption cells and the per cent transmission measured with reference to a reagent blank in the Beckman model DU spectrophotometer using monochromatic light of 660 millimicra wavelength and a slit width of 0.24 mm. Using the accompanying calibration curve, the per cent transmission was converted to mg. of desoxycorticosterone which was chosen as the reference standard, *i. e.*, all results are reported as mg. of desoxycorticosterone per 24 hours. The 24 hour value is obtained by multiplying the value from the curve by the 24 hour volume divided by 100.

III. Administration of Adrenocorticotropin.*

Procedure

No food is permitted after 8:00 p. m. On the following day water is allowed ad libitum, and in addition 200 cc of water is given at 6:00 a. m., 8:00 a. m., and 10:00 a. m. A control urine specimen is collected from 6:00 a. m. to 8:00 a. m., and an eosinophil count is done at 8:00 a. m. Immediately thereafter 25 mg. of A. C. T. H. is injected intramuscularly. Urine is collected from 9:00 a. m. to 12:00 n., and the eosinophil count is repeated at 12:00 n. The percentile decrease in circulating eosinophils is calculated, the two urine specimens are analyzed for uric acid and creatinine, and the change in uric acid-creatinine ratio is computed.

IV. Test of Pituitary Adrenal Response**

Procedure

No food is permitted after 8:00 p. m. On the following day water is allowed ad libitum, and in addition 200 cc of water is given at 6:00 a. m., 8:00 a. m., and 10:00 a. m. A control urine specimen is collected from 6:00 a. m. to 8:00 a. m. and an eosinophil count is done at 8:00 a. m. Immediately thereafter one starts the intravenous administration of 1.5 mg. of epinephrine hydrochloride in 200 cc of saline which is given over a one hour period. Urine is collected from 9:00 a. m. to 12:00 n. and the eosinophil count is repeated at 12:00 n. The percentile decrease in circulating eosinophils is calculated, the two urine specimens are analyzed for uric acid and creatinine, and the change in uric acid to creatinine ratio is computed.

V. RESULTS

Table I	17-Ketosteroids and Cortin Estimation Normal Men and Women
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V. RESULTS

TABLE I

17-Ketosteroids and cortin estimation—Normal men and women.

No.	Name	Sex	Age	Cortin	17-K.S.	Average	Range
1.	R.K.	M	28 yrs.	1.9 mgm.	10.0 mgm.	Cortin	Cortin
2.	C.G.	M	30 yrs.	1.7 mgm.	12.5 mgm.	1.7 mgm.	1.25-2 mgm.
3.	J.P.T.	M	40 yrs.	2.0 mgm.	14.0 mgm.	17-K.S.	17-K.S.
4.	K.M.	M	22 yrs.	1.85 mgm.	14.2 mgm.	11.5 mgm.	8-14.2 mgm.
5.	E.Y.	M	25 yrs.	1.5 mgm.	9.6 mgm.		
6.	D.D.	M	29 yrs.	1.25 mgm.	8.0 mgm.		
1.	J.M.	F	21 yrs.	1.6 mgm.	10.0 mgm.	Cortin	Cortin
2.	O.G.	F	24 yrs.	1.1 mgm.	9.0 mgm.	1.3 mgm.	1.2-1.6 mgm.
3.	D.H.	F	35 yrs.	1.4 mgm.	6.5 mgm.	17-K.S.	17-K.S.
4.	R.M.	F	30 yrs.	1.2 mgm.	7.0 mgm.	8.0 mgm.	6.5-10 mgm.
5.	M.T.	F	24 yrs.	1.3 mgm.	8.5 mgm.		

The same method was used in our laboratory for some other work.

The average 17-Ketosteroids excretion was 10.9 mgm. (23 men), the range being 5.9-18.0 mgm.

TABLE I.
17-Ketosteroids & Cortin Estimation—Hypertensive Patients.

No.	Name.	Sex.	Age.	Disease.	Urine Albumin.	B. P.	Eye Fundi.	Cortin.	17-K.S.	Eosin.
1	W. P.	F	22	Essential Hypertension	traces	240 / 154	Gr. II	1.8 mgm.	5.0 mgm.	200
2	M. F.	F	41	..	+	230 / 130	Gr. I	2.6 mgm.	5.2 mgm.	142
3	S. H.	F	30	..	nil	190 / 120	Gr. I	2.1 mgm.	5.5 mgm.	186
4	M. W.	F	40	..	nil	190 / 130	Gr. I	2.2 mgm.	5.8 mgm.	133
5	T. B.	F	55	..		262 / 150	Gr. II	1.2 mgm.	4.2 mgm.	..
6	G. G.	M	33	..		220 / 130	Gr. II	2.2 mgm.	6.5 mgm.	133
7	M. M.	F	42	Hypertension, hirsutism, obesity	traces	182 / 104	Gr. I	3.2 mgm.	14.0 mgm.	120
8	M. C.	F	43	..	traces	184 / 112	Gr. II	2.9 mgm.	5.0 mgm.	103
9	G. C.	M	27	Essential Hypertension & Rheumatic Heart Disease	nil	190 / 40	Gr. II	3.2 mgm.	5.5 mgm.	300
10	M. B.	F	64	Hypertension & Arteriosclerosis	traces	185 / 110	Gr. I	1.3 mgm.	3.5 mgm.	..
11	M. H.	F	52	Essential Hypertension & Diabetes	nil	228 / 130	Gr. II	2.2 mgm.	4.2 mgm.	180
12	B. G.	F	66	..		180 / 110	Gr. IV	4.5 mgm.	3.2 mgm.	20
13	A. H.	F	49	..	traces	240 / 140	Gr. III	2.4 mgm.	3.2 mgm.	200
14	H. R.	M	28	Essential Hypertension & Obesity	+	160 / 100	normal	1.6 mgm.	5.8 mgm.	260
15	J. F.	M	45	..	++	185 / 140	Gr. III	3.4 mgm.	4.8 mgm.	..
16	T. J.	F	62	..	++	200 / 110	Gr. III	2.7 mgm.	3.0 mgm.	..
17	G. N.	M	62	..	traces	170 / 90	Gr. I	2.4 mgm.	5.8 mgm.	..
18	E. T.	M	58	..	nil	170 / 110	Gr. I	2.7 mgm.	3.45 mgm.	50
19	E. M.	M	23	Diabetes & Hypertension	++	170 / 100	Gr. IV	3.4 mgm.	3.5 mgm.	178
*20	F. S.	F	48	.. (k.s.w.) ..	++	266 / 142	Gr. IV	3.65 mgm.	2.8 mgm.	5
21	G. L.	M	26	2 ..	++	210 / 120	Gr. IV	3.2 mgm.	4.0 mgm.	..
22	R. R.	M	19	Renal Rickets, Hypertension, uremia	++	150 / 105	Gr. II	2.8 mgm.	3.2 mgm.	72
*23	V. F.	F	48	Hypertension, nephrosclerosis, uremia	++	260 / 170	Gr. III	4.0 mgm.	2.5 mgm.	6
*24	A. F.	M	48	Chr. Pyelonephritis and	++	185 / 105	Gr. IV	4.8 mgm.	2.0 mgm.	5

* Decea-

SURGICAL & MEDICAL NEWS

JANUARY 1957

In all hypertensive patients the urinary 17-ketosteroids are decreased except in one and that patient has hirsutism. Out of 24 patients, 4 had normal urine cortin excretion and in the rest it is increased—more so in patients having kidney damage and congestive failure.

- * F. S. Adrenal cortex normal in size and shape; microscopic revealed hyperplasia of adrenal cortex.
- * A. F. Adrenal cortex normal in size and shape; microscopic revealed few adenoma here and there.
- * V. F. Adrenal cortex normal in size and shape; microscopic normal.

TABLE III
17-Ketosteroids and Cortin Estimation—Rheumatic Diseases.

No.	Name.	Sex.	Age.	Blood Sed. Rate	B. P.	Cortin.	17-K. S.	Eosin.
1	B. H.	F	15	22 mm.	145 / 80	2.85 mgm.	4.8 mgm.	50
2	A. L.	F	12	21 mm.	105 / 65	2.2 mgm.	3.45 mgm.	272
3	A. B.	F	6	42 mm.	80 / 50	2.0 mgm.	1.5 mgm.	216
4	E. D.	F	12	48 mm.	125 / 50	2.6 mgm.	2.0 mgm.	666
5	J. L.	F	12½	34 mm.	120 / 80	2.5 mgm.	2.9 mgm.	486
6	M. F.	F	12	20 mm.	95 / 55	2.3 mgm.	1.8 mgm.	220

In Rheumatic Disease the urinary cortin is increased and 17-ketosteroids is decreased.

TABLE IV
17-Ketosteroids and Cortin Estimation
CIRRHOSIS OF LIVER

No.	Name.	Age.	Sex.	B. P.	Cortin.	17-K. S.	Eosin.
1	L. F.	58	M	116 / 68	4.5 mgm.	1.6 mgm.	100
2	* T. W.	58	M	118 / 62	3.8 mgm.	0.75 mgm.	140
3	K. K.	54	M	112 / 72	3.3 mgm.	1.8 mgm.	343
4	A. M.	32	M	98 / 56	4.3 mgm.	1.2 mgm.	66
5	P. W.	52	M	108 / 62	5.7 mgm.	2.2 mgm.	121
6	B. F.	60	M	128 / 70	3.8 mgm.	1.4 mgm.	143

In Cirrhosis of the Liver the urinary cortin is increased and 17-ketosteroids is decreased.

* T. W. Deceased.

Both kidneys and adrenal cortex, macroscopically and microscopically normal.

TABLE V
17-Ketosteroids and Cortin Estimation
HYPO & HYPERTHYROIDISM

No.	Name.	Sex.	Age.	B. M. R.	Cortin.	17-K. S.
1	D. T.	F	15	-30.0	0.8 mgm.	1.65 mgm.
2	A. M.	F	11	-25.0	0.45 mgm.	1.8 mgm.
3	J. L.	F	63	+47.0	3.0 mgm.	3.5 mgm.
4	M. L.	F	49	+59.0	2.65 mgm.	4.5 mgm.
5	B. R.	F	12	+50.0	2.16 mgm.	3.0 mgm.
6	M. F.	F	13	+32.0	2.4 mgm.	3.6 mgm.
7	L. K.	F	34	+81.0*	0.95 mgm.	5.0 mgm.

In Hypothyroidism both the urinary cortin and 17-K. S. are decreased.

Out of five cases of hyperthyroidism in four the urinary cortin is increased and 17-K. S. is decreased.

* In one, both the urinary cortin and 17-K. S. were decreased.

TABLE VI
17-Ketosteroids and Cortin Estimation
DIABETES MELLITUS

No.	Name.	Sex.	Age.	Cortin.	17-K. S.
1	M. B.	F	17	1.55 mgm.	4.5 mgm.
2	D. G.	M	17	1.46 mgm.	5.0 mgm.
3	G. M.	M	15	1.4 mgm.	4.25 mgm.
4	M. H.	F	18	1.7 mgm.	5.5 mgm.
5	C. S.	M	24	1.9 mgm.	6.2 mgm.

In diabetes mellitus the urinary cortin is normal but the 17-ketosteroids is decreased.

TABLE VII
17-Ketosteroids and Cortin Estimation
CHRONIC LYMPHATIC LEUKEMIA

No.	Name.	Sex.	Age.	Cortin.	17-K.S.	Lymph.	Eosin.	A.C.T.H.
1	J. F.	M	58	2.6 mgm.	3.8 mgm.	31,869	1357	50.0 mgm.
	After A. C. T. H.			4.2 mgm.	6.6 mgm.	39,206	549	
	Percent of Change					18.2% Up	59.5% fall	
2	L. D.	M	43	3.6 mgm.	1.75 mgm.	31,870	14	25.0 mgm.
	After A. C. T. H.			3.4 mgm.	2.2 mgm.	35,280	11	
	Percent of Change					10.7% Up	21.4% fall	

In Chronic Lymphatic Leukemia the urinary cortin is increased and 17-ketosteroids is decreased.

Administration of 50.0 mgn. of A.C.T.H. did not produce any significant change in the lymphocytic count.

TABLE VIII
17-Ketosteroids and Cortin Estimation.

IN A CASE OF ANOREXIA NERVOSA
Result of Administration of A.C.T.H. and Epinephrine

J. S.	Boy 17 yrs.	Before A.C.T.H.	After A.C.T.H.	After Epinephrine.	% of fall in Eosinophils.
17-Ketosteroids		1.75 mgm.	3.8 mgm.	2.1 mgm.	After A. C. T. H. 62. 4%-normal response
Cortin		0.53 mgm.	1.53 mgm.	0.8 mgm.	
Eosinophils		444	167	336	After Epinephrine 24. 3%-poor response. Mild insufficiency

In the above case of anorexia nervosa, both urinary cortin and 17-ketosteroids are decreased.

TABLE IX
17-Ketosteroids and Cortin Estimation.
IN SURGERY

No.	Name.	Sex.	Age.		Pre-operative.	1st day	Post-operative. 3rd day	10th day
1	E. E.	M	47	Cortin	1.86 mgm.	3.2 mgm.	3.4 mgm.	2.5 mgm.
				17-K.S.	9.0 mgm.	10.2 mgm.	8.0 mgm.	6.0 mgm.
2	H. H.	M		Cortin	1.6 mgm.	2.7 mgm.	2.4 mgm.	2.2 mgm.
				17-K.S.	6.8 mgm.	7.0 mgm.	5.8 mgm.	4.0 mgm.
3	A. P.	F	49	Cortin	1.2 mgm.	3.0 mgm.	2.8 mgm.	2.0 mgm.
				17-K.S.	8.5 mgm.	8.0 mgm.	6.0 mgm.	3.3 mgm.

Following surgery there is increase in cortin but no significant change in urinary excretion of 17-ketosteroids.

On 10th post-operative day, 17-ketosteroids urinary excretion is decreased but excretion of cortin still elevated.

27. Evans, G. "The Adrenal Cortex and Endogenous Carbohydrate Formation". *Am. Jr. Physiol.* 114:297, 1936
28. Long, C. N. H. et al. "The Adrenal Cortex and Carbohydrate Metabolism". *Endocrinology* 26:309, 1940
29. Ingle, D. J. et al. "A Comparison of Acute Effects of Corticosterone and 17 Hydroxy-corticosterone on Body Weight and Urinary Excretion of Sodium Chloride, Potassium, Nitrogen and Glucose in Normal Rats". *Endocrinology* 39:52, 1946
30. Conn, J. W. et al. "Production of Temporary Diabetes in Man". *Jr. of Lab. and Clinical Med.* 33:651, 1948
31. Joffe, H. L. "The Influence of Supra Renal Glands on Thymus". *Jr. Exper. Med.* 40:325, 1924
32. Ingle, D. J. "Effect of Two Steroid Compound on Weight of Thymus of Adrenalectomized Rats". *Proc. Soc. Exper. Biol. & Med.* 44:174, 1940
33. Dougherty, T. F. et al. "Pituitary Adrenocortical Control of Lymphocytic Function as Experimental X-ray Radiation." *Endocrinology* 39:370, 1946
34. Dougherty, T. F. et al. "Effect of Pituitary Adrenotrophic Hormone on Lymphoid Tissue". *Proc. Exper. Biol. & Med.* 53:132, 1943
35. Dougherty, T. F. et al. "Functional Alteration in Lymphoid Tissue induced by Adrenal Cortical Secretion". *Am. J. Anat.* 77:81, 1945
36. Hills, A. Gorman et al.: "Changes in Circulating Leukocytes induced by Administration of Pituitary A. C. T. H." *Blood, Jr. of Hæmatology* 3:755, 1948 (July)
37. Swingle, W. W. and Pfiffner, J. J. "The Revival of Comotosed Adrenalectomized Rats with an Extract of a Supra Renal Cortex". *Science* 72:75, 1930
38. Hartman, F. A. and Blomwell, K. A. "The Hormone of Adrenal Cortex". *Science* 72:76, 1930
39. Mason, H. L. et al. "Chemical Studies of Supra Renal Cortex". *Jr. of Biol. Chem.* 116:267, 1936
40. Defermery, P. et al. "Corticosterone, a Crystalline Compound with Biological Activity of the Adrenal Cortical Hormone". *London, Nature*, 139:26, 1937
41. Reichstein, T. et al. "Desoxycorticosterone." *Helvt. Chem. Acta.* 20:1164, 1937
42. Reichstein, T. and Von Euw, J. "Isolation of Desoxycorticosterone from Adrenal Cortex". *Helvt. Chem. Acta.* 21:1197, 1938
43. Wintersteiner, O. and Pfiffner, J. J. "Chemical Studies on Adrenal Cortex". *Jr. Biol. Chem.* 116:291, 1936
44. Reichstein, T. "Adrenosterone". *Helvt. Chem. Acta.* 19:223, 1936
45. Pfiffner, J. J. and North, H. B. "17 beta-hydroxyprogesterone" *Jr. of Biol. Chem.* 132:459, 1940
46. Selye, H. "Steroids Isolated from Adrenal Cortex". *Encyclopedia of Endocrinology*, Sect. 1. Steroid. Vol. 4, page 10 of Synoptic Chart. 1943
47. Kendall, E. C., "Adrenal Cortex". *Arch. Path.* 32:474, 1941
48. Ingle, D. J. "The Effect of Cortin Like Compound upon Body Weight and Work Performance of Adrenalectomized Rats". *Endocrinology* 27:297, 1940
49. Ingle, D. J., "Problems Relating to the Adrenal Cortex". *Endocrinology* 31:419, 1942
50. Sayers, G. et al, "Preparation and Properties of Pituitary Adrenotrophic Hormone". *Jr. Biol. Chem.* 149:425, 1943
51. Li, C. H. et al. "Adrenotrophic Hormone". *Jr. Biol. Chem.* 149:413, 1943
52. Albright, F. "Cushing's Disease". *Harvey Lect.* 38:123, 1943
53. Selye, H. "Production of Nephrosclerosis by Over Dosage with Desoxycorticosterone Acetate". *Canad. M. A. J.* 47:515, 1942
54. Sayers, G. et al. "The Effect of Pituitary Adrenotrophic Hormone on Cholesterol and Ascorbic Acid Content of Adrenals of Rat and Guinea Pig". *Endocrinology* 38:1, 1946
55. Long, C. N. H. "The Relation of Cholesterol and Ascorbic Acid to the Secretion of Adrenal Cortex. Recent Progress in Hormone Research." *New York Academic Press* 1:99, 1947



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56. Callow, N. H. et al. "The Colorimetric Determination of Substances Containing the Grouping CH_2CO in Urine Extract as an Indication for Androgen Content." *Bio. Chem. J.* 32: 1312, 1938
57. Zimmerman, W. "The Color Reaction of Sex Hormone and its Application to Colorimetric Determination". *Ztschr-Fur-Physio. Chem.* 233-257, 1935
58. Zimmerman, W. "Colorimetrische Bestimmung der Keimdrusen hormone". *Ztschr-Fur-Physiol. Chem.* 245-241, 1936
59. Wu, H. and Chou, C. Y. "Contents of Sex Hormones in Normal and Pathological Urine". *Chinese J. Physiol.* 11: 413, 1937
60. Callow, N. H. "Excretion of Androgens by Eunuchs and Isolation of 17-Ketosteroids from Urine". *Bio. Chem. Jr.* 34: 276, 1940
61. Callow, N. H. et al. "Isolation of 17-Ketosteroids in Normal Women". *Bio. Chem. J.* 33: 931, 1939
62. Hirshman, H. "Androgen from Urine of Ovariectomized Women". *Jr. Biol. Chem.* 130: 421, 1939
63. Hamblen, E. C. et al. "Urinary Excretion of 17-Ketosteroids in Ovarian Failure". *Jr. Clin. Endo.* 1: 724-763, 1941 (Sept.)
64. Callow, N. H. et al. "The Differential Diagnosis of Forms of Basophilism, particularly by Estimation of Urinary Androgens". *Quart. Jr. Med.* 8: 233, 1939
65. Mason, H. L. et al. "Isolation of Steroid from the Urine of Patient with Adrenal Cortical Tumor and Hyperplasia". *Jr. Biol. Chem.* 161: 235-257, 1945 (Nov.)
66. Venning, E. H. et al. "Isolation of Androsterone Sulphate". *J. Biol. Chem.* 146: 369-379, 1942 (Dec.)
67. Dorfman, R. I. et al. "Conversion of the Human Testis Hormone Testosterone into Urinary Androgens and Androsterone". *Jr. Biol. Chem.* 130: 285-295, 1939 (Sept.)
68. Dorfman, R. I. et al. "Concerning the Metabolism of Testosterone to Androsterone". *Jr. Biol. Chem.* 133: 763-780, 1940 (May)
69. Albright, F. et al. "A Syndrome Characterized by Primary Ovarian Insufficiency and Decreased Stature". *Am. J. Med. Sci.* 204: 625-48, 1942
70. Cahan, R. L. et al. "Urinary 17-Ketosteroids in Metabolism; standardized Chemical Estimation." *Jr. Biol. Chem.* 152: 489-499, 1944
71. Hershberg, F. B. et al. "A Rapid Extractor for Urinary Steroids". *Jr. Biol. Chem.* 133: 667-673, 1940 (May)
72. Drechter, I. J. et al. "A Rapid Method for the Determination of Total Urinary 17-Ketosteroids". *Jr. Clin. Endocrinology* 7: 795-800, 1947 (Dec.)
73. Pincus, G. et al. "New Color Reaction for Certain Urinary 17-Ketosteroids". *Endocrinology* 32: 176-184, 1943 (Feb.)
74. Nathanson, I. T. et al. "Excretion of Sex Hormones in Abnormalities of Puberty". *Jr. Clin. Endocrinology* 3: 321-330, 1943
75. Talbot, N. B. et al. "Excretion of 17-Ketosteroids by Normal and by Abnormal Children". *Am. J. Dis. Child.* 65: 364-375, 1943 (March)
76. Bachman, C. et al. "Day and Night Excretion of Pregnanediol-Glucuronide and Neutral 17-Ketosteroids in Pregnancy". *Jr. Clin. Endocrinology* 1: 142-146, 1941 (Feb.)
77. Forbes, A. P. et al. "Individual Variation of 17-Ketosteroids Excretion." Paper Read Before 25th Annual Meeting of Association for Study of Internal Secretions.
78. Werner, S. C. "The Daily Variation in 17-Ketosteroids Excretion of Men and Women". *Jr. Clin. Endocrinology* 1: 951-954, 1941 (Dec.)
79. Talbot, N. B. et al. "The Colorimetric Assay of Total alpha and beta 17-Ketosteroids in Extracts of Human Urine". *Jr. Biol. Chem.* 132: 595-603, 1940
80. Dorfman, R. I. et al. "Metabolism of Steroid Hormones-Studies of 17-Ketosteroids and Androgens". *Endocrinology* 41: 470-488, 1947
81. Deakins, M. L. et al. "Some Effects of Testosterone Propionate, Stilbestrol, and X-ray Therapy with Cushing's Syndrome." *Jr. Clin. Endocrinology* 4: 376-384, 1944
82. Kepler, E. J. et al. "Adrenocortical Tumor Associated with Cushing's Syndrome". *Jr. Clin. Endocrinology* 8: 499, 1948
83. Landau, R. L. et al. "The Effect of Starvation on Urinary 17-ketosteroid Excretion". *J. r. Clin. Endocrinology* 8: 133, 1948
84. Levin, L. "The Urinary 17-Ketosteroid Level of Human Leukemic Subjects". *Jr. Clin. Endocrinology* 8: 487, 1948

85. Miller, S. et al. "Excretion of 17-Ketosteroid by Diabetes". *Jr. Clin. Endocrinology* 5: 220, 1945
86. Pearlman, W. H. "Steroid Excretion in Cancerous and Non-cancerous Patients". *Endocrinology* 30: 270, 1942
87. Cutler, H. H., Power, M. H. and Wilder, R. M. "Concentration of Sodium Chloride and Potassium in the Blood. Their Diagnostic Significance in Adrenal Insufficiency". *Jr. Am. Med. Assn.* 111: 117, 1938
88. Robinson, F. J. Power, M. H., and Kepler, E. J. "Two New Procedures to Assist in the Recognition and Exclusion of Addison's Disease". *Proc. Soc. Staff. Meet. Mayo Clinic* 16: 577, 1941
89. Wilson, D. M. et al. "Alkalosis and Low Plasma Potassium in a Case of Cushing's Syndrome. A Metabolic Study." *Jr. Clin. Invest.* 19: 701, 1940
90. Venning, E. H. et al. "Biological Assay of Adrenal Corticoids". *Endocrinology* 38: 79, 1946
91. Talbot, N. B. et al. "The Colorimetric Assay of Urinary Corticoid Like Substance". *Jr. Biol. Chem.* 160: 535, 1945
92. Heard, R. D. H. and Sobel, H. "A Colorimetric Method for the Estimation of Reducing Steroids". *Jr. Biol. Chem.* 165: 687, 1948
93. Daughaday, W. H. et al. "Chemical Assay for Cortin." *Jr. Clin. Endocrinology* 8: 166, 1948
94. Robbie, W. A. and Gibson, R. B. "Rapid Clinical Determination of Urinary 17-Ketosteroids". *Jr. Clin. Endocrinology* 3: 200, 1943
95. Thorn, R. W. et al. "Test for Adrenal Insufficiency". *Jr. Am. Med. Asso.* 137: 1005, 1948
96. Recant, L. et al. "Observation on Pituitary Adrenal Response Following Epinephrine Infusion in Man". Abstract from the Paper Read Before 30th Meeting of the Association for Study of Internal Secretion, June 1948.
97. Sayers, G. et al. "The Assay of Adrenotrophic Hormone by Adrenal Ascorbic Acid Depletion Method." *Endocrinology* 42: 379, 1948
98. Heard, R. D. H. and Sobel, H. and Venning, E. H. "The Neutral Lipide Soluble Reducing Substances of Urine as an Index of Adrenal Cortical Function." *Jr. Biol. Chem.* 165: 699, 1946
99. Folin, O. and Wu, H. "A Simple and Improved Method for Determination of Sugar." *Jr. Biol. Chem.* 41: 367, 1920

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A CASE OF STENOSIS OF THE AQUEDUCT OF SYLVIIUS DUE TO TUMOUR

By F. L. DAVIES, F.R.C.S., & P. S. ANDREWS, M.B., B. Chir.

from Department of Neurosurgery and Bland-Sutton Institute of Pathology, Middlesex Hospital, London, W. 1., England.

STENOSIS of the Aqueduct of Sylvius is a condition of considerable interest not only as a pathological study but also from the aspects of diagnosis and treatment. The case presented below illustrates both the difficulty of differentiating neoplastic from benign forms of stenosis and the problems involved in the treatment of these cases.

CASE HISTORY

A female aged 18 years. Three and a half months prior to admission she complained of early morning frontal headaches with bouts of vomiting; at first she had a few days respite between attacks but later vomiting occurred daily and she noticed pain in the occipital region, and at the back of the neck. She had double vision occasionally on looking to the left but had not noticed any blurred vision, weakness nor unsteadiness.

PREVIOUS HISTORY

Her mother had a prolonged and difficult labour but the child was apparently normal. Two years prior to admission her parents noticed a sudden change in her personality. She left Grammar School, where she had been doing well, and took a simple filing job in an office. Her menstrual history was normal.

CLINICAL FINDINGS

She was a pleasant, well-built, healthy looking girl. She was alert, of average intelligence and emotionally labile. Skull was normal externally; neither cracked-pot sound nor bruit were present. There was no neck stiffness. Bilateral papilloedema was present and greater on the left than the right. Visual acuity was 6/5 in each eye. The visual fields were full to confrontation, the pupils were large and reacted to light and accommodation. The left external rectus muscle was weak and there was diplopia on looking to the left, there was no nystagmus. The other cranial nerves were normal. Her gait was normal. Muscle tone, muscle power and sensation were normal in all the limbs. Reflexes were brisk, more so in the right leg than the left. The

plantar responses were flexor. Both outstretched arms were easily displaced.

INVESTIGATIONS

X-rays of the chest were normal. Straight X-rays of the skull showed increased convolutional markings with widening of the sutures and a small posterior fossa. Electroencephalogram was consistent with increased intracranial pressure and did not show any lateralising features. Ventriculogram (24-4-56) revealed a pressure in the lateral ventricles of 50 mm. C. S. F., the lateral ventricles were symmetrically dilated as were the third ventricle and upper $\frac{1}{3}$ of the aqueduct. The appearance of the stenosed aqueduct as shown by the Myodil (Fig 1) is very suggestive of a non-neoplastic stenosis, while the antero-posterior view (Fig. 2) shows no lateral displacement of the third ventricle or the upper part of the aqueduct. A diagnosis of non-neoplastic stricture of the aqueduct was made.

OPERATION

(24-4-56) A Torkildsen's operation was performed but in view of the very high intracranial pressure



Fig. 1. Ventriculogram. Air outlines the dilated anterior horns of the lateral ventricles and the anterior part of 3rd ventricle. Myodil is shown in the posterior part of the 3rd ventricle and upper $\frac{1}{3}$ of dilated aqueduct. Ventricular catheter is shown in situ.

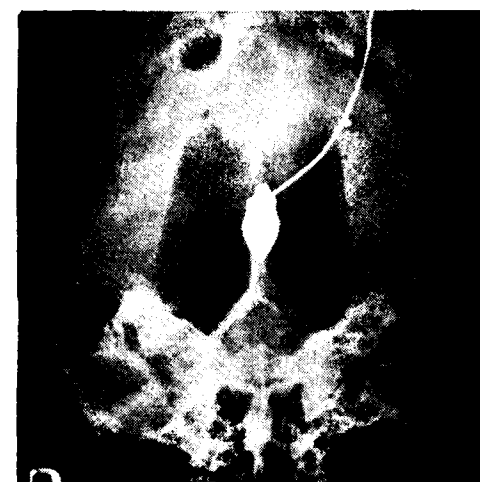


Fig. 2. Ventriculogram. Symmetrical dilatation of lateral ventricles. There is no lateral shift of dilated 3rd ventricle and upper part of aqueduct.

present, a catheter was inserted into the opposite ventricle and controlled drainage was instituted in order to lower the pressure gradually. The patient's immediate post-operative condition was satisfactory but two days later she suddenly developed a severe headache, increasing drowsiness and irregular gasping respiration.

SECOND OPERATION

An emergency cerebellar decompression with removal of the posterior arch of the atlas was performed the same day. Despite drainage of the lateral ventricle, the pressure in the posterior fossa was extremely high, the left cerebellar lobe protruded out of the wound and tonsils had herniated below the arch of the atlas. No evidence of tumour was found in the cerebellum and the wound was closed with difficulty after administering 60 ml. of 50 per cent sucrose solution intravenously.

The immediate post-operative course was satisfactory, ventricular catheter was removed in two days, the pressure gradually returning to normal. In two days the patient was up and walking in the ward. A nystagmus to the left, which was noticed immediately post-operatively, had disappeared; the papilloedema was gone and no other abnormal signs were present. She remained symptom free until 14-5-56 when the headache and vomiting recurred, the left upper limb became unsteady, and the nystagmus reappeared. Deep X-ray therapy to the pons was commenced. Despite this treatment the intracranial pressure increased and the patient began to deteriorate. On 11-6-56 she had a fit, became rigid, rolled her eyes from side to side and lost

consciousness for a few minutes. The radiotherapy was discontinued. On the 14-6-56 she vomitted frequently and was found to have increased papilloedema, visual acuity of J16 in each eye, left sided ankle clonus and a temperature of 103°F. On the 19-6-56 she complained of severe headache, was very drowsy and vomitted; the decompression was tense. It was decided to re-explore the posterior fossa to re-establish, if possible, the flow between the lateral ventricles and the cisterna magna. The patient died suddenly before the wound was completely reopened. The immediate cause of death was established as due to air embolism.

POST-MORTEM FINDINGS

Air embolism. Astrocytoma of the midbrain. Occlusion of the aqueduct of Sylvius.

The calvaria was thin and the inner table showed marked convolutional impressions. The dura and arachnoid were normal outside the areas of surgical intervention. The point at which air entered the circulation was not found. Air bubbles were present in the cerebral vessels. The heart chambers contained frothy blood, post-mortem coagula and air.

The lateral and third ventricles were dilated. The aqueduct, dilated in its upper third, gradually narrowed until it would admit only a fine bristle. The stenosis was caused by a tumour, almost spherical in shape, measuring 1.3 cm. in diameter, which surrounded the aqueduct (Fig. 3). The tumour had a well-defined edge and was firmer and darker than the brain tissue around it. The fourth ventricle was normal.



Fig. 3. Section through the brain stem showing the tumour surrounding the cerebral aqueduct which lies slightly to the left of the midline.

MICROSCOPICALLY

The tumour is a fibrillary astrocytoma (Fig. 4). The cells show a small variation in size and staining; occasional giant cells are present. The cells, a few of which are in mitosis, resemble astrocytes and lie in the meshes of a loose, fibrillary network which is condensed and coarser beside the right half of the aqueduct. The ependymal lining of the latter is regular and complete. Blood vessels are plentiful in the tumour; they show endothelial proliferation and are surrounded by a mantle of lymphocytes, plasma cells and a few neutrophils. There is no sign of degeneration in the tumour.

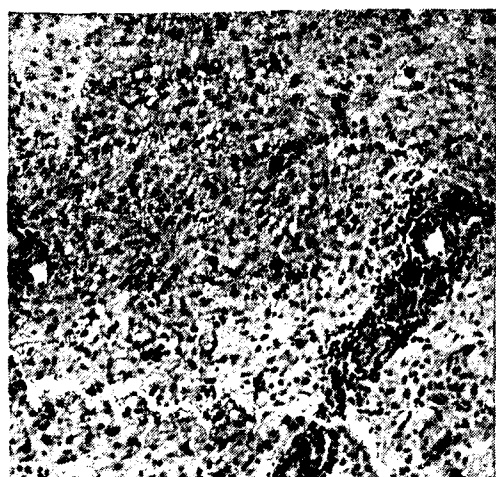


Fig. 4. Section of the tumour showing the cells lying in a loose meshwork of fibres. The vascular changes are marked.
H. & E. x 110.

DISCUSSION

This case is presented as it illustrated the difficulty and virtual impossibility, of making an accurate pre-operative diagnosis even with aid of modern methods of investigation.

The short history in an otherwise healthy young woman was suggestive of a rapidly progressive posterior fossa tumour. The age of the patient however does not exclude a non-neoplastic stenosis of the aqueduct (Spiller, 1902; Pennybacker, 1940; Russell, 1949 and Paine and McKissock, 1955).

The physical signs were predominantly those of increased intracranial pressure and are similar to those described as the "adult" type found in the older age group by Pennybacker (1940). Other features of non-neoplastic stenosis of the aqueduct have been reported by Orton (1931), Parker and Kernohan (1933), Stookey and Scarff (1936) and Petit-Dutaillis et al. (1951).

The radiological appearances were considered typical of non-neoplastic aqueduct stenosis. The signs of generalised increased pressure, such as the increased convolitional markings, and the partial separation of the sutures, when taken in conjunction with the small posterior fossa were suggestive of benign stricture. The ventriculogram seemed to confirm the diagnosis, as it satisfied the criteria put forward by Twining (1939), Bull (1950), Sutton (1950) and Paine and McKissock (1955).

Operations to overcome the obstruction to the flow of cerebrospinal fluid have been described by Dandy (1920, 1922), Mixter (1923), Stookey and Scarff (1936) and Pennybacker (1940). At the present time, the most satisfactory treatment of non-neoplastic aqueduct stenosis is Torkildsen's procedure (Penfield, 1942; Paine and McKissock, 1955), while the same operation holds the only hope of relief in those cases in which a neoplasm is the cause of the stenosis.

That Torkildsen's operation alone may not be sufficient to give immediate relief is illustrated in this case and has been noted by other authors (Paine and McKissock, 1955). It appears that the immediate cause of failure is the very high intracranial pressures encountered in these patients and the unavoidable changes in the cerebrospinal fluid and vascular pressures consequent upon the ventriculographic investigation. Sudden release of the ventricular fluid may invoke cerebral oedema which will increase the intracranial pressure directly and indirectly by completely occluding the already narrowed aqueduct.

It is suggested that to minimise the effect of these immediate complications a preliminary controlled ventricular draining by an indwelling catheter together with a Torkildsen's operation with the judicious use of hypertonic solutions, such as sucrose, might tide the patient over the crisis. If these measures are unsuccessful, a posterior fossa decompression should be performed.

The value of radiotherapy in these cases is doubtful as the nature of the lesion is often unknown. Its use in this patient was indicated after the second operation when a pontine tumour was suspected.

The pathological aspects of aqueduct stenosis have been classified by Russell (1949) according to certain criteria. The diagnosis of gliosis of the aqueduct was considered as a cause of this patient's illness. Although gliosis may occur after the first decade of life (Pennybacker, 1940), the clinical history was short and histologically the aqueduct was not subdivided, subependymal gliosis was confined to one area contiguous with

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ANTIBIOTICS IN DENTISTRY

Penicillin and other antibiotic drugs in recent years have become useful adjuncts in many dental procedures and powerful weapons against dental infections. Dr. Edward L. Sleeper of Tufts College in the United States has reported that some abscessed teeth so loose that "they could have been extracted with one's finger", have been saved by treating the infection with aureomycin or penicillin. Dr. Lester Hugh Roth, of the University of Pittsburgh, last year credited aureomycin with preserving the teeth of 31 patients with "poor to hopeless" chances of keeping them.

Antibiotics—sometimes in combination with the triple sulfa drugs, sulfadiazine, sulfamerazine and sulfamethazine—deal effectively with dental infections. Indeed, so effectively that the wholesale removal of teeth is no longer ordered with the idea of eliminating infections that are causing trouble elsewhere in the body.

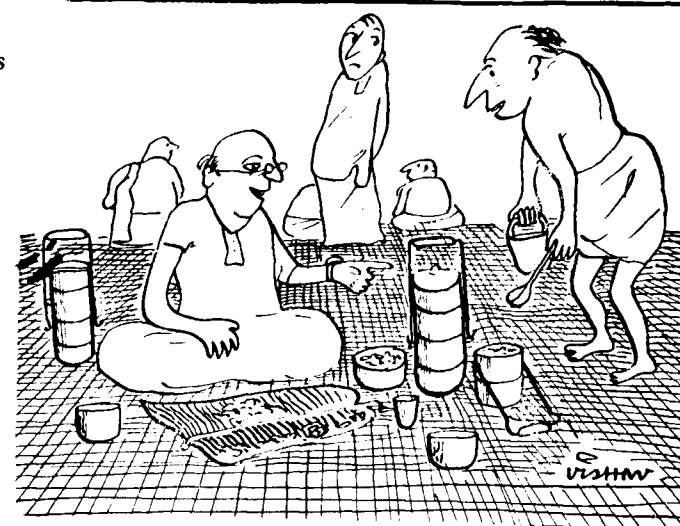
NEW SNAKE-BITE TREATMENT RAISES SURVIVAL CHANCES

A new treatment which increases the chances of survival after a bite from a poisonous snake has been developed by Dr. E. R. Trethewie, of the Department of Physiology at Melbourne University, Australia. The new technique was developed through a series of tests with mice, and the results have been published in the Australian Medical Journal.

The death rate from a severe snake-bite is about 50 per cent, but Dr. Trethewie claims by his method of injections survival after a bite is prolonged, giving more time for anti-venom or other treatment and also giving the body a greater chance of dealing with the venom naturally.

£500,000 FOR U. K. CANCER RESEARCH

Contributions to the British Empire Cancer Campaign reached £500,000 last year. Announcing this at the campaign's annual meeting in London recently the Duke of Gloucester commented: "So Lord Horder, a member of the Organisation, reach his goal in the last year of his life". Announcing three big donations to the campaign, the Duke said one of them was £100,000 from the Government, another £100,000 from the Duke of Edinburgh, and a third £100,000 from the Duke of Kent.



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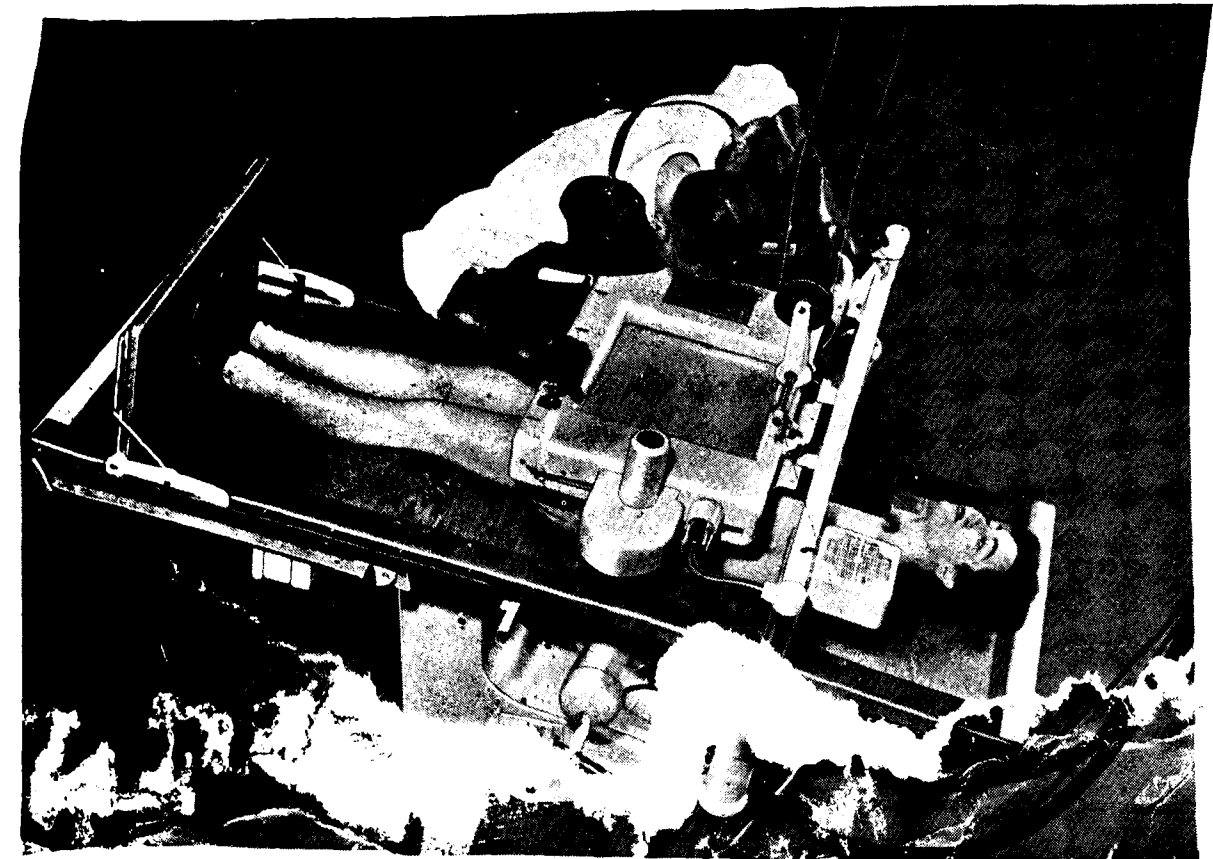
under covenant for the provision of a cobalt 'gun' at Westminster Hospital; it would make it the first London teaching hospital to have this equipment. There was also a donation from the Civil Service Sanatorium.

Duke said: "We can now go forward with every confidence in the importance of our cause, and determined year by year to intensify the efforts being made to solve the riddle of cancer so as to end misery and fear which that word has evoked in the past."

INDIAN SURGEON STUDYING IN U. K. UNDER COLOMBO PLAN

Dr. R. V. R. Saha, lecturer in surgery at the Patna Medical College, has entered a four-month course in surgery in the United Kingdom under the Technical Co-operation Scheme of the Colombo Plan. According to present plans, the Patna Medical College Hospital is to be enlarged in the next few years and is expected to become one of the big post-surgical hospitals in the East. A modern university centre is to be established there under Dr. Saha's charge.

Dr. Saha will study the organisation, equipment and research facilities at similar centres in the U.K. He will spend some time at the University of Manchester, at London University, and will also visit the University of Birmingham.



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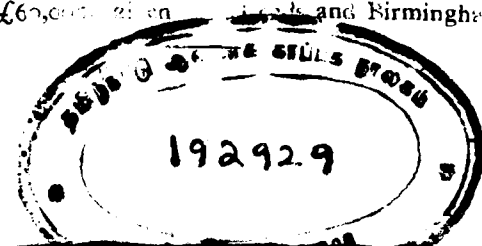
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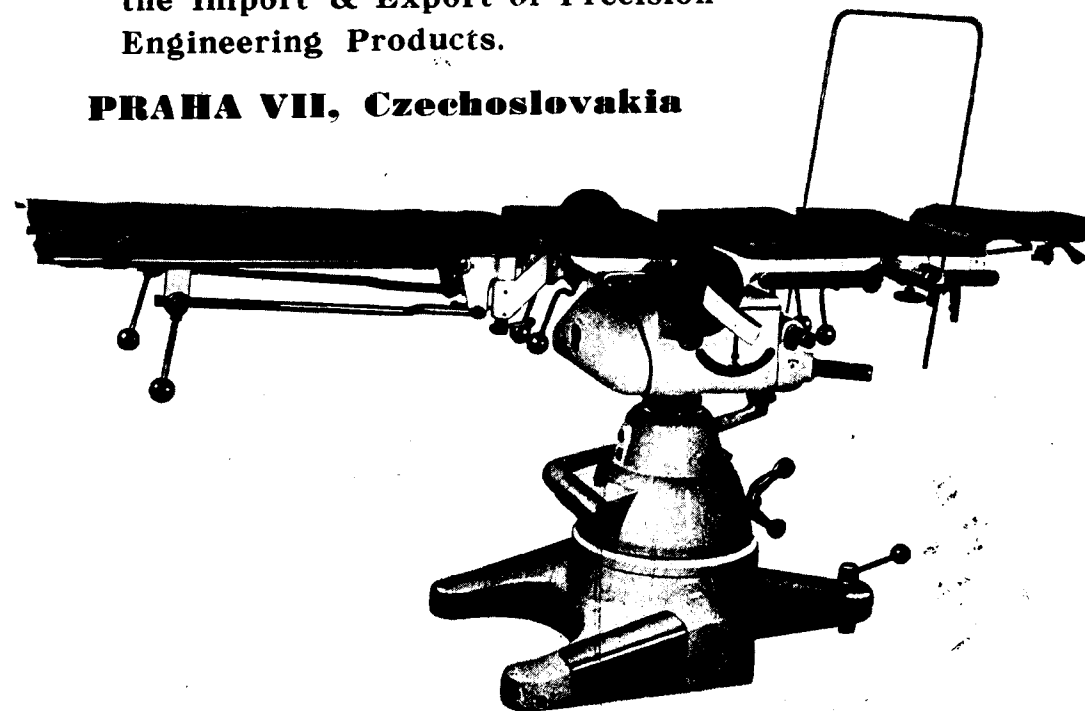
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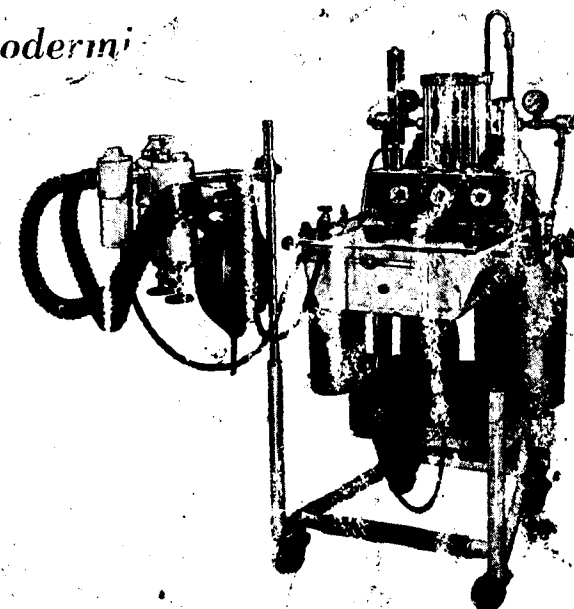
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