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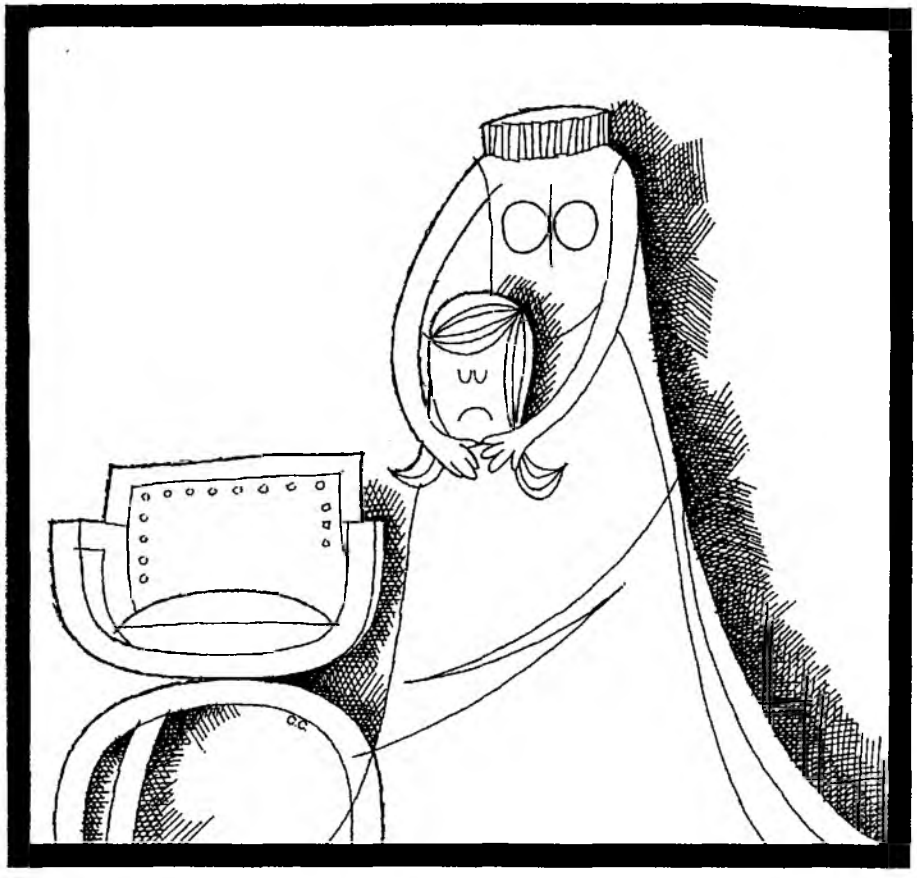

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NEUROLOGICAL EXAMINATION

The first of two articles written for Res Medica by
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Neurological Unit, Northern General Hospital.

Wilfred Trotter has said that the performance of a refined neurological examination is "a job for men". Certainly performing a full neurological examination seems to separate the men from the boys and many medical students are often unnecessarily alarmed at the prospect. Much of this anxiety can be dispelled, however, if the logic of the examination is appreciated. A greater number of objective signs can be elicited in the examination of the nervous system than in any other system and this profusion of signs, at first so unnerving, can be a positive advantage in providing sufficiently precise information regarding the site of dysfunction in the nervous system. After the examination has revealed this anatomical diagnosis, the physician, by taking into account the details of the evolution of the disease revealed in the history, can usually reach a final conclusion regarding the nature of the disease which is causing the dysfunction in the nervous system. This is the final or pathological diagnosis.

The following account deals briefly with the correct methods of eliciting the physical signs and is not primarily concerned with neurological history taking. The importance of taking a careful history, however, cannot be over-emphasised, in neurology as in any other branch of medicine. A well-known neurologist has said that if he does not have a pretty shrewd idea of what is wrong with a patient when he puts his pen down at the end of taking the history he probably never will know. Not only does the history reveal important information, but the intelligent use of this information will often direct the neurologist's attention to those parts of the physical examination which are particularly revealing in the patient concerned.

EXAMINATION OF THE CRANIAL NERVES

First cranial nerve. The sense of smell should be tested by the use of various aromatic odours, such as coffee, oil of almonds or peppermint. The method is to occlude one nostril

and to ask the patient to sniff the sample presented through the other nostril. This procedure is repeated on the opposite side. The patient may smell nothing (anosmia), or he may say that he can smell some odour but is unable to identify it (hyposmia), or he may be able to identify the odour correctly, in which case he has certainly got normal olfactory sense. The sense of smell may be lost unilaterally with lesions of the olfactory tract and is not uncommonly lost altogether following head injury.

The second cranial nerve. There are three aspects of the function of the second cranial nerve which have to be tested. These are the visual acuity, the fields of vision and the appearance of the fundus. *Visual acuity* is tested ideally for both far and near vision. At the bedside, however, usually only near vision is tested. To do this the patient covers one eye with his hand and is given the near-vision type card and is requested to read the smallest type that he can see. This is N5 on the standard near-vision test. Each eye is tested separately. *The fields of vision* are tested by confrontation. The examiner faces the patient at a distance of 18″ to 2′. One of the patient's eyes is covered and he is instructed to look at the opposite eye of the examiner. In this way the patient will be looking with, for example, his left eye into the examiner's right eye. The patient is instructed to keep his eye fixed on the examiner's eye and the examiner then proceeds to test the extent of the patient's peripheral field by direct comparison with that of his own eye. A small object such as the head of a hatpin is introduced from the periphery towards the centre until the patient declares that he can see it. This procedure is carried out around the whole circumference of the field of vision and any constriction of the field or sector defect is readily apparent. The method of confrontation can also be used to determine the presence of a central scotoma. In this case the object is held a few degrees outside the line of fixation of the patient's eye and he is asked to say whether the object appears clearer in this position or when it is brought immediately in front of his fixation point. Normally the latter position is, of course, the clearer. *The examination of the fundus* requires the use of the ophthalmoscope and this can only be acquired by considerable practice. The examination of the fundus is, of course, part of the general physical examination, but from the neurological standpoint certain features are especially important. These are (a) the appearance of the disc: This is normally of a pinkish-white colour, paler than that of the surrounding retina, and in the centre of the disc the optic cup can be seen, from which the retinal vessels emerge and run over the disc to reach the periphery of the retina. In optic atrophy the disc is paler than normal, and the edge sharper, and in raised intracranial pressure, papilloedema occurs in which there is marked swelling of the optic disc. Swelling can be suspected when the disc is pinker than normal, and when the optic cup is filled up and when the edges of the disc become blurred as the oedema masks the junction with the surrounding retina. (b) The vessels of the retina: Careful examination may reveal differences in calibre of the arteries, and in the arterio venous ratio, indicating the presence of atheroscelerosis, or may show the presence of arterial or venous thrombosis. (c) The appearance of the retina itself: The presence of haemorrhages or exudates is of importance, since these occur not only in general medical diseases, such as hypertension, renal disease, and diabetes, but will also occur when there is gross raised intracranial pressure with papilloedema. The retina may also show signs of old choroiditis or other inflammatory disease, such as tuberculoma, toxoplasmosis, etc., which may have a bearing on the neurological condition.

Third, fourth and sixth cranial nerves. At this point it is convenient to examine the orbit for the presence or absence of proptosis, as well as testing the integrity of the muscles innervated by the third, fourth and sixth cranial nerves, which also include the levator of the upper lid and the pupil. Proptosis is best detected by examining the patient from behind. Ptosis is usually noted early on meeting the patient and is conveniently measured by the degree to which the upper lid in the normal open-eyed position covers the upper part of the limbus. To examine the ocular movements the patient is first asked to look directly ahead. In this position it is possible to detect any squint, that is to say to detect whether the visual axes appear parallel or not. The patient should then be asked to fix his gaze on the examiner's finger held at a distance of about 2′ from the patient. The finger is then moved with the patient's eyes following it to the extreme positions of lateral gaze to either side and also vertically upwards and downwards. The patient is asked whether he sees double

in any position of the eyes and if he does the direction of gaze which produces maximum separation of the images is determined. At the extremes of gaze, attention should also be paid to the presence of nystagmus.

The pupils: These are normally equal in size and regular in shape. They should constrict to a light stimulus, direct or consensual, and on accommodation/convergence. The light reflex is tested by covering one eye and shining a lighted torch on the other eye. The pupil of the eye so stimulated should contract and remain constricted so long as a light is shone on it. If at the same time the hand covering the other eye is raised, it will be seen the pupil of this eye normally contracts consensually when light is thrown on the other eye. This procedure is carried out on each side. Accommodation/ convergence is tested by asking the patient first to look into the distance and then to look at the observer's finger placed one foot in front of him. The two eyes should converge and the pupils contract when the patient focuses on the finger.

Fifth cranial nerve. The sensory, motor and reflex functions of this nerve must be tested. Sensation to light touch and pin prick is examined in the territory of the three divisions of the nerve. Motor function of the muscles of mastication, the masseters, temporales and pterygoids, is also tested. This is done by asking the patient to open or close the jaw against resistance. If the muscles of mastication are paralysed on one side, the jaw will deviate towards that side when opening. The reflexes of the trigeminal nerve are the corneal reflex, which is tested by lightly applying a wisp of cotton wool to the cornea, and the jaw jerk which is the tendon reflex of the muscles of mastication. The patient is asked to open his jaw half-way and the jaw is grasped between the thumb and forefinger of the examiner's hand. A blow with the patella hammer on the examiner's thumb will then elicit the jaw jerk.

The seventh cranial nerve innervates the muscles of the face. It also carries the sensation of taste from the anterior two-thirds of the tongue through the chorda tympani nerve. The facial muscles are tested by asking the patient to wrinkle his forehead, to frown, to screw his eyes up tight, to smile and to whistle. In upper motor neurone weakness the movements of the lower part of the face only are involved, but in a lower motor neurone palsy the whole of the musculature on the affected side is paralysed. *Taste* is a relatively crude sensation and comprises the distinction of sweet, sour, salt and bitter. Other more delicate flavours which we loosely call taste are in fact the properties of the first cranial nerve. Taste on the tongue is tested by applying a small amount of sugar, citric acid, salt or quinine with an applicator stick to the protruded tongue, the patient being asked to identify the taste without withdrawing his tongue into his mouth. He should be instructed to raise his finger to indicate when he has appreciated the taste. He can then be allowed to withdraw his tongue and to announce what he tasted.

Eighth cranial nerve. Hearing is tested at the bedside by the distance at which the patient can hear the whispered voice while one ear is occluded. Normally the distance should be over three feet. If there is depression of hearing of one or both ears then the tuning fork tests should be carried out. There are two of these tests: 1) Rinné's test consists of a comparison of bone and air conduction of sound. The vibrating tuning fork is placed against the mastoid process and the patient asked to say as soon as he can no longer hear the note. The tuning fork is then removed and the vibrating end presented close to the external auditory meatus when, if air conduction is (as normally) better than bone conduction, the patient will again hear the note. This procedure is carried out on each side. (2) Weber's test is performed by placing the vibrating tuning fork on the midline of the head either at the forehead or the vertex and asking the patient whether he hears the sound. With normal hearing the sound is described as in the middle of the head or all over the head, but when there is impaired hearing the sound may be localised to one side. If the deafness is associated with depressed air conduction and Weber's test is lateralised to the same side, this indicates a middle-ear deafness. If in the deaf ear air conduction is better than bone conduction, while both are depressed, and Weber's test is lateralised to the normal ear, then the deafness is caused by nerve deafness.

The ninth and tenth cranial nerves innervate the soft palate and the muscles of the pharynx and larynx. The ninth nerve also carries the

sensation of taste for the posterior third of the tongue. The function of these two nerves can be tested by observing the movements of the palate when the patient says 'Ah', and by eliciting palatal and pharyngeal reflexes. Touching the soft palate with an applicator stick causes a brisk contraction with elevation of the palate, and touching the posterior pharyngeal wall causes gagging with contraction of the wall of the pharynx. If there is paralysis of one side of the palate or pharynx then these movements will be assymmetrical, the movement appearing only on the normal side. Taste over the posterior third of the tongue is tested as described under the facial nerve.

The eleventh cranial nerve innervates the sterno-mastoid and the upper part of the trapezius muscles. The sterno-mastoid is tested by asking the patient to turn his head to the opposite side against resistance when the contracting muscle can be seen and its power estimated. The trapezius is tested by asking the patient to shrug his shoulders upwards towards his ears, while the examiner presses down on the shoulders to assess the power.

The twelfth cranial nerve, the hypoglossal, innervates the tongue. The tongue should first be inspected for any muscle atrophy, fibrillation or tremor. The patient should then be asked to protrude his tongue which normally protrudes in the midline. If there is paralysis of one side then the tongue will deviate towards that side. If this paralysis is of upper motor neurone type, there will be no wasting of the tongue. If it is of lower motor neurone origin, there will be atrophy and possibly fibrillation of the paralysed side.

(To be continued)

THE FIELD OF ALLERGY

by K. K. Adjepon-Yamoah, B.Sc.

A review based on a dissertation read before the Society on 10th December, 1965.

This article concentrates on (i) the immunological basis, (ii) pathophysiological mechanisms, and (iii) control (theoretical and practical) of the immediate-type allergy.

PART I — IMMUNOLOGICAL BASIS

Introduction

Antigen-antibody reactions constitute an important group of defences, facilitating phagocytosis and blocking the toxic effects of parasitic poisons. The reaction confers 'immunity'. The combination of antigen and antibody is, however, not always beneficial. Pathological reactions as severe or more severe than the effect of the antigen alone are sometimes noticed. Hypersensitivity or allergic reactions form major examples of such conditions. Allergy or hypersensitivity may be defined as a state in which the animal reacts in an excessive way to the introduction of an antigen or a hapten even though the antigen or hapten may be innocuous. Not all instances of hypersensitivity enjoy the identification of the exciting antigens, the mediating antibodies and the mechanisms of tissue damage.

Classification

Experimentally two types of hypersensitivity reactions can be demonstrated. They are: (a) the 'immediate type' and (b) the 'delayed type' reactions. Some of the main differences are summarised below.

	Immediate Type	*Delayed Type*
1. Speed of onset of reaction following antigen introduction	Immediate	Delayed 24-72 hours
2. Type of anti-bodies	γ - globulins	As yet Unidentified
3. Chemical medi-ators	Histamine 5 HT, SRS-A, ? Bradykinin. (Depending on species)	As yet Unidentified ? Bradykinin
4. Transfer from animal to animal	Possible with serum in many instances	Not possible with serum. Possible with cells in animals. In man extracts of cells are effective.
5. Types	Anaphylactic shock, Arthus reaction serum sickness, atrophy e.g. asthma, some drug sensitivity, Allergic rhinitis.	Bacterial allergy e.g. Tuberculin type reaction. Contact sensitivity to simple chemical, e.g. contact dermatitis.

Anaphylaxis

Portier and Richet (1902) found that whereas the first intravenous injection into dogs of an extract of sea anemones was relatively harmless, a second injection some 2 weeks later resulted in violent symptoms and often in the death of the dogs. Instead of 'phylaxis' (i.e. immunity), anaphylaxis developed. Soon Theobald, Smith, and Otto independently showed that the guinea pig could likewise be made hypersensitive even to non-poisonous extracts. To explain these facts two schools of thought developed. The first and now defunct theory was the 'anaphylatoxin hypothesis' led by Portier and Richet. The second and now widely accepted theory is the 'cellular hypothesis' supported by Dale. Briefly, this cellular theory maintained that the anaphylactic reaction was the result of union between antigen and antibody which had become 'fixed' to the living cell surface — Dale and Schultz independently showed that the phenomenon of anaphylaxis could be demonstrated in isolated tissues without the presence of blood. Dale showed that the uterus of a sensitised guinea pig (i.e. guinea pig which had received small injections of egg ovalbumin three weeks earlier), when suspended in a nutrient fluid at 37° C and oxygenated, would contract upon the addition to the bath of a small amount of the substance against which the guinea pig had been sensitised. The effect was quite specific since unrelated antigens gave no reaction. Furthermore, after the uterus had once responded by contraction to the antigen in question, a second addition of the same amount of the same antigen produced no effect. The tissue had thus become desensitised. Other workers have shown that other smooth muscle strips from sensitised guinea pigs behave in the same 'Schultz-Dale' manner as the myometrium. It is now possible to sensitise guinea pig tissues passively by soaking them in antibody solution (e.g. I^{133} labelled egg ovalbumin). There is ample evidence that antibody fixation to certain tissues is a necessary prerequisite for anaphylaxis.

Desensitisation

Guinea pigs sensitised to anaphylactic shock can be desensitised by repeated small injections of antigen. It has been shown that during the process of desensitisation a very high titre of circulating antibody is produced, and if antigen is administered to such an immune animal, anaphylactic reaction does not develop because the amount of circulating antibody is sufficient to neutralise all the injected antigen. Serum from such an immune animal is capable of inducing 'passive' sensitisation to anaphylaxis, thus demonstrating that the antibodies involved are of the same type.

Species variation

There is considerable species variation in the manifestations of generalised anaphylaxis. In the guinea pig there is severe bronchospasm leading to asphyxia and death. In the rabbit death is ascribed to corpulmonale. In the dog, death is due to hepatic congestion and peripheral circulatory failure. Man resembles the guinea pig in that there is acute respiratory distress of asthmatic type and generalised oedema. Anaphylactic reaction in man is in fact rare but when it does occur, it usually follows repeated injections of therapeutic serum (e.g. ATS), or certain drugs (e.g. penicillin and neoarsphenamine).

There is experimental evidence that cot deaths, which are responsible for about 2,000 infant deaths per year, may be due to hypersensitivity to cow's milk protein.

The disturbances in generalised anaphylaxis are fundamentally the same in all species. The main effects are: (a) spasm of smooth muscle, and (b) damage to endothelium of blood vessels and an increase in permeability, giving rise to generalised oedema.

Anaphylaxis has been used as an experimental model in the study of allergy. The basic mechanisms are not fundamentally different from other types of immediate hypersensitivity.

Atopy, Food, Dust and Drug Sensitivity

This group of allergies occur after the ingestion of certain foods and drugs, the inhalation of antigens like pollen, and the injection of drugs. There is considerable variation in symptomatology which seems to be dependent upon the route of absorption and the nature of the antigen or hapten.

Examples:

(a) Inhalation antigens, e.g. pollen, gives rise to respiratory symptoms such as allergic rhinitis, hay fever and asthma.

(b) Ingested substances, e.g. mushrooms, shellfish, give rise to gastro-intestinal symptoms and rashes. There is possibly absorption of

whole protein from the gut, so providing an antigen.

(c) Injected drugs, e.g. streptomycin and penicillin, usually give rise to skin rashes.

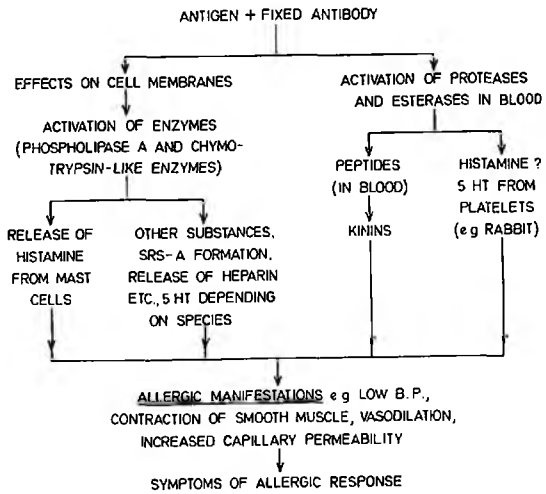
There seems to be a genetic basis in these types of allergy — hence the name atopy.

Miscellaneous Examples

Other examples of immediate hypersensitivity are Arthus reaction and serum sickness, but these conditions seem to be dependent on antigen-antibody complexes.

Many diseases have been labelled allergic although their pathogeneses are by no means clear. Examples are Type I nephritis, rheumatic fever and polyarteritis nodosa. A number of drug 'diseases' have also been documented as being allergic, and chlorpromazine obstructive jaundice is a well known example of this group.

PART II — MECHANISMS



The mechanism by which antigen-antibody combination brings about the release of pharmacological agents is far from being well understood. Briefly — antigen combines with fixed antibody. This 'reaction' is believed to lead to activation of tissue enzyme systems which include chymotrypsin-like enzymes and phospholipase A (Austen and Brocklehurst, 1961, etc.). Complement may or may not play a part at this stage.

Activated enzyme systems cause changes in the cells, such as mast cells which release pharmacologically active substances notably histamine, heparin, SRS-A, 5 HT, and bradykinin. The pattern of release is to some extent dependent on the species. The activation of tissue proteases and esterases may act on substrates such as peptides in the blood to release vasoactive substances such as kinins.

The symptoms of hypersensitivity result from the actions of these pharmacological agents. A summary of the evidence supporting the above statements is made below.

Enzymic Participation

The influence here stems from indirect evidence in which the effects were observed of pH change, temperature change, calcium lack and specific enzyme inhibitors on certain standard tests, e.g. Schultz-Dale type of test. Mongar and Schild concluded (1962) that the enzymes were calcium requiring and heat labile.

Role of Histamine

As Schachter states "Ever since that time that the similarity between the symptoms of histamine intoxication and acute anaphylactic shock was pointed out by Dale and Laidlaw (1910) an impressive body of evidence implicating histamine in anaphylaxis has accumulated." Many workers have demonstrated the release of histamine from sensitised organs both *in vitro* and *in situ* by specific antigen. Histamine liberators, e.g. 48/80, are able to reproduce many of the symptoms of anaphylactic shock when administered to animals. Schayer, and others, using radioactive histidine, have concluded that not only do mast cells store histamine, but also form histamine from histidine. Extrusion of mast cell granules, which are thought to contain histamine-heparin complexes, have been observed during antigen-antibody reaction. The evidence for the release of histamine in anaphylaxis is overwhelming and the release of this substance has been assumed to occur also in other immediate-type allergic reactions.

Slow Reacting Substances of Anaphylaxis (SRS-A)

Kellaway and Trethewie (1940), reported the occurrence of a slow reacting substance from a sensitised tissue following a challenge

with an antigen. The perfusate from guinea pig lung was assayed on guinea pig ileum and these workers recognised that the contraction differed from that caused by histamine in that the gut was slower to relax.

Brocklehurst (1952) noticed that high concentrations of antihistamines were unable to abolish SRS-A response. SRS-A does not appear to exist in preformed state, but is generated by events set in motion by antigen-antibody 'reaction' (Brocklehurst). In the tissues of sensitised guinea pigs and in human asthmatic lungs challenged with the appropriate antigens SRS-A is released along with histamine, but the peak release of SRS-A occurs later than that of histamine and moreover the release of SRS-A continues longer. SRS-A can cause a strong and well-maintained contraction in isolated human bronchioles and it is presumed to play an important role in asthma and so to be as least part of the cause of therapeutic failures of antihistamines in this condition. Herxheimer and Stressman (1961) have shown that whereas impure SRS-A aerosol decreased the vital capacity in asthmatic patients, it had only a small effect in normal subjects.

Other Substances

5 HT has been shown to be important in some species (rabbit and mouse) but not in man.

Bradykinin is present in the blood during anaphylaxis in several species of animals and can mimic some of the changes which are not abolished by antihistamines and presumably cannot be attributed to histamine. An enzyme capable of forming bradykinin in plasma, from dog plasma pseudoglobulin and from Mawer Fraction C is rapidly released from sensitised guinea pig lung or skin when these blood-free tissues are challenged with specific antigens (Brocklehurst).

Some of the inflammatory changes accompanying antigen-antibody 'interaction' might be due to bradykinin generated locally.

PART III — CONTROL OF ALLERGY

Theoretically the allergic reaction can be prevented in a number of ways:—

(a) The first anti-allergic step, often impractical, is the avoidance of contact with known antigens.

(b) By preventing antibody synthesis, e.g. by total body irradiation, antimetabolites and corticosteroids. The obvious disadvantages here far out-weigh any possible therapeutic advantages.

(c) By preventing antibody fixation to tissues. (This has not been possible.)

(d) By inhibiting enzymes involved in the allergic process. Little is known about these cellular enzymes, although it is possible they have normal physiological functions, and so it follows that inhibition of these enzymes may interfere with some vital metabolic processes (Brocklehurst, 1962).

(e) By desensitisation. This method has been tried, but the results are often disappointing even when the existing antigen has been indentified.

(f) The last, and at present most simple method of controlling the allergic symptoms is the inhibition or destruction of the pharmacological substances released during antigen-antibody 'reaction'.

There is no satisfactory way of antagonising SRS-A although it has been reported that homochlorcyclizine is a useful therapeutic agent in several allergic conditions including asthma. This drug has multiple actions — anti 5HT, antihistamine, antiacetylcholine and weakly anti-SRS-A. It is therefore difficult to predict which action is responsible for the clinical improvement.

Theoretically there are three ways in which a drug can oppose the actions of histamine:

(i) by physiological antagonism — e.g. adrenaline which has many of its pharmacological actions opposite to those of histamine.

(ii) the drug might destroy histamine, e.g. formaldehyde, nitrates and the enzyme diamine oxidase. These drugs are of very limited therapeutic value.

(iii) by preventing histamine from reaching its site of action, e.g. by competition — the antihistamines. The last measure has proved to be the best therapeutic method of controlling the allergic reaction at present.

Antihistamines

These drugs oppose all the effects of injected histamine except that on gastric secretion. The use of antihistamines in allergy, however, has certain serious disadvantages. I shall summarise these under three short paragraphs.

Disadvantages of the drugs. These include multiple actions of these antihistamines. All of them depress and sometimes stimulate the C.N.S. About 20% of people on antihistamines complain of minor and moderately severe side effects. Few complain of serious side effects such as blood dyscrasias, the paradoxical occurrence of hypersensitivity reactions.

Therapeutic uses of antihistamines. The best therapeutic results have been obtained in acute uticaria and seasonal hay fever. In perennial vasomotor rhinitis, chronic urticaria, angioneurotic oedema and allergic reactions to various allergens including drugs, the results of antihistamines are less gratifying. In serum sickness they are of symptomatic value.

For acute anaphylactic reactions the antihistamines are not as effective as adrenaline or the corticosteroids. Antihistamines have failed to benefit patients with bronchial asthma in spite of the undoubted allergic basis of the condition. Again these drugs have not been shown to be of any therapeutic value in the so-called allergic diseases like polyarteritis nodosa, acute rheumatic fever and type I nephritis.

Possible interference with a physiological role of histamine. Histamine is widely distributed in the organism. It is stored in a readily releasable form. Again, Schayer has shown recently that histamine is readily formed evern from tissue free of mast cells in response to stress. He has postulated a microcirculation regulator role for 'inducable' histamine (which is perhaps stretching conclusions too far). Kahlson (1962) has also shown increased production of 'nascent' histamine in rapidly growing tissues, e.g. granulation tissue, tumour cells and rat embryos. Many other observations have forced Kahlson to conclude that 'nascent' histamine formation is an integral part of the metabolism of certain rapidly growing tissues. I find it hard to believe that the presence of histamine in the complicated and homeostatically balanced organism is simply to cause pathological changes. A physiological role for histamine is a very distinct possibility and has to be studied. Blocking the actions of histamine in certain clinical situations may have other dangers and possibly what one gains on the roundabout is lost on the swings.

PART IV — CONCLUDING REMARKS

The immunological basis of the allergic process is undoubtedly proved, but the reaction sequence after antigen-antibody combination is still not clear. Progress has been made in the study of the pharmacological agents thought to be responsible for the allergic symptoms, but here too, there are gaps. Why should the protective action of antigen and antibody combination result in detrimental reactions in certain individuals? Is this due to an inborn error? If so, what is the basic biochemical abnormality that is involved? What is the agent responsible for the propagation of the allergic process once started? The fertile soil of the delayed-type hypersensitivity has not yet been cultivated.

It is estimated that about one person in ten in Great Britain suffers from one kind of allergy. It is also thought that in spite of individual susceptibility anyone is liable to develop a type of hypersensitivity reaction if exposed to the antigen for a certain time. Allergic reactions to drugs and antitoxins pose more problems in therapeutics. Many of these considerations given above make a thorough understanding of the allergic process highly desirable.

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RES MEDICA

ABORTIVE LEGISLATION?

For the back-street abortionist business is booming. It is commonly estimated that some 100,000 criminal abortions are performed annually in England and Wales alone. Maternal deaths from these are, according to Goodhart (1964) of the order of 35 per year in England and Wales, giving a surprisingly low maternal mortality of 0.35 per 1,000 which equals maternal mortality from all other causes. Serious maternal morbidity, however, defies estimate but must be alarmingly high. Even in hospital, the operation carries serious risk of complication, which is obviously greatly increased in a tenement kitchen. Cervical incompetence, causing repeated miscarriage, serious infection, especially pelvic peritonitis, and severe anaemia from haemorrhage are but some of the scars which a woman may carry for many years, as a result of such treatment. The scar of the psychological trauma may well be carried for life.

An attempt must obviously be made to put this deplorable situation to rights. Will the proposed reform of the abortion law do this?

Lord Silken's Bill, introduced in the last Parliament, emerged battered from its passage through the Lords, barely recognisable through deletions and amendments only to die a sudden death on the dissolution of Parliament. A modified version will again grind through the legislative cogs of Westminster later this summer. If successful this will certainly clarify the legal position on abortion. It specifies who may perform such an abortion and in what circumstances. Thus an NHS gynaecologist, registrar or above — in agreement with the patient's G.P. — may terminate for the following reasons: if the mother's physical or mental health would be endangered by continuation of the pregnancy; if she were aged under 16 at conception, or mentally defective; or finally if the child would be likely to suffer from a defect which would prevent reasonable enjoyment of life. (Grounds of rape and that the woman would make an inadequate mother were later deleted.)

This attempt at clarification is welcomed by many practitioners for whom the burden of decision is eased. Some, however, consider that the present law (which rests largely on the Bourne case judgement of 1938) allows considerably more freedom. Yet others feel that the change is not liberal enough and should take fuller account of social and economic factors as ground for termination.

In its present form the bill would do little towards eliminating the criminal abortionists. Many of their patients are not those provided for by the bill but physically and mentally healthy women, notably the single girl and the widow, whose pregnancy is looked upon with distaste by Society. For them the law will be effectively unchanged. For them the criminal abortionist will provide the only acceptable solution.

This situation could be improved to some extent by liberalising the law — though not to the extent of "abortion on demand" as practiced in Japan and Czechoslovakia. The Swedish system of a panel considering each case on its merits, including socio-economic factors, has much to commend it.

An even more effective step would be widespread education in the most efficient methods of contraception. Yet even with better contraception unwanted pregnancies will occur. If we are ever to be rid of criminal abortions and their dire sequalae, Society must view the unwelcome pregnancy through more sympathetic eyes.

OVER-PRESCRIPTION

Overprescription of drugs has often been in the news in the light of the Annual Drug Bill, but recently another aspect has become prominent. It concerns the prescription of large quantities of sedatives, anti-depressants and tranquilizers to a population which is increasingly employing them for self-poisoning rather than as remedial agents.

Unfortunately the people who are most likely to use these drugs for self-poisoning are those to whom large quantities are given — the depressed and the unstable. Surely it is time that other methods of making these drugs available were used. Kessel has already made this appeal in a recent article in the B.M.J. and Res Medica.

Could not greater control over prescriptions

be exerted? A weekly 'recurring' prescription requiring a weekly 'cancelling' signature from the pharmacist would limit the number of tablets issued at one time and incur no extra work for the GP. The wider use of emetic charged barbiturates might be a worthy investment of the extra cost and more widespread dealing with the dangers of storing old tablets etc. would undoubtedly help. Some measures might be more time consuming for the GP. in that he, as the 'family doctor' has the opportunity to warn of the potential dangers of these drugs; put tablets into the custody of another member of the patient's family when necessary, and deal more thoroughly with psychiatric problems. But it remains the responsibility of the medical profession to consider priorities when discussing this problem.

THE SOCIETY

Office-bearers for the 230th session will be as follows :

Senior President
M. H. KAUFMAN

1st Junior President
R. J. NIXON

2nd Junior President
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House—Miss N. BAKER
Library—M. F. MACNICOL
Museum—J. WALLWORK
Dinner—R. J. NIXON

The Society's first year in Hill Square has been extremely successful in both Public and Private business.

PUBLIC BUSINESS

We have again been fortunate in having many distinguished guest speakers to address us. These included Professor F. J. Gillingham, Dr. W. I. Card, Dr. J. D. Roberston and Dr. Cicely Williams. Guest of honour at the President's dinner was Sir Dugald Baird whose address on some of the more amusing aspects of his career provided one of the highlights of the year. To these, as to all our other guests, we extend once more our thanks and appreciation.

PRIVATE BUSINESS

The Private Business meetings have been described as the most important activity of the Society: this may or may not be true, but certainly they provide an opportunity for every member to be active in discussion. The value of this is twofold; it encourages members to learn to express their ideas in a more confident manner in public, and it is a stimulus to a wider interest in the art and science of medicine.

The meetings of the past session were organised with this in mind. The majority of the meetings were introduced by a brief talk by a member and this was taken as the topic for discussion: topics ranged from "Prematurity" to "Exercise" and included many instructive clinical presentations. In each term two speakers were invited. In the first term Mr. J. Chalmers spoke on "Bone Growth" and Dr. R. A. Cumming on "The Blood Transfusion Service"; and in the second term Dr. M. Gaze spoke on "Micro-electrode Recording From The Human Brain" and Professor D. Whitteridge gave "Some Recollections Of Sir Charles Sherrington".

Essentially, however, Private Business meetings are what members make them: the more members that attend, the more members contribute, the more valuable are the meetings.

REVISION OF LAWS

The Society's Laws have again undergone extensive revision by a committee set up for the purpose. The changes are concerned mainly with technicalities related to the election of office-bearers. One welcome innovation, however, means that members may now entertain guests in the coffee lounge at any time.

SEX CHROMOSOME ABNORMALITIES IN THE MALE

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This article does not set out to give a comprehensive review of sex chromosome abnormalities in Man, nor even in phenotypic males. Its purpose is more to outline a few general principles and show how they apply to one group of individuals with one class of abnormality, namely males with abnormalities of number of either the X chromosome, or the Y chromosome or of both.

Man has 46 chromosomes consisting of 22 pairs of autosomes, which are common to both sexes, and two sex chromosomes an X and a Y. Normal females have two X chromosomes which are morphologically indistinguishable from one another, while males have one X chromosome and one Y chromosome, which are morphologically dissimilar. (Fig. 1, Fig. 2). The main two criteria used in recognition of chromosomes are their length and the position of the centromere or primary constriction. On the basis of these criteria only 4 pairs of autosomes can be recognised with certainty, whilst the others can only be recognised as belonging to one of a number of groups. Some of these groups contain only two pairs of chromosomes, whilst the largest group, consisting of medium sized submetacentric chromosomes, contains as many as seven pairs of autosomes. Unfortunately the X chromosome falls into this category of medium sized submetacentric chromosomes and, therefore, cannot be distinguished morphologically from autosome pairs 6-12. Normal males, therefore, have 15 chromosomes in this group — 14 autosomes and a single X chromosome, while normal females have 16 — 14 autosomes and two X chromosomes.

The Y chromosome, however, is one of the smallest chromosomes in the human complement with its centromere very near one end (acrocentric). It can usually be distinguished from the autosomes that it most closely resembles, those of pairs 21 and 22, by virtue of

the fact that it never has small satellites on its short arms, and also because the constituent chromatids of the Y chromosome tend to be close to one another and are often rather fuzzy in appearance. Little difficulty, therefore, arises when dealing with abnormalities of number of the Y chromosomes as these can be easily recognised. The X chromosome cannot, however, be distinguished morphologically from the autosome pairs 6-12. It is therefore necessary, when deciding whether or not one is dealing with an abnormal number of X chromosomes to consider, as well as the cytogenetic findings, the evidence from three other sources, namely the nuclear sex, the clinical findings and the results of autoradiography undertaken to determine the time at which the chromosomes synthesise DNA.

Nuclear Sex

In a proportion of nuclei of non-dividing cells of normal females there is a small body about 1μ in diameter attached to the nuclear membrane. Such a body is never found in similar nuclei from normal males (Fig. 3). This body was first described by Barr and Bertram in 1949[1] and is, therefore, referred to as the Barr body or sex chromatin body. Individuals having this body are said to be Barr positive or chromatin positive, whilst those in whom it is absent are said to be Barr negative or chromatin negative. There has been much speculation since the first observation of sex chromatin as to its nature, but it is now known that it represents an X chromosome which is in a different state of condensation from the other chromosomes of the cell. While the latter are uncoiled and genetically active, the sex chromatin body consists of the whole, or the greater part, of an X chromosome which is condensed and presumably relatively inactive. It appears that for normal function the cell needs only one X chromosome, and any further X chromosome present is, to a greater or lesser extent, inactive, and represented by a sex chromatin body. Thus the maximum number of sex chromatin bodies is one less than the number of X chromosomes in the cell. Sex chromatin can be seen in the cells of a great many tissues in the body, but it is often studied in cells from the buccal mucosa, because these are very easily obtained. Such studies enable large populations to be screened for their X chromosome status by means of a simple and quick technique. The sex chromatin status of the individual gives valuable information as to the number and, in favourable circumstances, the size of the X chromosome, as abnormalities of size of the X chromosome are reflected in abnormalities of size of the sex chromatin body. It must be emphasised, however, that it gives no information about the Y chromosome. Thus individuals who are lacking a sex chromosome, XO females, and also normal XY males are both chromatin negative, while both XXX females and males with Klinefelter's syndrome and an XXXY sex chromosome complement have two sex chromatin bodies in a proportion of their cells.

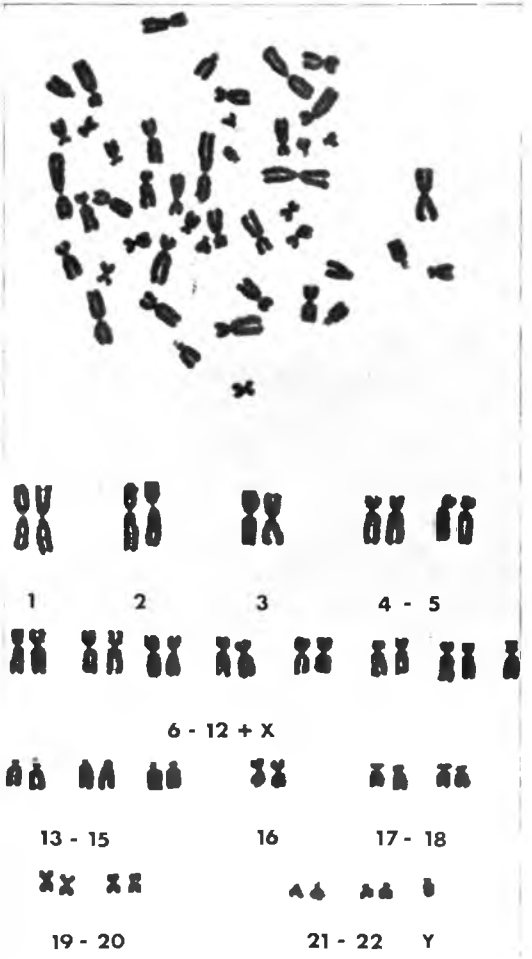

Fig. 1. Cell and Karyotype from a culture of the peripheral blood lymphocytes of a normal male.

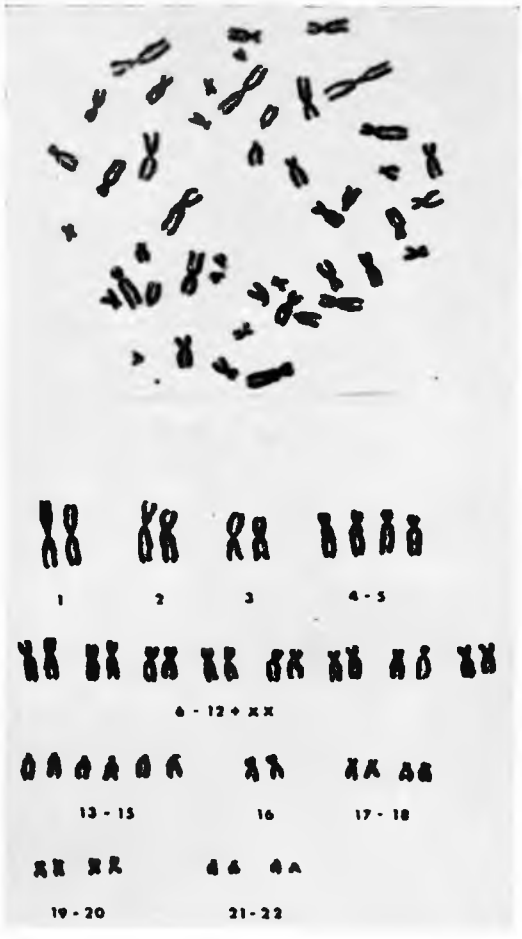

Fig. 2. Cell and Karyotype from a culture of the peripheral blood lymphocytes of a normal female.

Clinical Features

Much work remains to be done on the clinical expression of abnormalities of the chromosomes in man. Yet it is clear that in general, abnormalities of the autosomes give rise to very much more severe and widespread anomalies than abnormalities of the X and Y. Furthermore where there are clinical manifestations of abnormalities of the sex chromosomes these tend to affect mainly the primary and secondary sexual development, though they may also affect the mental development and behaviour of the affected individual. Thus the presence of an additional small autosome in group 21-22 results in the profound disturbance of virtually every system in the body characteristic of mongolism. On the other hand the presence in an individual of an additional Y chromosome, which is of a comparable size, may be associated with no phenotypic abnormalities at all.

Fig. 3. Cell from the buccal mucosa of a normal female showing a single sex chromatin body (Barr body).

Autoradiography

By treating cultures of human cells with tritium labelled thymidine (a specific radioactive precursor of DNA), during the time the chromosomes are duplicating their material prior to division, it can be shown that there is a medium sized submetacentric chromosome in females. This synthesises DNA somewhat out of phase with all the other chromosomes in the cell, in that it both starts and finishes later. No such chromosome is present in cells from normal males. This chromosome is presumed to be the "inactive" X which also forms the sex chromatin body, and it has been shown that the number of late-synthesising X chromosomes is one less than the number of X chromosomes present in the cell. To determine whether such a chromosome or chromosomes are present in the cell tritium-labelled thymidine is usually added to the cultures some three to four hours before harvesting, when the majority of the chromosomes have completed or are in the final stages of synthesis. Single layers of the cells are then prepared on a microscope slide and covered by a layer of photographic emulsion which blackens when suitably exposed to a radio-active source. By this means any chromosome, or chromosome region, which is actively synthesising DNA later in the synthetic period can be recognised (Fig. 4).

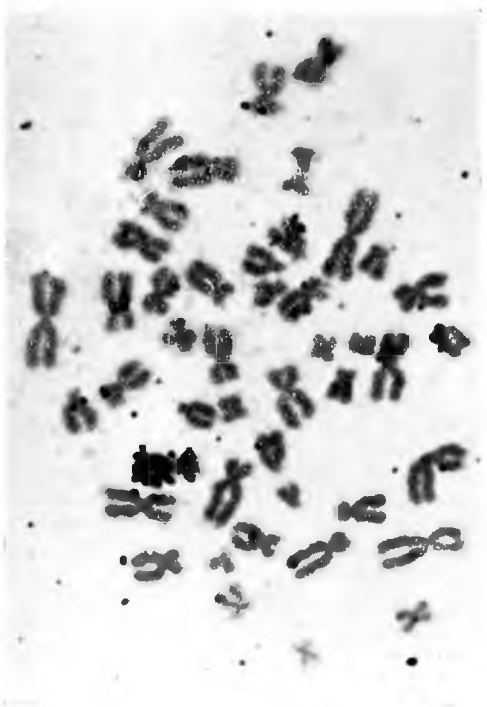

Fig. 4. A normal female cell subsequent to treatment with tritium labelled thymidine which shows one very heavily labelled medium sized submetacentric chromosome.

By way of illustration of how evidence from sex chromatin, clinical findings and autoradiography are correlated with the cytogenetic observations two cases can be considered. From cultures of both skin fibroblasts and peripheral blood leukocytes, both of these were shown to have 47 chromosomes, the additional chromosome being a medium sized submetacentric chromosome indistinguishable from the chromosomes of group 6-12 - X. The first patient was a 28 year old man who presented at a subfertility clinic, his wife having failed to conceive after 5 years of marriage. He was of average intelligence and the only clinical feature of note was the presence of small testes and azoospermia. The cells of his buccal mucosa were chromatin positive and autoradiography showed that he had a medium-sized submetacentric chromosomes which synthesised DNA late in the synthetic period. It was, therefore, concluded that the additional chromosome was an X and the patient an example of Klinefelter's syndrome with an XXY sex chromosome constitution. The second patient was an 8 year old mentally retarded boy who was noted at birth to have a cleft soft palate and who had subsequently been hospitalised on a number of occasions for severe respiratory infections. He also had a number of congenital anomalies, including hypomandibulosis, a sinus on bridge of his nose, abnormal dentition, curious facies and a systolic murmur. Repeated observations on cells from a number of tissues showed him to be chromatin negative and autoradiography did not reveal any chromosome which synthesised DNA out of phase with the others. It was, therefore, concluded that the additional chromosome was not an X chromosome, but was an autosome belonging to group 6-12 and that the patient was trisomic for one of these autosomes.

Abnormalities of the Sex Chromosomes

The more commonly encounted numerical abnormalities of the sex chromosome in males are listed in Table 1, together with the sex chromatin and autoradiographical observations in these individuals. While these are the only abnormalities which will be considered in the present article it must be remembered that abnormalities of structure of both the X and Y chromosomes are encountered which may replace a normal sex chromosome or be additional to them. Furthermore it is very common to find, especially in individuals with abnormalities of the sex chromosomes, that not all the cells of the body have a uniform constitution, but that there are two or more cell lines present which can be distinguished cytogenetically, usually because they differ in their number of chromosomes. One of the cell lines may be normal or all may be abnormal, and the resulting clinical picture depends on the constitution of the constituent cell lines and their relative frequency and distrib-

TABLE 1

Chromosome Constitution	Sex Chromatin	No. of Late Synthesising Medium Sized Chromosomes
XXY	+ve	1
XXXY	++ve	2
XXXXY	+++ve	3
XXYY	+ve	1
XYY	−ve	0

ution in the body, especially in the gonads. Thus an individual who has two cell lines, one with 46 chromosomes and an XXY sex chromosome complement may, if his gonad is largely comprised of XY cells, be clinically indistinguishable from a normal male. Conversely, if his gonad is largely comprised of XXY cells he may be clinically indistinguishable from a "pure" XXY individual.

XXY Males

The presence of a single extra X chromosome is by far the commonest abnormality of the sex chromosome complement found in man. This is associated with the features of seminiferous tubule dysgenesis or Klinefelter's syndrome. These features are somewhat variable but hypogonadism is always present. Before puberty, however, regressive changes take place characterised by marked degeneration and hyalinization of the seminiferous tubules, unusual numbers of Leydig cells and the absence of spermatogenesis. These features may be accompanied by abnormalities of development of the secondary sex characters such as sparse growth of facial hair, female head or body hair distribution and development of breast tissue. Furthermore XXY males tend to be rather tall and eunoichoid in proportion, their leg length being long in relation to their height. The I.Q. of males with an extra X chromosome is on average lower than that of the normal population, such males being found significantly more often in institutions for the mentally defective than in the general population.

XXXY

Males with two additional X chromosomes are much less common than males with a single additional X chromosome. They also exhibit the features of Klinefelter's syndrome but they are much more severely affected. Their testes are very small and the abnormalities of development of the secondary sex characteristics are usually very marked. Furthermore all XXXY individuals so far described have been mentally retarded — the majority of them being found amongst lower grade mental defectives.

XXXXY

Males with three additional X chromosomes are, as expected, even more uncommon and more severely affected than those with two additional X chromosomes. They also show a number of additional congenital abnormalities. Their testes are usually extremely small and often cannot be defined clinically. Some underdevelopment of the penis or scrotum is usually found, sometimes linked with hypospadias, and the degree of underdevelopment of the secondary sex characters is often very marked. There are usually marked skeletal abnormalities present, among them some degree of fusion or synostosis of the ulna and radius. All XXXXY individuals described have been low grade mental defectives.

XXYY

Males with an additional X and an additional Y chromosome are clinically similar to the XXY male. They have small testes and show a similar range of abnormalities of development of the secondary sex characters. They are fairly uncommon, and all those so far described have been mentally defective. There is also some suggestion that they are taller than the XXY males and that they are unusually prone to the development of acromegaly. XXYY males were also found to comprise one third of all chromatin positive males in an institution for criminal and hard to manage mental defectives — a proportion far higher than that found in ordinary mental defective institutions. It has therefore been suggested that the presence of an additional Y chromosome may be a predisposing factor to criminal behaviour[3].

XYY

Until recently relatively little was known about males with one additional Y chromosome. Such individuals seem to be rare and the few cases described in the literature ranged from a normal fertile male examined because one of his children was a mongol, to a number of mentally retarded children with undescended testes. However, no clear picture of the XYY male had emerged, partly because they are indeed rather uncommon and partly because there is no easy way such as nuclear sexing, of recognising them in the population. Recently, however, a chromosome survey of the inmates of a hospital for psychopathic criminals and for criminal and hard to manage mental defectives has been completed

and it was shown that 9 of the 314 men examined had an XYY sex chromosome constitution[3]. Clinical examination of the 9 XYY males showed them to be unremarkable, with apparently normal testes and genitalia.[4] However, they were significantly taller than the other males in the institution — in fact in this particular institution one in three of the males 6 ft. and over in height had an additional Y chromosome. While the frequency of XYY males in the general population is not known there is no doubt that their frequency in this particular group of patients is very much greater than could be expected by chance. This data suggests that the XYY male is a clinically unremarkable tall male, who is unusually predisposed to aggressive and criminal behaviour.

In conclusion it must be remembered that, while some of the more bizarre abnormalities of the sex chromosomes which have been described in this article are extremely rare, chromatin positive males are common. Their incidence at birth is about 2 per thousand, which, if we assume there is no differential mortality, means that there are about 100,000 such individuals in the population of Britain at present. They form about 1% of all male mental defectives and have been shown to comprise over 10% of all azospermic and oligospermic males attending a subfertility clinic[5]. Furthermore there is growing evidence that the presence of an additional Y chromosome may contribute to psycopathic and criminal behaviour. It is, therefore, evident that males with abnormalities of the sex chromosome complement contribute very significantly to human pathology.

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HEADACHE

by Duncan L. Davidson, B.Sc.

From a dissertation read before the Society on February 4th, 1966.

Headache is a symptom which may be a feature of a wide range of conditions, arising not only with pathology in the head but also in cardio-vascular, renal, metabolic, orthopaedic and psychiatric conditions. It is extremely common, and usually transitory. Yet it may be a symptom of great significance in clinical practice. The underlying mechanisms are largely unknown. The explanations of the cause of headaches have a long history, and it is on the actiology of headache that this discussion will centre.

Headache can be a dramatic symptom and presumably has been ever since primitive man drank a fermented juice to excess and had his first hangover, or woke up with his first post-concussional headache to find that his wife had been kidnapped.

The first recorded description of headache comes from the 'Book of Prognoses' which is a series of tablets inscribed by the Physician-Priests of Mesopotamia probably before 2,500 B.C. These writings contain a mixture of clinical observations, which are often very astute, with statements on crude drug therapy, magic and religion.[1] One section on headache has been translated thus:

'when his brow pains a man and he vomits and is sick, his eyes being inflamed, it is the hand of a ghost; then reduce to ashes human bones and bray them; and anoint him with them in cedar oil and he will recover.'

It was serious enough having the 'hand of a ghost' causing these afflictions but worse still

'not only the hand of a ghost but the hatred of a goddess against his life causes a man's right temple to hurt, his right eye to swell and tears to flow.'

While it is clear from the remains of neolithic skulls that trephing was performed at that time, and perhaps more surprising, that patients recovered, the precise indications for trephing are unknown. Perhaps an indirect indication may be considered from the finding that primitive groups in the South Sea Islands were trephing skulls during the last century. Possession by evil spirits was considered the cause of headache, epilepsy and mental disorders; these spirits were released by trephining.

The contribution of Greek medicine to our understanding of headache is the recognition that a particular group of clinical features constitute a distinct entity, the migraine syndrome. No advance in knowledge of the actiology of headache occurred with the Greeks, nor has it occurred until the present era.

Now, in our age of 'scientific enlightenment' we seek a more precise and objective description of the pathophysiological mechanisms than

demon possession, the hands of ghosts, and the hatred of goddesses.

In an article of this length the central mechanisms of pain perception cannot be discussed. Our concern here is with the disturbances which give rise to abnormal patterns of sensory input to the brain, and not with discussion of the fibres involved, the abnormal patterns themselves, and the central interpretation of these changes.

Sources of Headaches

Knowledge of which structures in the head may give rise to pain comes from two main sources. The first of these is the correlation of clinical observations, e.g. an occipital headache, with pathological findings, e.g. an infra-tentorial tumour. The second source is from neuro-surgical operations under local anaesthesia in which records are made of the site of referred pain which is elicited by such crude methods as crushing, stretching, distending, burning and electrically stimulating various structures of the head.[2] There is, however, a great difference between eliciting pain in an operation and demonstrating the mechanisms which operate in the clinically occurring headache. The following results, therefore, are but crude pointers to the sites at which pain may arise. The scalp, as expected, is pain-sensitive while the cranial bones are insensitive. The dura appears to be insensitive to pain-producing stimuli except in the vicinity of arteries, venous sinuses and their tributary veins, and the floor of the anterior and posterior fossae. Pain is particularly easily elicited from the large arteries at the base of the brain. Cranial nerves V, VII, IX and X, all nerves with a sensory component, and also CI, 2 and 3 are pain sensitive. No pain was elicited from the pia and arachnoid mater, the parenchyma of the brain or the linings of the ventricles. As the supra-tentorial dura is innervated by branches from the Trigeminal Nerve, pain arising in this region is usually referred in the distribution of the nerve producing peri-orbital, frontal and temporal headaches. Infra-tentoral disease, on the other hand, is largely referred via Cranial nerves IX and X to the auricular region and via the upper cervical nerves to the occipital region and the upper part of the neck.

The causes of headache have, inevitably, been classified. One simple and useful approach is to consider that headaches may arise in any, or a combination of five general ways;

(1) traction upon intra-cranial structures
(2) intra-cranial inflammation
(3) vascular changes
(4) sustained contraction of scalp and neck muscles
(5) spread of pain from diseases of the eyes, ears, nose and throat.

Traction Upon Intra-Cranial Structures

Headache may occur with expanding intra-cranial lesions whether these be neoplasms, sub-dural or intra-cerebral haematomas, or abscesses. It is almost always a presenting symptom in infra-tentorial lesions presumably because expansion occurs within a confined space in a region which contains a number of pain-sensitive structures. With expansion of the lesion distortion of the normal anatomy occurs, and pain arises from traction on and displacement of nerves and vessels. In supra-tentorial lesions headache occurs as a presenting feature in only about a third of all cases, presumbaly because greater expansion may occur before pressure and traction effects become prominent.

Intra-Cranial Inflammation

The intra-cranial inflammation that occurs in meningitis or sub-arachnoid haemorrhage is associated with severe headaches. The pain probably arises in part from vascular changes presently to be discussed, partly from traction and pressure effects, and perhaps from direct stimulation of nerves by the ill-defined entity 'toxins' and the breakdown products of affected cells.

Diseases of Eyes, Ears, Nose, Throat and Teeth

Diseases of the eyes and orbit, E.N.T. conditions like sinusitis and acute otitis media, as well as dental abscesses may produce pain. In general the pain is at first localised at the site of the lesions, but with progress of the disease process it may radiate in the distribution of the nerve involved.

Headaches of Vascular Origin

The vascular changes which occur in a number of conditions, for example, hypertension, migraine, uraemia, and febrile illnesses appear to be related to the headaches. The subject is perhaps best approached through an experimental model, the headache induced by the intravenous injection of histamine. Within a few seconds of injecting histamine there is a flushing of the skin, hypotension and a rise in C.S.F. pressure. In about 30 seconds the blood and the C.S.F. pressures return to nor-

mal, and it is at this time that the headache begins. It is a bilateral, throbbing headache which usually lasts between 10 and 20 minutes. There is only indirect evidence that the headache is related to intracranial vasodilatation and the evidence is as follows. The oscillations in C.S.F. pressure that are in phase with the arterial pulse are increased during the headache. The headaches are reduced by manoeuvres which reduce the intracranial arterial pressure. The headaches are intensified or diminished by lowering or elevating the C.S.F. pressure respectively.

Wolff has applied these methods to patients with headaches and finds that a number of headaches are altered by these manoeuvres in a similar manner to the histamine induced headaches. This group includes the headaches of uraemia, all the febrile illnesses, post-seizure and post-concussional (in part). As vasodilatation is common to all these states it is commonly stated that dilatation of the vessels, perhaps with stretch of the fine nerve endings in the wall, is the cause of the headache. But it is an inadequate explanation, for it does not recognise that there may be a process which has in common vasodilatation and pain stimulation. Recent work on the headaches of the migraine syndrome suggests that, in migraine, arterial dilatation is only part of the story. And so it may be revealed with further investigation that the headaches due to intracranial vascular changes have mechanisms similar to that in migraine.

The headache in the migraine syndrome is classically a unilateral throbbing headache that may be peri-orbital, frontal, temporal, or occipital. It may last from under half an hour to several hours. But the headache is only part of a syndrome which may be very variable in presentation. In about 15% of patients there may be prodromal symptoms occurring between 20 and 40 minutes before the onset of the headache. These may include a variety of visual changes, such as scintillations, scotomas, or even hemianopia. There may be paraesthesia, ataxia, vertigo, or changes in consciousness or mood.

But what is known of the underlying mechanisms in this condition? When the vessels of the bulbar conjunctiva are directly examined and photographed, arteriolar constriction is found in the prodromal phase. The finding that E.E.G. changes are consistent with focal cerebral ischaemia, and that the prodromata can be reduced or abolished with breathing 10% CO_2 mixtures suggests that arteriolar constriction with areas of cerebral ischaemia may underlie the prodromal phase.

The origin of the headache of migraine in the extra-cranial arteries is suggested by a number of observations. Pain can be reduced or abolished by direct pressure or procainisation of the extra-cranial arteries. Unlike the histamine induced headaches it is unaffected by manoeuvres which alter intra-cranial pressure. During a headache the superficial vessels become tender, painful and surrounded by oedema fluid. Simple measurements with a tambour show increased amplitude of pulsations during the headache. Three changes must be explained during the headache phase; (1) vasodilatation, (2) oedema formation, (3) pain production. What may be implicated as the perpetrator of these changes.

The release of endogenous histamine from a bound form has been considered an unlikely mechanism as the headache differs in its characteristics from a histamine induced headache. Also, the migraine headache is unaffected by anti-histamines in contrast to the reduction in pain that is produced in the rarer, rather bizarre condition 'histaminic cephalgia' or 'cluster headaches'. Recently, however, Schayer[3] using radioactive tracer techniques, has shown the existence of an 'induced' form of histamine, that is unaffected by anti-histamines, and has a longer time course of action than 'bound' histamine. Its precise role is as yet speculative. But histamine cannot yet be dismissed as having no role in the headaches of migraine.

May 5 H.T. or a kinin be a cause of the vascular changes? To investigate this, small quantities of tissue fluid have been aspirated from the vicinity of the temporal arteries during and immediately after the migraine headaches and also in headache-free intervals. These were then compared with the aspirates from normal subjects by a number of pharmacological assay methods.

Chapman[1] claims to have found in the tissue fluid a polypeptide and also an enzyme that, on incubation with plasma, is capable of producing increased quantities of the polypeptide. This polypeptide is similar but not identical to bradykinin, and clearly differs from 5 H.T. The levels during the headache period were on average about 8 times that of normal subjects, and it was stated that the level correlated very well with clinically estimated severity of the headache. Here, of course, is an illustration of one particular difficulty in work on pain — that of estimating the severity of pain and comparing the severity of pain in one person with that

in another. This polypeptide has been labelled 'neurokinin'. While it does fulfil our three criteria, those of vasodilatation, increased permeability with oedema formation, and pain production, this work is rather tentative. It may be that the improved methods of separation and characterisation of the kinins involved will throw more light on the subject. It may become evident that a multi-factorial mechanism is responsible for the headache. It must also be pointed out that no progress has been made on the questions of what initiates the whole process, why the headache should be unilateral, and why the changes should occur only in the external carotid vessels? The autonomic changes which may occur in association with the headache are varied; there may be lacrimation, bradycardia, sweating, nasal congestion, constipation (or even diarrhoea). It may eventually be shown that the migraine syndrome takes origin in a disturbance of autonomic function.

The headaches of hypertension, on the same evidence as in migraine, appear to originate in changes in the extra-cranial arteries. The headaches do not, however, relate directly to the level of the blood pressure except during acute attacks. The fact that the arterial pressure is elevated throughout the body, but only the extra-cranial vessels become painful suggests that there may be some intrinsic difference in the extra-cranial arteries that renders them liable to develop pain. Little work has been done on the headache in hypertension so that it is only an interesting speculation that the mechanisms may be similar to those of migraine.

Muscle-tension Headache

The other common chronic headache, a cause of distress to thousands of patients, is one which often arises in relation to stress or anxiety and is called a 'tension' or 'muscle-tension' headache. Its characteristics are that it is non-pulsatile, fairly constant in intensity, being a dull ache rather than an acute pain. Patients describe it variously as a 'tight band' or cap or as an oppressive pain on the top of the head. Often it is bilateral in the occipital region, extending into the neck, but it may vary and be either unilateral or bilateral, and may occur in the frontal or parietal areas. It may occur primarily in a neurotic type of reaction or in anxiety producing situations, but it may arise secondary to pain elsewhere, e.g. migraine, or secondary to degenerative changes in the cervical spine.

The term 'muscle-tension' headache has evolved because one feature of the headache is a sustained contraction of the occipito-frontalis, temporalis or the muscles of the neck. E.M.G. recordings from these muscles showed increased activity during the headache periods which was approximately related to the 'clinical anxiety level' (again a very subjective and unreliable estimation). There is, however, another factor besides increased muscular activity, and this is the observation that arteriolar constriction occurs in the bulbar conjunctive during the headaches. As the headaches are intensified by vasoconstrictors and relieved by vasodilator drugs it is reasonable to infer that constriction may be occurring in the vessels of the active muscles and that this contributes to the headache. Presumably, therefore, headache arises from a combination of ischaemia due to vasoconstriction and increased metabolism of sustained muscular contraction.

Conclusion

Headaches are often trivial and transitory and as such tend to be ignored clinically. But they are important in two ways. Firstly, the chronic, recurring headaches cause considerable misery in the community. Secondly, headaches may be of great clinical significance, for example in hypertension and in intra-cranial tumours. The explanation of the causes of these headaches have varied through the ages, and even now ideas change as information increases. Some current ideas have been outlined in this article. As knowledge increases in the future so should the treatment of the underlying causes improve.

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BOOK REVIEWS

CALLING THE LABORATORY. Editor: W. A. R. Thompson, M.D. 2nd edition. E. & S. Livingstone, Ltd. 1966. 17/6d. pp. 126.

This book, although designed for use by general practitioners, will fill a long-felt need of both students and hospital staff.

It gives a brief outline of the various laboratory tests commonly in use today, with an explanation of the indications for such tests, and the principles and methods underlying them. Perhaps most useful of all, and certainly most practical, it tells doctors the correct way in which to present the specimen under test to the laboratory — surely a sore bone of contention between doctor and laboratory for many years.

As a practical review of laboratory tests it is admirable, and fully recommended. Its title and cover illustration, however, could well be improved.

D.B.

GLAUCOMA: EPIDEMIOLOGY, DIAGNOSIS AND SOME ASPECTS OF TREATMENT. Proceedings of a symposium held at the Royal College of Surgeons of England 1965.

The practical difficulties in mass screening of the population to detect unsuspected glaucoma in its early stages are enormous. This is especially so if one realises that "suspects", when discovered, constitute about 10% of the population and that further investigation of these will lead to discovery of the disease in about 1%. Unfortunately the problem does not end there.

This small thought-provoking volume will be of interest to ophthalmologists and those specially interested in glaucoma. It contains the result of 4 glaucoma screening programmes, as well as 2 studies of close relatives of glaucoma patients. A further portion is devoted to problems of epidemiology and difficulties in recommending and assessing surgical and medical treatment. The symposium ends with a critical review of methods of detecting glaucoma.

Not a recommended buy for the student unless he, for better or worse, wishes to complicate his thoughts on glaucoma.

B.C.

TEXTBOOK OF MEDICAL TREATMENT. Edited by Sir Derrick Dunlop and Stanley Alstead. 10th edition. E. & S. Livingstone, Ltd. 1966. 70s. pp. 1003.

Since is conception in 1939 this text book has consistently proved one of the most popular of its kind, both in this country and overseas. The 10th edition will certainly be no exception. The authors, all clinical teachers from the Scottish Medical schools, have again produced a text which is both authoritative and comprehensive. The treatment of most conditions likely to be encountered in any branch of Medical practice is set out clearly, and with humbling attention to detail. In fields where controversy exists, such as anticoagulants, steroids and certain antibiotic regimes, full and fair consideration is given to all views. Where, on the other hand, a well-proven treatment is advocated, the authors do not hesitate to be dogmatic.

One refreshing feature throughout the book is the presentation of therapeutics not as a mere exercise in applied pharmacology but as treatment of "the whole Man" with due regard being paid to nursing care, diet, exercise, mental welfare and rehabilitation. Metric measures and official drug names are used throughout in an attempt to make the present pharmaceutical Tower of Babel a little less bewildering.

Like its predecessors this edition will surely remain the safe and complete guide to medical treatment for students and practitioners alike.

I.C.M.

A GUIDE TO CARDIOLOGY. By J. C. Leonard and E. G. Galea. 2nd edition. E. & S. Livingstone, Ltd. 1966. pp. 306.

Cardiologists seem to delight in writing short volumes for students, young doctors and General Practitioners. These books carry explanatory titles such as 'Essentials', 'A Clinical Introduction', 'A Primer', and 'An Approach'. And now there is the second edition of 'A Guide to Cardiology'.

In the Preface to the First Edition the authors said that the "emphasis throughout has been placed on the clinical features, diagnosis and treatment of the commoner diseases of the heart." This indeed has been done. The book is modern in outlook and up to date in most details. The text is perhaps rather fuller than that required by most medical students, but is written in a straight-forward manner. It is well illustrated by X-rays and electrocardiographs. After comparing this book with others of its kind, it emerges as the best in its field at the present time.

D.L.W.D.

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