

STUDY OF AUTONOMIC FUNCTIONS IN LEPROSY WITH SPECIAL REFERENCE TO DRUGS

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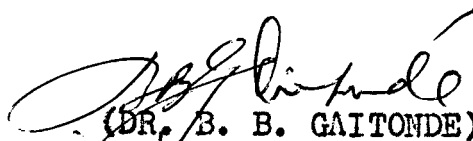
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This is to certify that Dr. V.R.Dabholkar M.B.B.S. has carried out the work on '' A STUDY OF AUTONOMIC FUNCTIONS IN LEPROSY WITH SPECIAL REFERENCE TO DRUGS'' under my guidance and direction at Haffkine Institute and to my satisfaction.



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* INTRODUCTION *

I N T R O D U C T I O N

Leprosy is one of the most crippling diseases that one encounters particularly in tropics. It is the disease with the longest incubation period ranging from 3 months to 3 years. It is so insidious in its onset that its manifestations become hardly perceptible till it invades the organism to a significant extent.

It has been mentioned in Sushruta Samhita as Kushtha Rog. It is evident from the history that the origin of it lies in the continent of Africa. Then it spread to Far East. Later on it spread to America and finally it entered in Europe too.

It has been mentioned in Sushruta Samhita (600 B.C.) that the disease was then well known by the name Kushtha Rog. It was then treated by Chaulmugra Oil which was called as at that time by the name Tuvarka. In Manu Smriti the disease is distinguished from Leukoderma. A reference of Leprosy occurs in Atharva Veda.

In Egypt the disease was prevalent as far as back as 1400-1300 B.C. It has been mentioned in Ebers Papyrus in 1555 B.C. by the name of Uchedu.

In China the disease was evident in 600 B.C. It has been mentioned in Chao's Anthology in 7th century A. D. In China Leprosy is called Tai-Fung. Even China during those days Chaulmugra Oil

was the only remedy till 14th century.

The disease further spread to Asia Minor and then it migrated to Greece some time in 350 B.C. From Greece it started its spread to other countries like Denmark, Germany, Germany, France, Great Britain and Italy. The spread of the disease was chiefly due to malnourishment lack of sanitation and poverty as it can be seen that the entity called Leprosy was only known after 13th century.

It is interesting to know that the evolution of Leprosy was documented in Old Testament as Zarath and in New Testament as Lepra. Even during those days preventive measures like that of quarantine was observed at least in Arabia. The quarantine was then called as Juzam.

Lastly it did invade the continent of North and South America. In those continents the disease is hardly in existence today, as it was eradicated as rapidly as it spread.

Perhaps the only continent is Australia where this disease has not reached as yet.

Statistically (Dharmendra 1967, J.E. Park 1972) it is noted that there are in all 5 million cases of Leprosy in the whole world. But about 95% of the cases are distributed in Asia and Africa.

The major foci are in India, China, and Africa where 1 million cases are distributed in each of those areas. In a recent survey it has been observed that the prevalence of Leprosy in India is 5 per 1,000 population.

According to latest information a survey done by Ganapati et.al.(1975) in school children in Bombay has shown that the prevalence rate in some schools is as high as 10.8/1,000 being maximum at Khar-khari village and Mahim-Dharavi areas. Further, it is the least in Vikhroli-Park side and Colaba-Sassoon Dock side. The prevalence is highest among 14-16 years of age and it is more in males than in females. It is the highest in Kanada, Tamil and Marathi speaking community and least in Sindhi community. It is to be noted that the incidence of this disease is highest in South than in Punjab.

From the overall observation it can be seen that lack of education, dense population, humid climate and undernourished conditions are the predisposing factors in Leprosy.

Aetiology of Leprosy: In olden days Leprosy was thought to be inherited, as it was found in families. The strongest supporter of this theory was the well known leprologist called Danielssen. Later on it was discarded when Henson, another leprologist discovered and identified the causative organism a bacillus called *Mycobacterium Lepae*. Sir Jonathan Hutchison had postulated a fish theory in which eating fish with or without milk and eating putrified fish were thought to be causative agents.

In 1871-74 it was confirmed that the disease is definitely caused by Mycobacterium Leprae, thanks to the brilliant work in the field by Hansen of Norway.

Clinical Classification: Sushruta, in ancient times classified Leprosy into three varieties as Vata-Rakta, Vata-Shonita and Arun-Kushtha. The term Vata-Rakta denotes the disease with sensory changes which resembles polyneuritic form of modern classification. While Vata-Shonita is with deformities. Arun-Kushtha is a form in which there are skin lesions which resembles Lepromatous. It is further divided into one with ulceration and the other where prominent symptoms are sensory changes, which is similar to maculo-anaesthetic. Later on Danielson and Boeck (1847) divided Leprosy into nodular and anaesthetic forms. This classification is called pre-Manilla Classification. Further Hansen and Looft (1894) divided the disease into Tubercous (Nodular) and Maculoanaesthetic. Neisser (1903) described this disease under three forms Lepra Tuberosa, Cutanae and Nervorum. Jadassohn (1905) and Darrier (1923) followed this classification and used the term tuberculoid. Rogers and Muir (1925) described it as 'A' for neuroanaesthetically positive but Bacteriologically negative. 'B' for Bacteriologically positive and 'BA' for Bacteriologically positive with secondary neural lesions.

Manila classification was the first internationally accepted classification where it was designed in 1931 and divided Leprosy into Cutaneous, Neural and Mixed.

Later on in Cairo (1938) the International Leprosy Congress adopted a classification where the disease was divided into Neuromacular simple, Neuromacular Tuberculoid and Neuro-anaesthetic. Further, in Rio-de-Janeiro the second pan american conference divided Leprosy into Lepromatous, Uncharacteristic and Tuberculoid and these three groups were further divided into various sub-types. In 1948 Havana Classification modified the American one replacing the term Uncharacteristic into Indeterminate.

Although these are the important classifications there are several others which are of minor importance.

At present there are two modern classifications of Leprosy. One is called as Indian Classification and the other one is that of Ridley's Classification which is based on histology of Leprosy lesion

The Clinical Manifestations of the Disease.: Clinically Leprosy can be distinguished into Polyneuritic, Maculoanaesthetic , Tuberculoid and Lepromatous as per Indian Classification.

Polyneuritic: In this type there is a predominance of sensory nerve's affection than that of motor and can thus be differentiated from

other types of polyneuritis. The nerves commonly affected are Ulnar, Lateral and Medial Popliteal and some times Facial and Trigeminal Nerves too. The Median Nerve is seldom affected. The lesion produces loss of temperature, pain, light touch in that order. The sensation of pain on deep pressure is hardly affected. The motor changes migrate from distal to proximal end and it produces lower motor neuron type of lesions, giving rise to hypotonia areflexia etc. It is also accompanied by trophic changes like wasting of muscles, diminution or suppression of sweating, glossy skin with loss of hair, decalcification and gradual atrophy of bones.

Thus a predominantly sensory polyneuritis without acid fast bacilli in the skin but positive nerve biopsy for bacilli characterise the type called as polyneuritic. The lepromin test is mostly variable.

Maculoanaesthetic :As name suggests it can be defined as a patch which is in level with the rest of the skin with anaesthesia. Here the lesion lies almost exclusively in the skin of face, trunk and extremities in that order. It is worth noting that the lesion in quiet a good number of cases occur on covered parts of the body especially on buttocks. The patches are hypo-pigmented but not apigmented as in Leucoderma. They are in flush with the skin and are anaesthetic.

The loss of sensation being first of that of temperature, pain and lastly touch with or without deep pressure. The lesions are scattered and may be unilateral, quite a few have smooth glossy surface. In this type acid fast bacilli may or may not be present and if present they will be only plus one. The involvement of nerves is minimal and can be hardly detected.

Tuberculoid: This form draws attention even when a lay man sees it as typical raised elevated and rough lesion with loss of sensation as a distinguishing character. The lesions are variably distributed all over the body. The surface is dry, the margins are very well defined with firm consistency. It can be further divided into major and minor depending on the severity. The above mentioned typical tuberculoid patch has to be accompanied by anaesthesia to prove itself as a case of tuberculoid. Usually the nerves if at all thickened are towards and near the site of the patch. The lepromin test is positive and acid fast bacilli are usually absent or only 1 plus.

Thus to summarise Maculoanaesthetic is self explanatory, tuberculoid as raised patches accompanied by loss of sensation and polyneuritis typified by neuritis of sensory type are the three different forms of the predominantly neuritic type of Leprosy as compared to that of opposite end of the spectrum.

Lepromatous: The typical of this lesion is a leonine facies. This type is qualified by thick, red, shiny, diffuse infiltrative type of lesion with or without loss of sensation. Further, it is

invariably positive for acid fast bacilli. The lesions are usually symmetrical and diffuse. A variant of it is called as Lucio type, in which it is accompanied by polyneuritic changes also. Thirdly a type only recently introduced called as Histoid is further accentuated by nodular lesion filled with dense collagenous tissue developed from spindle cells.

Borderline: This type lies between the tuberculoid and lepromatous end of the spectrum. The type is an indeterminate form between tuberculoid and lepromatous. Nothing typical is of it except perhaps circular and /or annular lesions with only peripheral loss of sensation.

Indeterminate: This is a very vague term and the diagnosis is perhaps conclusive when it has progressed from its indeterminate form to either tuberculoid or lepromatous.

Erythema Nodosum Leprosum (E. N. L.): This reaction occurs only in lepromatous form while similar reaction can also occur although rare in other types. This can be precipitated by drug therapy of D.D.S. or D.A.D.D.S. Therapy with other drugs only rarely gives this form of reaction. There are various views about it but the recent trend is to accept it as an immunological phenomenon occurring due to either unknown factors or due to the rapid

lysis of bacilli. The reaction if present for long time may produce complications particularly neurological. Similar but less fulminant reaction also occurs in other types of Leprosy.

Autonomic Nervous System: (A.N.S.): It is also known as vegetative, visceral or involuntary nervous system. It regulates the functions of Heart, Blood vessels, glands and smooth muscles all throughout the body. The word autonomic is used for two reasons: 1) The ganglia of this system are situated outside the central nervous system 2) Many of the organs innervated by this system have spontaneous activity independent of its innervation. In intact animals the activities of this system are co-ordinated with the somatic nervous system. For example : Rise in pulse rate is accompanied by physical or mental exertion.

Essentially it consists of two complimentary sub-parts of it. Parasympathetic and Sympathetic. In sympathetic system the mediator is nor-adrenaline at post synaptic nerve endings except at that of sweat glands, which are predominantly cholinergic while parasympathetic post ganglionic nerve endings liberate acetylcholine as a neurohumoral transmitter and 5-H.Tat some of the nerve endings too. All the preganglionic nerve endings liberate acetylcholine.

Parasympathetic reactions are generally discrete while sympathetic participates in mass reactions. Parasympathetic

activity results in the conservation of body energies, while symphathetic one results in the dissipation of body energies.

Regulation of Innervated Organs:

Eye: The parasympathetic nerve's stimulation causes constriction of the muscle called as constrictor pupillae which results in miosis. It also causes contraction of ciliary muscles. While symphathetic nerve stimulation causes dilatation of pupils called as mydriasis.

Heart: The parasympathetic stimulation by vagus nerve causes slowing of heart rate and decreased in force of contraction of myocardium. While symphathetic nerve stimulation via plexuses causes rise in blood pressure and increased or decreased in the heart rate. The increase in heart rate is more frequent than the decrease.

Blood Vessels: The parasympathetic stimulation causes dilatation of blood vessels while symphathetic stimulation causes constriction of the vessels. The symphathetic tone is dominant than the parasympathetic.

Sweat Glands: The symphathetic cholinergic nerve stimulation causes secretion of sweat by the sweat glands while parasympathetic nerves do not supply the sweat glands at all. Adrenaline when injected also causes sweat but sometimes only.

The extirpation of Sympathetic system results in derrangement of the control of the body like temperature regulation, fight or flight response etc. But this system is not essential to the body. While total extirpation of the parasympathetic counterpart may endanger the survival.

Regulationn of Heart:The cardio-inhibitory centre i.e. dorsal vagal nucleus gives rise to the nerve fibres which pass along the vagus nerve and end in the cardiac ganglion in the superficial cardiac plexus. From there the nerves pass to the heart at S.A. node, A. V. Node and all the portions of the atria and the base of the ventriclès. Vagus nerve does not supply the apical portion of the ventricle.

The Vaso-Motor-Centre(V.M.C.) and Dorsal Vagal Nucleus is connected with the carotid and aortic sinuses via glossopharyngeal nerve for the former and vagus nerve for the later. These are called as baro-receptors or presso-receptors. Increase in pressure due to systole stretches the nerve endings which lie in the tunica adventitia of these structures and carry the inhibitory impulses to the V.M.C. and stimulatory to the cardio-inhibitory centre, as a result the heart rate and the blood pressure is regulated. In addition inspiration increases the heart rate and blood pressure while expiration results in the reverse. This is achieved by the impulse firing from the respiratory center to the V.M.C. and Cardio-inhibitory centre.

In addition baroreceptors are also present along the common carotid, at the origin of the right subclavian, atria and other minor structures.

The symphathetic nervous system supplies all the portion of the heart and its fibres originate from thoracic segments of the spinal cord. The final symphathetic control is by hypothalamus and cerebral cortex.

Regulation of the tone of the blood vessels: The blood vessel's tone is predominantly at the arterioles and the capillaries. These structures are innervated by symphathetic outflow which comes from thoraco-lumbar symphathetic chain.

Pathophysiological Changes in Autonomic Nerves: The process of degeneration and regeneration in the autonomic system are similar to that in peripheral nervous system. Degeneration is the process of pathological changes which lead to abnormal physiological changes elicited by stimuli like pressure, extremes of temperature changes, trauma due to poison like lathyrism or polio-myelitis and perhaps Leprosy. The degeneration starts in the distal stump predominantly and also ⁱⁿ the proximal stump to a lesser extent. The changes start within seconds after the lesion but becomes appreciable within twenty four hours. At first the axoplasm splits into pieces and finally within a span of 8-10 days it turns into a

mucilagenous mass. The myelin sheath when present turns into fat droplets within 8-10 days time and thus ultimately the fibres dwindle off. The regeneration starts after 21 days from the beginning of the process of degeneration by the proliferation of Schwann cells to the extent of 1 m.m. in length per day. Thus the tunnel is created connecting the two cut ends and neurilemmal tube so formed is filled in by the axoplasm and thus the nerve regenerates.

Local Axon Reflexes: Most of the reflexes in the body either pass through the spinal cord or the rest of the central nervous system or both but there are certain reflexes like Histamine triple response which are not passed through them. These reflexes are mediated by the local stimulation of the nerve which releases neurohumour at the effector site and thus results in the response. There are cutaneous sensory nerves which carry impulses of pain and itch towards dorsal nerve cells. These nerve fibres give rise to collaterals along their course and these collaterals end on the arterioles. Stimulation of the path by stroking the skin results in the conduction of impulse along these path and end in the release of Histamine at the effector cells of the arterioles. Further, series of triple response appear. The denervation results in loss of flare.

Sweat Glands: Sweat glands are of two types, eccrine and apocrine but majority of them are of eccrine type. The sweat so produced may be due to emotions, when seen particularly on palms and

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soles of the hands and feet. While the thermogenic sweat is distributed on the forehead, arms and thighs. The sweat can also be produced by neurochemicals, like Carbachol or Acetylcholine.

The sweat glands are supplied by sympathetic nerve fibres which are cholinergic as they release acetylcholine instead of nor-adrenaline on stimulation. The receptor at the sweat gland surface also responds to exogenously injected acetylcholine or like substances. The adrenergic sweat stimulation is not always positive.

Cold Pressor Test: The method of this test will be described in the chapter on Materials and Methods. Here the physiology of this test is described.

The afferent impulses of cold are perceived by the organs of Krause's end bulb of the hand deeped in the cold water maintained at a temperature of $0-2^{\circ}$ C. These impulses are carried by the afferent nerves present in the mixed somatic nerves to the dorsal root ganglion and further to dorsal spinothalamic tract. This tract carries those impulses to thalamus and then these impulses are finally relayed to hypothalamus and cerebral cortex. In cold pressor test it is the hypothalamus which is of concern for the blood pressure changes.

The hypothalamus releases its impulses from its dorsal nucleus

through its efferent limbs and these impulses pass down the spinal cord via midbrain and medulla to end in lateral horn of the spinal cord. Further, the grey lateral horn of the spinal cord gives rise to sympathetic pre-ganglionic nerve fibres which end in the respective para-vertebral ganglia and they give rise to post-ganglionic fibres to end at the blood vessels and heart. The impulses are carried along this pathway. The mediator is nor-adrenaline.

Secondly there is dilatation of capillaries and constriction of arterioles of hand deeped in water and release of adrenaline from adrenal medulla in response to cold. Further, there is a constriction of thoroughfare channels performing arterio-venous anastomoses which raises the diastolic pressure.

Lastly the sensation of cold is also carried away by the cool blood reaching to the heart and thus provoking the response.

The combined effect of these factors is a rise in blood pressure in both systolic as well as in diastolic with shortening of pulse pressure and variable change in pulse rate. The blood pressure change is predominantly dependent on the reflex arc and the breach of reflex arc will abolish the reflex.

Valsalva's Manoeuvre: Valsalva's Manoeuvre is performed in

daily life very inadvertently as in the act of defaecation, lifting heavy weights or even a long stretched yawn. In general this manoeuvre is performed in cases where there is straining against closed glottis. Professional trumpet blowers and aviation people and some of the Yogic exercises are nothing but the Valsalva's Manoeuvre.

This manoeuvre first causes an increase in the intrathoracic pressure which causes a rise in systolic and diastolic pressure with shortening of pulse pressure. In the next stage the intrathoracic pressure is so raised that it impedes the venous return of the heart and thus there is decreased venous return and fall in arterial blood pressure for few seconds followed by rise in pressure due to reflex vaso-constriction and tachycardia due to removal of stimulation of baroreceptors as there is impedance to arterial blood flow at this stage.

The third phase comes where there is release of pressure which results in the sudden gush of blood in the ventricles and the blood pressure falls. But in the next stage which is the last stage there is increased ventricular feeling to increase the cardiac output and thus stimulation of carotid sinus and aortic baroreceptors giving rise to bradycardia.

These various responses to the manoeuver are determined partly by mechanical changes in the thoracic cage and partly by the way of baroreceptors stimulation. This test shows the sensitivity of baroreceptors to the fluctuations in the intrathoracic pressure. The real crux of Valsalva's Manoeuver is the bradycardia observed in the last stage.

*
* L I T E R A T U R E *
* R E V I E W *
*

SWEAT FUNCTION TEST.

In 1889 Father Joseph Damien de Veuster was the first to note the absence of sweat at his own macule of Leprosy.

In 1930 Dr. E. Muir of Calcutta had modified the needle designed by the Phillipines Medical Service. The needle so modified was used by the author. The needle consisted of only 2 m.m. in length so that it entered only in the intradermal layer when injected with an acute angle. The needle so designed was used to test sweat function and it produces safer results than otherwise.

Further, the controversy was going on for a long time about the mechanism of sweat function and piloerection. In 1940 J.M. Coon and Stephen Rothman studied the phenomenon of this function on dead cats and human beings. They found that piloerection response produced by epinephrine lasts for about 1/2 an hour while that by acetylcholine lasts for few minutes in humans. Similarly it was tried on cat's tail and found that piloerection is present for 10 minutes on death after epinephrine and it can be elicited 5 minutes on death after acetylcholine. Atropine did not antagonise, while ergotamine abolished the response to acetylcholine. All this evidence was in favour of nicotinic action of acetylcholine. The local anaesthetics like cocaine and procaine inhibit pilo-motor erection at a concentration lesser than that needed for anaesthesia. Further, blocking of a nerve say for example radial do not have any effect on piloerection.

Further, it was found by Bruck that the action of acetylcholine is nicotinic on piloerection. In smaller doses it produces piloerection while in higher doses it depresses.

To substantiate further, Kolliker has elicited pilomotor erection in man 72 minutes after the death by electrical stimulation. It was found that the sweating can be abolished by atropine but not piloerection. To be brief in conclusion it is reported that the nerve fibres which are sweat producing are muscarinic while those producing piloerection are nicotinic.

In addition to above J.M. Coon and Stephen Rothman (1941) studied the sweat response to drugs with nicotine like action. It has been found that sweat is produced due to muscarinic as well as by nicotinic actions. The acetylcholine induced sweat occurs by activation of both the types of receptors. It is noted that pilocarpine acts directly on the sweat glands.

Further, in cat's foot pad the injection of saline produced sweat but it was considerably less than that produced by the injection of nicotine. The response of sweat to nicotine was abolished by previous injection of local anaesthetic. The sweat response to nicotine disappears after nerve section. Atropine abolishes sweat response but not the pilomotor response. They concluded that the smaller the diameter of the nerve fibre the greater is its sensitivity. It is postulated that the sweat gland response is produced

by local axon reflex mechanisms. The sweat gland's receptors behave as a ganglion.

Further, Arnold in 1948 showed that sweat is absent in oval hypopigmented facial macules of so called 'Achromia Parasitica'. Histologically such patients do not show any signs of Leprosy but the great majority of such patches disappear after the external application of either ammoniated mercury or White's crude coal tar paste.

Dr. Felix Cinreas of Spain (1949) has studied the utility of sweat function test in the diagnosis of Leprosy. He concluded that the old pilocarpine test suggests that in tuberculoid Leprosy the test shows anhydrosis of the macules and the persistent sweating in the healthy regions but the author believes that better results are obtained with histamine triple response. In Lepromatous Leprosy sweating disturbances are more extended than the anaesthesia.

In 1949 Dr. J. Bedizoso Crucet developed upon sweat function test and histamine triple response test. He used formic acid to elicit itching in normal persons. In Leprosy patient's this itching phenomenon is absent at the site of skin lesion. The response is normal in normal, unaffected skin. This test has an advantage in that it can be elicited even in dark skin.

Harry L. Arnold (1949) studied the sweat function in Leprosy. He found the following findings. He found that there is anhydrosis in the skin whose nerve supply have been denervated. This can happen in both types of Leprosy cases i.e. Tuberculoid and Lepromatous. The anhydrosis frequently precedes thermal, tactile, and pin-prick anaesthesia. This anhydrosis probably occurs at the same time at which histamine test becomes capable of demonstrating nerve damage. Further, Arnold used the following method. He used 1% acetylcholine which when injected produced sweat with fleeting goose flesh. The sweat is visualised by Minor's method which consists of painting the skin with 2% Iodine and 10% Castor oil in absolute alcohol before injection of acetylcholine. The dusting is made with powdered starch afterwards. Each droplet appears blue or black spot.

Further, both sweating and goose flesh are absent with in the areas of Leprosy macule and will help in differentiating vitiligo, tinea versicular and alopecia areata. But sometimes the test is false positive, as in achromia parasitica. It has one striking advantage over histamine test in that it can be produced even in dark skin people.

Later on in 1952 T.M. Chalmers and C.A. Keele studied the nervous and chemical control of sweating. They found that heating the body leads to profuse sweating which is most marked on forehead, dorsum of hand, chest and neck while emotional sweating is most profuse on palms and soles. This type is also called as emotional

sensory sweating. The emotional sweating can also occur in axilla. The thermal sweating is controlled by anterior hypothalamic nuclei. The emotional sweating is probably governed by centres in the cerebral cortex. Further, the relay of these pathways occur along the descending tract and via thoracic and lumbar segments of spinal cord by its sympathetic outflow. These fibres function independently after the section of cord and sweat profusely. This is called as mass reflex response. The sweat glands are finally innervated by post ganglionic sympathetic fibres. Coon and Rothman has stated that locally injected acetylcholine may stimulate sweat glands by two mechanisms: 1. A direct muscarinic like action on the sweat glands 2. A nicotine like action on nerve endings causing sweating due to axon reflex. It has been found that there is no significant difference between males and females.

Further, during hot weather the response to acetylcholine is increased. The cholinesterase inhibitors induce the reduction in the threshold of sweat glands by inhibiting the destruction of acetylcholine and thus increasing its concentration. While atropine blocks the cholinergic muscarinic receptors for acetylcholine. Hyaluronidase increases the area of sweating. Further, they had found that preganglionic sympathetic denervation does not change the response to sweat. Post-ganglionic sympathetic denervation reduces the response and this is peculiar finding as there is ^{no} denervation supersensitivity, to administered acetylcholine. It has been

shown that in horses the injection of adrenaline induces sweat but in cat it is not so instead it is the acetylcholine which induces sweat.

It has been found that in man adrenaline can also produce sweat by its direct action on sweat glands which is not blocked by atropine but by tolazoline. But the thermal sweat response is not blocked by tolazoline. Thus thermal sweating is actively due to cholinergic transmitters. The same thing holds good for emotional sweating. Thus although the sweat glands which are involved in emotional and thermal sweating are stimulated by adrenaline or nor-adrenaline to produce sweat, normally catecholamines are not the transmitters. Lastly ganglionic blocking drugs may reduce hyperhidrosis.

In 1953 Harry L. Arnold studied the pilomotor response to intradermally injected nicotine. Further, the author has said that this can aid in diagnosis of Leprosy. He injected 0.1ml of 1:50,000 or 1: 1,00,000 of nicotine picrate solution. The drug nicotine was more reliable than acetylcholine in producing piloerection. It has been found and concluded that the absence of sweat or piloerection does not suggest anything while a normal pilomotor or sweat response eliminate the possibility of Leprosy.

Stephen and Rothman had suggested the mechanism of axon reflex.

The sweat glands are innervated by post-ganglionic sympathetic cholinergic nerve fibres the collaterals of which supply the skin overlying the sweat glands. The injection of cholinomimetic drugs in the skin causes stimulation of the nerve endings of the skin which carries impulses to the collaterals supplying the sweat glands. Secondly the drug also does act on the receptor of the sweat glands per-se. Post-ganglionic denervation inhibits this conduction of impulse and thus abolishes the response.

In 1961 W.C.Lobitz and R.L. Bobsen studied the structure and function of eccrine sweat glands. They found that 1. The sweat gland undergoes certain changes during the process of sweating. 2. Its function is dependent upon internal conditions of the body and external environment 3. Interpretation of the function of sweat gland is considerably influenced by the method of sweat collection, the area from which the sweat is collected and the method employed to produce sweat.

The eccrine gland consists of a simple, tubular duct and coiled portions. The duct itself is composed of a short coiled portion, a long and relatively straight portion extending from the coil through the dermis to the epidermis. Further, they have studied the composition of sweat. The ultimate sweat composition is dependent upon the activity of the duct but the initiation of it is done by the secretory coil.

The sweat gland undergoes fatigue when repeatedly stimulated by heat or by methacholine and thus produced diminished secretion. This occurs after 4-6 hours of stimulation.

In 1966 one more research worker Dr. A. C. Parikh studied the acetylcholine test for anhidrosis in Leprosy.

He studied the sweat glands and found that they are supplied by non-medullated sympathetic cholinergic nerve fibres which form a close plexus on the outer surface and give off fibrils to the glandular cells. The anhidrosis present may be due to deficiency, destruction and absence of the secretory apparatus. It may result from congenital ectodermal defects.

In Leprosy the anhidrosis is due to early denervation of sweat glands.

The interpretation of the sweat function is as following:

1. Normal: Number of blue spots close to each other with no appreciable difference as compared to the normal control area.
2. Slightly diminished: Number of spots more than half but yet less than in the normal or control area.
3. Markedly diminished : Number of blue spots less than half the number found in the normal or control area.
4. Absence of sweat: No blue spots on the paper.

Karat et.al improved the sweat function test by producing sweating under cellulose tape. They reported that in routine sweat function tests the area is left uncovered except that of the dye as a result of which the measurement of sweat shows less amount due to evaporation. This holds good for whatever method used. Karat et.al. had used quinazarin powder. The area where the powder was used were covered with cellophane tape and then the sweat measured after exposure to heat and it was shown that the covered area showed more sweating than the uncovered area. Further, they had said that sweat can be detected by various methods like ferric chloride and tannic acid, quinazarine compound, pilocarpine and heat craddle or faradism and also by starch and iodine.

In 1971 N.K.Mathur et.al. compared cutaneous autonomic and somatic nervous functions in the lesions of Leprosy. They reported that Leprosy is a disease which involves peripheral nerves both somatic and autonomic. They studied the sweat and vasodilatation response and compared with the sensory functions of somatic nervous system.

They injected 0.1ml of Carbachol (25 micrograms) intradermally. Whatman No.1 filter paper strips were impregnated with 1% acetone solution of Bromophenol Blue. The grading of sweat response obtained on Bromophenol Blue paper was done as following.

- Nil : Indistinct sweat spots less than 10
1+ : 10 to 100 spots over an area of 1 square inch.
2+ : 100 to 200 " " " " " 1 " "
3+ : More than 200 spots.
4+ : Large smudges of sweat.

The central smudge produced by the point of injection is excluded from the count. The vasodilatation produced by Carbachol is observed as redness so produced. It is finally concluded that sweat function is impaired in cases of Leprosy but there is no difference between dimorphic, maculoanaesthetic and tuberculoid types. Secondly there is no correlation between impairment of autonomic nervous system and sensory nervous system.

It was reported by Khanolkar in 1951 that it is the perineural infiltration of the disease that causes loss of sensation and sweat. When specific anti-leprosy therapy is given it reduces perineural infiltration and thus there is return of function of cutaneous nerves.

Further, V.N. Sehgal and A.N. Manerkar studied the significance of sweat response in the diagnosis of Leprosy. They concluded that the sweat function test is helpful in cases which gives equivocal evidence for the diagnosis of Leprosy by testing temperature pain and touch. It is concluded that the loss of sensation of these modalities goes hand in hand with the loss of sweat response, in majority of cases.

Carbachol produces sweat by vasodilatation. Formerly this test was used in the diagnosis of atrophic skin changes, in Leprosy.

In 1974 Yewalkar and Sanjana studied the effect of D.D.S. therapy on the acetylcholine induced sweat function test in fifty cases of tuberculoid and maculoanaesthetic types of Leprosy. They concluded that sweat response is affected by humidity and temperature. Further, they have concluded that there is no improvement in Sweat Function Test with in one year of treatment with D.D.S.

In 1976 P.B. Joshi studied the pilocarpine test in assessing the therapeutic efficacy in Maculoanaesthetic Leprosy. They concluded that maculoanaesthetic type is commonest type found in India. Further, it is well known that Pilocarpine is the well known drug to test the sweat function. It decides the integrity of nerves. Further it is much better to assess sweat glands than to assess the neurological function by way of touch, temperature and pain sensation as these latter tests can be affected by the method of clinician and patient's apprehension, alertness, intelligence etc. The test is very sensitive as it can be effective in a concentration of pilocarpine upto 1:10,000,000 (1 in 1 Billion). The impairment in sweat function is due to involvement symphathetic nerves as well as sweat glands. The sweat response to Pilocarpine persists inspite of nerve fibres being blocked by lignocaine thus it shows that it acts distal to the nerve block. Similarly after surgical

section of peripheral nerves with adequate time for degeneration of the nerve fibres the response to pilocarpine is markedly diminished. This shows that the drug acts on the terminal arborisation of sudomotor nerve fibres. However Langley and Anderson conclude that Pilocarpine acted directly on sweat glands probably upon receptive substance in them. The injection of Pilocarpine is given and then the tincture of Iodine is painted and starch powder is sprinkled so that the blue spots can be noted and counted. The recovery or deterioration of the sensory nerves can be seen by sweat response at a patch and compared it with that of normal site. It is to be noted that intradermal injection of this drug also has variation such as the exact selection of site, amount of solution injected, exact level of injection in skin.

Acetyl-choline gives erratic response. It has been noted that it has two actions 1. Direct muscarinic like on gland cells. 2. Nicotinic like action on nerve endings, causing sweating by mean of axon reflex. The response to Acetylcholine, Carbachol and Pilocarpine will differ quantitatively. In 1874 Pilocarpine was at first shown to be sudorific by Brazilian physician Coutinhon, In his opinion it is muscarinic in action and not nicotinic.

Circadian Variation: It has been shown that sweat is susceptible to circadian variation. This finding is reported by Jean Timbal (1975) et.al. They measured sweat rate and body temperature during day and night time . It was observed that the latent period for the sweating to the thermal stimuli is not significantly altered. The

mean body temperature is raised at the time of sweating during night time was closer to the basal body temperature. On the contrary during day time there was a considerable difference. This change may be due to increased conduction and vasodilatation during night time than during day time. During day time the condition is usually reversed. The sweat response and basal body metabolic rate and body temperature were Night < Morning < Evening. Further, authors have said that the drug can be given in skin by various methods.

1. Inunction 2. Iontophoresis 3. Intradermal injection or puncture. In intradermal injection the drug is placed between epidermis and dermis while in puncture it is only intraepidermal. This can be demonstrated by Histamine induced pruritus. For injection into most superficial layers of the skin the needle is inserted almost parallel to the skin surface with the bevel facing upwards having entered the skin the needle is then advanced towards the skin surface until the bevel can be seen throughout the intact skin.

Thus finally the fluid is injected with the needle in its position. But many such syringes leak under pressure.

Finally V. N. Sehgal (1976) have found that it is sweat function which improves then the other functions, like that of sensation gradually.

HISTAMINE TRIPEE RESPONSE

The Histamine triple response is first described by Eppinger in 1913. Later on in 1917 Sollman and Pilcher elaborated it. But the investigations in depth was done by Lewis and Grant 1927. Hence this response is popularly called as Histamine Triple Response of Lewis. Lewis's triple response is full development of reaction to histamine injected intracutaneously consisting of local redness, the flare and the wheal or wheel formation in succession. For example when a dilute solution of histamine is injected or pricked into the skin a reaction takes place as described by Lewis(1927).

Within first 20 seconds there is an appearance of circular, sharply defined local reddening surrounding the prick and measures when fully developed to about 2-4m.m. in diameter. This is followed by another fifteen to thirty seconds by a flush or flare that appears on the surrounding skin. The flare is dark red or scarlet red in colour while the local red reaction is of brighter red in colour. The flare so produced has crenated borders which spread 2-3 cms from the centre of the reaction. Soon after the flare develops a wheal appears within 3-5 minutes of injection and this is elevated for about 1-2 m.m. and is 2-3 cms in diameter.

This Lewis's triple response is a characteristic of the reaction of the normal skin following injury by heavy stroking, pricking, scratching, freezing, heating, electrical shocks as well as by irritants like acids, alkalies, mustard oil, cantharidine, nettle sting and morphine like drugs etc.

In short any substance which is capable of releasing histamine from mast cells or cutaneous histamine producing tissues is capable of producing histamine triple response of Lewis. The reaction develops fast in above cases of agents. But it develops slowly in cases when ultra-violet rays, sunlight, bacterial poisons and chemicals like dichloroethyl sulphide.

Further, Lewis had shown that the local redness and wheal are due to direct actions of the injury or irritant on the capillaries while flare is produced by the dilatation of the arched arterioles and is reflex in nature being dependant upon integrity of the cutaneous nerves. Further, the arteriolar dilatation is mediated by a purely local nervous axon reflex and does not depend upon a spinal reflex arc. This has been shown by Lewis by performing the test on anaesthetised skin where all the 3 responses are obtained. But if sufficient time is allowed for a nerve to degenerate or anaesthetic to act then it has been found that the flare is lost while oedema and local red reaction persists in normal skin reaction. Thus the loss of flare after the injection of Histamine is the sign of degeneration of sensory nerves supplying the skin tested.

The above phenomenon was employed by Jose Rodriguez and Fidel Plantilla as an aid in the diagnosis of Leprosy.

To elucidate the mechanism of Histamine triple response further Herbert H. Gass in 1954 studied the progress of lesions and found that Leprosy 1st starts in peripheral twigs and then it spreads centripetally. The sensation of touch was observed over the lesion when only hair were present. The touch sensation disappeared when the hair were shaved. This shows that it is the stimulation of hair root that causes sensation of touch. According to Decoud the nerve fibres persist for a long time in Lepromatous cases while in tuberculoid lesions they are destroyed early. Further, V. R. Khanolkar has suggested that the bacilli travel along the axons and Fite has described the occurrence of bacilli in the axons of nerves. In tuberculoid fibres there is a marked inflammatory reaction hence the fibres are destroyed faster while in Lepromatous that is not so.

In 1970 C. A. Keele studied the chemical causes of pain and itch. He found that body pain/itch can be considered as a sense of injury and itch and pain is due to changes in the chemical environment of the nerve. Itch is superficial while pain is superficial as well as deep. Histamine when injected produce itch or burning sensation for quite a some time. They have also studied the chemical causes of itch. This can be produced by mechanical, chemical thermal stimuli which are ultimately chemical stimuli. Lewis had said that moderate noxious stimulation produce itch with triple response while severe one produces burning pain. The itch and triple response is due to the Histamine release. There is a str-

tified sensation in the skin. Superficial itch, deeper pain, and deepest ache. This strata of pain is shown by the injection of methyl bromide, which is a fat soluble drug. For example Histamine by local application on a unbear skin, pin-pricks, iontophoresis and intraepidermal injection produced itch while intradermal injection produced pain.

Further, Histamine liberators like L.1935 produces itch, wheal and flare but its repeated administration causes depletion of Histamine and then itch do not occur. The itch produced by Histamine liberators is inhibited by anti-histaminic drugs. Itch powder or cow hage *Mucuna Pruriens* produces itch that is not mediated by Histamine release but by direct action. Certain venoms also contain Histamine or Histamine releasing substances.

Further, in 1974 Lahiri et.al have shown that in Leprosy patients there is absence of Prausintz-Kustner reaction while normal patients do give this reaction when tested with homologous reaginic sera. It is further noted that reaction of Histamine is decreased in cases of Leprosy. Secondly the histamine content of reactional lesions is considerably low than the plane tuberculoid lesions. This shows that there is some thing wrong with histamine catabolism and that is why authors have studied histaminase levels in serum. It has been found that serum histaminase levels are increased in pregnancy, asthma, anoxia, anaphylaxis, hepatic damage, myocardial infarction etc.

Further, it has been found that increased histaminase levels is a response to tissue injury. In the same study authors have found that high histaminase levels are present in Lepromatous and Tuberculoid cases together, as compared with normal and higher levels with reaction when compared with any types of Leprosy. Histaminase levels are known to be enhanced by immediate type of hypersensitivity reactions and hence in Erythema Nodosum Leprosum. Histaminase levels may be of diagnostic and prognostic value in evaluating Leprosy.

COLD PRESSOR TEST.

Hines and Brown in 1933 measured the increase in Blood pressure response to immersing hand at 4°C, and found that there is a rise in systolic and diastolic blood pressure in the subjects with the ages of 17 to 50 years. The rise was 8.9 m.m. in systolic and 7.5 m.m. in diastolic. It was 20.1 m.m. and 21.1 m.m. respectively in subjects of potential hypertension. Similar rise was found in subjects with labile hypertension. The rise in blood pressure was 13.1 m.m. and 10.8 m.m. in patients with arteriolosclerosis without hypertension.

Thus they concluded that the hyper reactive vasomotor system was typical of essential hypertension and also of those who are destined to develop it. They concluded that the rise in Blood pressure in old subjects is more than in younger ones. Thus a positive test indicates over activity of the sympathetic system.

In 1964 Harlon, Osborne and Graybiel concluded that the test is not at all affected by the variation in age.

So far upto date no reference of Cold Pressor test in relation to Leprosy has been observed.

VALSALVA'S MANOEUVRE.

This Manoeuvre was first described by Valsalva in 1707 for testing the effect of sudden increase in intrathoracic pressure on air filled cavities.

During those days the concept developed was intrathoracic pressure changes due to any cause lead to changes in blood pressure for a second or few seconds. Thus the curious idea arose due to the fact that immediate rise of peripheral arterial pressure with the Valsalva's Manoeuvre was due to squeezing of blood out of the heart and lungs.

The actual procedure of the manoeuvre is described in the Chapter on Materials and Methods.

Hand-Book of Physiology(1965) mentions about the test of Valsalva's Manoeuvre. At first there is an immediate sharp rise of B.P. at the onset of blowing with little or no change in pulse pressure or heart rate. The magnitude of this rise of Blood pressure is related to the pressure blown. Most adults can blow upto 40m.m. of Mercury. The young and healthy can blow upto 60m.m. Professional trumpet blowers and children can blow upto 80m.m. and 160m.m. can be reached only by certain individuals and few of these can hold it for longer than 10 seconds. During coughing similar rise occurs depending upon the severity of cough.

In normal persons the arterial pulse and mean pressure decline over the next 6-7 seconds due to a decrease in effective filling of the heart. This fall is due to accumulation of blood in peripheral veins. This is due to prevention of forward flow of blood in veins due to increase in intrathoracic pressure creating an obstruction to the inflow. The cardio-vascular response to Valsalva's Manoeuvre is divided into 4 phases.

Ist Phase: It consists of rise in arterial pressure more or less equivalent to increase in intrathoracic pressure. In most cases there is little or no change in heart rate and pulse pressure and there is no change in transmural arterial pressure so that aortic baroreceptors are not stimulated but transmural pressure in carotid is increased.

IInd Phase: At this phase the intrathoracic pressure exceeds the pressure in great systemic veins. Venous return from outside the thorax and abdomen stops although that from within these cavities and cerebrospinal canal is not hindered by increase in transmural pressure. This causes decrease in cardiac output and as acceleration of heart rate is not much it results in decrease in pulse pressure and mean pressure. This decrease in mean pressure comes to an end in a few seconds and both transmural and intraluminal pressure may even rise. This increase is due to reflex vasoconstriction. It occurs despite the fall in pulse pressure and cardiac output.

IIIrd Phase: The strain is let off and the arterial pressure being no longer supported by intrathoracic pressure falls by an amount equal to the fall in the thoracic pressure.

IVth Phase: This is due to the increased venous return and consists of a rise in arterial pressure and of pulse pressure. Here it results in the stimulation of baroreceptors and thus the heart is slowed down. It is more than in the 1st Phase. The paradoxical role is of vasoconstriction in the fourth phase. The overshoot persisting probably from the Phase II and coinciding with the baroreceptors stimulation. This leads to cardiac inhibition which was not appreciated till 1936.

Vasoconstriction in this Phase was 1st postulated by Williams and Gulbertsons as they worked with the sympathectomised patients. During Phase II the effective redistribution of blood takes place mainly in the limbs as the intrathoracic pressure approximates intra-abdominal pressure. Further, in anaesthetised man the abdominal muscles are relaxed. Hence a small imposed rise in intrathoracic pressure leads to increased circulatory changes than in the un-anaesthetised subjects. With the sharp rise in intrathoracic pressure at the beginning of Valsalva's Manoeuvre peripheral venous valve shut and blood accumulates distal to them.

The rate of accumulation is influenced by 2 factors;

1. The degree of increase of supply of pressure and 2. The state of arterial vaso-motor tone at the moment the manoeuver is performed.

Hence the increase and more rapid decrease in cardiac filling pressure and stroke output is achieved when a high pressure is blown in the presence of peripheral vasodilatation. In suitable subjects a decrease in arterial pulse pressure of more than 80% may result in the time of span of 7 seconds and this represents about 1500 ml of blood redistributed to the periphery.

In cases like Tabes Dorsalis where afferent limb is affected there is no overshoot of blood pressure as in Normal in Phase IV. During heart failure there is no change in pulse pressure during the Valsalva's Manoeuvre and no subsequent overshoot.

Luisada(1970) has reported that during performance of Valsalva's Manoeuvre the normal heart size decreases. Also the athletes have smaller hearts. This responsiveness is apparently lost quickly as heart becomes inefficient. It is also decreased with advancing age. The loss of sinus arrhythmia runs parallel with the loss of Valsalva's effect on heart size. In the persons above the age of 35 years Valsalva's Manoeuvre may be used in assessing the functional capacity of heart. Hurst and Logue in (1968) had reported that if an E.C.G. is taken during the Valsalva's Manoeuvre it shows prolonged P-R interval during the Manoeuvre due to vagotonia.

Campbell (1970) has reported that in patients with neurological disorders the heart rate does not increase normally despite the profound fall of blood pressure on standing. Further, the Valsalva's Manoeuvre provokes no change in heart rate and no overshoot of blood pressure on release of expiratory effort. In few cases which have been studied at necropsy spinal cord damage has been demonstrated and the defect is presumably due to damage to efferent sympathetic fibres.

EFFECT OF INJECTION OF ADRENALINE.

Adrenaline is also called as Epinephrine, arterinol. This substance is a catecholamine and is found in adrenal medulla and to a smaller extent in post-ganglionic adrenergic nerve endings. In 1894 Oliver and Schafer discovered the pressor effect of an extract of adrenal medulla. Lewandowsky (1898) and Langley (1901) noted independently the similarity between the effects of the injection of extracts of the adrenal gland and stimulation of the sympathetic nerves.

In 1899 Abel named the extract from adrenal medulla as Epinephrine. In 1905 T.R. Elliot postulated that the sympathetic nerve impulses release minute amounts of an epinephrine like substance in immediate contact with the effector cells. In 1926 Loewi and Navartil found that stimulation of vagus nerve in frog during summer causes release of epinephrine.

In 1921 Cannon and Uridil reported that the liver upon stimulation of the sympathetic hepatic nerve releases an epinephrine like substance that raised the blood pressure and heart rate. Further, Cannon and Rosenbluth (1937) named the substance liberated from sympathetic stimulation as sympathin. In 1910 Barger and Dale reported that the effect of sympathetic nerve stimulation were more or less but not exactly similar to injection of sympathomimetic primary amine than that with epinephrine.

In 1946 Von Euler proposed that the sympathetic mediator is Nor-epinephrine and not epinephrine. In 1948 Ahlquist put forward

the concept of types of adrenoceptors namely Alpha and Beta. Further, in 1959 Ahlquist and Levy put forward the concept of Gamma receptors and Furchgott in 1959 put forward the concept of Delta receptor. The later two receptors were soon discarded.

There are various types of stimuli which cause release of adrenaline from the adrenal medulla. Stimuli like fright, mental stress, physical stress, exposure to cold etc leads to release of adrenaline from the adrenal medulla.

The effect of adrenaline on blood pressure varies depending upon the dose of the drug and the route of administration. The drug when given intravenously causes a rise in systolic and diastolic pressure and with widening of pulse pressure. The pressure then falls below normal before returning to the control level. The drug does not lead to tachyphylaxis. There may or may not be a bradycardia, at the peak rise of blood pressure. This bradycardia depends upon the vagal tone.

INSTILLATION OF HOMATROPINE.

Homatropine is used in the form of either hydrobromide or methyl-bromide in a strength of 1 to 2%. It is an ester of tropanol with mandelic acid. It gives quicker dilatation with less marked cycloplegia (Paralysis of accommodation). The effect lasts at the most for a day or two.

This drug has been used for about 80 years or more as mydriatic. Many times the drug is combined with Phenylephrine or Cocaine, to give better results.

So far there is no report of this drug being used in the cases of Leprosy.

Since the time of Sushruta (600 B.C.) Leprosy is well known as a disease of nerves. Various workers have studied the pathology, histology and functional abnormality due to the nerve lesions.

It was known as Vata-Rakta type where there were nerve lesions. Recently Dr.S. N. Chatterjee(1956) has pointed out that thickening of peripheral nerves, particularly of Ulnar is a useful sign to diagnose Leprosy. Similarly Dr.S. S. Pandya(1975) and others have studied innervation of muscle in Leprosy with special reference to muscle spindle. These are just a few example to show that the affection of peripheral nerves in Leprosy have been studied in a considerable depth as compared to other fields of nervous system, in Leprosy, in particular autonomic nervous system.

Further, it is well known that particularly at the tuberculoid end of the spectrum there is a massive perineural infiltration which compresses the nerve and makes the nerve to undergo degeneration. Antia and co-workers have shown that release of this compression revives the nervous function.

In Lepromatous (L.L.) cases there is degeneration of nerves without that much infiltration or fibrosis.

Since autonomic fibres make their course with the somatic nerves and blood vessels it is possible that the autonomic functions

are liable for derangement. So we took the problem for studying the autonomic functions in Leprosy. We have taken two types namely Lepromatous (L.L.) and Maculoanaesthetic (M.A.) which are the ends of the whole spectrum of the classification and clinical manifestations of this disease. Thus it was intended to know whether pathological changes particular to one type of this disease as pointed out earlier can change the neurological manifestations.

An extensive survey of the literature have shown that only Histamine triple response and Sweat function test have been studied so far. Even then no comparative data is available of these two tests within the same group of patients, although it is said that (Dr. Felix Cinreas 1949) Histamine triple response is better for assessment than the sweat function .

Further, N.K.Mathur (1971) had studied the sweat function in comparison with sensory nerve's lesions and had concluded that there is no correlation between the autonomic and sensory functions. It appears very bold to conclude such, as no other parameter of autonomic function has been studied, except that of sweat function which depends upon local axon reflex, and the conditions of the sweat glands. Thus that will obviously not reflect any systemic autonomic disturbances. So to investigate the correlation further, we selected Cold pressor test.

Thus considering the amount of work done on autonomic functions we selected various tests, including the two tests which have been already performed, namely Sweat function test and Histamine triple response.

The selection of the test was done with an intention to evaluate the autonomic functions with simple, less troublesome tests to the patients and with the aid of only routine simple instruments.

Further, the tests should give a reliable and coherent idea about the functions. We have used electro-cardio-gram at lead I to get accurate pulse rate.

The instillation of Homatropine in the eye will give information about the cholinceptive muscarinic sites in the sphincter pupillae muscle. The basal readings when compared with normal will give a comparative idea about the dominant tone on the pupil. The measurements were done by paper pupillometer for its simplicity, efficacy and reproducibility.

The act of Valsalva's Manoeuvre will tell us about the functional status about baroreceptors.

The cold pressor test was undertaken for the reasons already mentioned and to investigate the mass reflexes and sympathoadrenal discharge.

The sub-cutaneous injection of adrenaline will reveal the status of adrenergic receptors in Leprosy cases, in addition to the inferences from cold pressor test. This test will certainly have a therapeutic implication if the leprosy cases show either hyper or hypo reactivity.

It can be inferred from the literature review that so far the work done on Histamine triple response is mainly on white skinned people. Secondly the criterion taken for nerve lesion is flare, which is ofcourse a subjective assessment. Hence we have taken the final end point of intradermal injection of Histamine, the wheal so formed, which is an objective criterion.

The sweat function test will reveal although semi-quantitatively the status of sweat glands and the local axon reflex mechanism.

Further to get a clear idea of the autonomic functions only the chronic cases who have taken treatment for not less than 8 years and ^{not} more than twelve years were selected. The only chemotherapeutic agent used was D.D.S. with a dose of 50mg/day in the volunteers. This makes the trial a uniform trial with respect to the progress of the disease.

Lastly all these tests were done on patients of only Lepromatous and Maculoanaesthetic as these ^{are} extremes of the whole Leprosy

spectrum. Further, a control study was also undertaken to compare the responses in normal persons with respect to that in Leprosy cases.

In short this study is a controlled, open trial to evaluate the autonomic functions in the two leprosy groups.

*MATERIALS & *
*
* METHODS *

Selection of Persons for the trial: Ten persons of each group namely normal volunteers, patients of Lepromatous type and patients of Maculoanaesthetic types were selected at random. All the persons included in the trial were males. Further, they were in the age group of 20 years to 35 years as it is the commonest age group for the most cases of Leprosy and majority of the population of India is in the range of that age group. All the persons were of about average height and weight when taken for trial. (Please see under Results).

Normal volunteers were not suffering from any disease at the time the tests were performed. This was confirmed by taking their pulse rates, blood pressure, auscultations of chest for respiratory and cardio-vascular system, Palpation^{of} abdomen for any abdominal mass or tenderness and arm pit body temperature. History of exposure, diabetes, and signs of peripheral neuritis were sought.

Similarly were the examinations done for the Leprosy patients and their recent medical records were checked to exclude any possibility of the disease, except that of the Leprosy. An history of glaucoma was asked to the patients.

Normal volunteers were informed not to take any medicaments for forty-eight hours before the trial. Leprosy patients were only on D.D.S. with their usual dose of 50mgs/day.

The trial was performed in a monsoon season with a relative humidity of 75to80% and an ambient temperature of 30to33°C. It was conducted for normal persons in a well ventilated and lighted room. Similar location was also present for the patients at Acworth Leprosy Hospital.

Selection of Tests: Valsalva's Manoeuvre, Cold pressor test, instillation of 1% Homatropine-Hydro-Bromide in both the conjunctival sacs, intradermal injection of Histamine acid phosphate, intradermal injection of Carbachol and sub-cutaneous injection of adrenaline bi-tartrate were the parameters used for the trial.

In general the tests used were selected for their reliability simplicity, ease of execution, economy and the least bothersome to the persons as the tests used do not have any appreciable after effects.

In addition to these general advantages these tests have their own merits which is of more importance, to show the various profiles of the autonomic nervous system, by the individual tests.

Valsalva's Manoeuvre: This test is used to assess the baroreceptors of Cardio-vascular system.

Cold Pressor Test: This test is used to evaluate mass reflex

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response which is involving symphathetic component of cardio-vascular system.

Instillation of Homatropine in Conjunctival Sacs: This drug is a mydriatic of anti-cholinergic type with a reasonable duration for its mydriatic effect which lasts for not more than 24 hours. Further its cycloplegic effect lasts for only couple of hours.

Intradermal Injection of Histamine: This test is used to give an idea about the integrity of local axon reflex.

Intradermal Injection of Carbachol: This test is used to evaluate the sweat glands which are supplied by only cholinergic symphathetic nerves.

Sub-cutaneous injection of Adrenaline: This injection was for the study of the effect of adrenaline on cardio-vascular system.

DETAILS OF EACH TESTS:

At first the subject was requested to take his chair and was interogated casually. Then he was intimated about the nature of tests and was given a demonstration of Valsalva's Manoeuver. He was enquired about his dominant hand for cold pressor test.

Then the weight and height of the person was measured and noted.

Two E.C.G. leads namely right and left arm were connected to the patient. Then the blood pressure cuff was tied to the left arm which is not used for cold pressor test, 5 cms above the elbow crease. Further, the basal blood pressure is obtained by auscultatory method which was followed throughout the tests. The diastolic blood pressure was taken at a level of mercury where there is complete disappearance of sound. The systolic is obtained at a pressure where the pulse sound becomes first audible.

The heart rate is obtained by noting the E.C.G. tracing at lead one.

After obtaining the basal data at complete rest and relaxation all the six tests were performed in the same order for all the persons as described below.

VALSALVA'S MANOEUVRE.

The person blows the column of mercury manometer of the internal diameter of 2.5m.m. with the linear scale of millimeters to a level of 40m.m. and keeps the pressure steady for 15 seconds. An E.C.G. tracing is recorded the moment the person is also assuming a steady level of mercury. At the same time his blood pressure is also recorded. The blood pressure and pulse rate are again recorded at the time of release of pressure. The test is repeated

one more time and the average of the two readings is noted as a mean result. A rest period of 5 minutes is given to the person before repetition.

COLD PRESSOR TEST:

Three minutes after the last Valsalva's Manoeuvre this test is performed by patients's dominant hand. In this trial the patients were with right hand as a dominant one.

The person's wrist was marked with a felt pen from styloid process of radius to styloid process of ulna. Then his hand was dipped in a beaker of one litre capacity containing ice cubes and water maintained at a temperature of 0-2°C. upto the mark. The person was told to inform the time at which he feels the sensation of cold, sensation of pain and the time at which he is unable to bear the pain. The duration of time were noted for all these three sensations from the time of onset of the test which is taken as zero.

The pulse was recorded during the time between the sensation of pain and pain intolerance so also the blood pressure. Blood pressure and pulse rates were also noted 2 minutes after the removal of the hand from the ice cold water. The person was allowed to take his hand out of the beaker the moment it becomes unbearable.

The test is repeated for one more time and the results of the two were noted as mean results.

EFFECT OF INSTILLATION OF HOMATROPINE.

(Please see opposite page for a sample of PUPILLOMETER).

At first the person is shown the paper pupillometer(L.J.McLeod et.al. 1970) which is nothing but a sheet of card paper in which there are sets of pin holes. Each pair of pin holes is at a specified distance ranging from 1 m.m. to 8m.m. with an interval of 0.5m.m. between the consecutive pairs. The card is held vertically so that the pairs lie in a column. The pair of 1 m.m. being the topmost when so held. The person was asked to hold the pupillometer in front of one eye with the other being closed. The card was held such that it lies parallel to eyes. Now the person sees through only one pair at a time with each other holes being compared to see at what size they come just close together(Their borders touch each other).

The diameter of the pupil is the size of the hole at which the holes just touch each other. Thus the initial diameter of the pupil was obtained.

Then the person is asked to extend his neck and open his eyes. Then at first a single drop of Homatropine Hydrobromide of 1% strength was instilled in his left eye and the eyes were closed. Exactly after a minute another drop was similarly instilled in the

right eye, and the eyes were opened at the end of one minute. Then the reading of the diameter of the left would be obtained by the aid of pupillometer which would be the diameter at the end of two minutes after instillation.

Similar procedure was followed for the other eye and the same procedure was practised at 4 minutes, 6, 10, 15, and 30 minutes from the time of instillation of the eye drops. The person was enquired about any symptoms like halos around the vision, brightening of the vision, headache, blurring of vision etc, and the symptoms if any were noted.

At the end of fifteen minutes after the instillation the next test of Histamine triple response is performed.

HISTAMINE TRIPLE RESPONSE.

At first the site of injection was swabbed with rectified spirit . Then 0.05 ml of 1mg/ml of sterile, freshly prepared solution of Histamine Acid Phosphate is injected intradermally with a needle of 26 No. and Top Tuberculin syringe. At every time a volume extending from 0.2ml to 0.15 ml is injected with the same syringe so that only exact amount goes into the skin.

The size of the wheal was noted with a vernier calipers at the intervals of 1, 2, 3, 5, 10 and 15 minutes from the time of

injection. The measurement was taken 1. Parallel to the forearms and passing through the site of injection and 2. At right angles to the first. The average of the two is recorded.

The injection was given to all the persons at their upper one third and middle one third of forearm and in Maculo-anaesthetic cases at the site of hypo-pigmented patch on their backs.

SWEAT FUNCTION TEST.

At first the site of injection is swabbed with rectified spirit and allowed to dry. Then Carbachol of 0.2ml of 0.25mgs/ml (i.e. 50 mcg) is injected intradermally with a needle of 26 No and a tuberculin syringe at a middle one third and lower one third of the forearm. The needle was very slowly withdrawn so as to avoid leakage of drug from the site of puncture.

In Maculoanaesthetic cases similar procedure was followed at the site of patch on their backs. This site was at least 10cms apart than that for Histamine test.

Preparation of Bromophenol Blue Paper: No 42 Whatman filter paper were at first dipped in 1% solution of Bromophenol Blue dye in acetone kept in a large petridish. At a time only one paper was dipped so that the dye was equally impregnated on the filter paper.

The paper was picked up by pair of forceps and dried before the table fan. The dried papers were kept in a air tight poly-ethylene bags. The papers were cut with the pair of scissors at the time of tests to the size of 2.5cms x 2.5cms.

The paper so cut was kept over the injected site and was gently pressed over the skin. It was allowed to stay at the site for 10 seconds every time. The paper was stained with blue spots of sweat and the spots were counted with magnifying glass(Lens). The counting of the spots was only approximately done as at higher density the spots merge together. This procedure is performed at 5,10, 15, and 30 minutes interval and the spots were graded as following (N.K. Mathur 1971).

Nil: Spots less than 10.

1+: 10-200 spots over an area of 6.25 sq.cms.

2+: 100-200 " " " " " "

3+: 200 or more ----- do -----

4+: Large smudges of sweat -----do -----.

The next test is performed fifteen minutes after the injection of Carbachol.

INJECTION OF ADRENALINE.

At first the site of injection was swabbed with rectified

spirit and was allowed to dry. Then 0.2ml of 1mg/ml of adrenaline bi-tartrate was injected sub-cutaneously with a 23 No. short needle at the deltoid belly. The persons were told to inform for any symptoms. Pulse rate and blood pressure were recorded at 5, 10, 20 and 30 minutes from the time of injection.

After the observations of this test, the blood pressure cuff E.C.G. electrodes were detached from the persons and they were asked to report the next day. Next day they were enquired for any residual effects and the pupillary diameter were measured.

The same method was followed for all the persons who had undergone this trial. Separate syringes were used for the respective drugs and the same syringes were maintained for all the persons. Similarly the Manometer for Valsalva's test, Sphygmomanometer (B.P. Apparatus) and E.C.G. Machine were the same. Further, the weighing machine, the tape for measuring height were also the same.

The drugs used were Adrenaline Bi-tartrate (Burroughs-Wellcome), Histamine Acid Phosphate (B.D.H.), Carbachol (Bengal Immunity) and Homatropine Hydrobromide 1% (Bell pharma)...

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Table No: 1. Showing mean with range of age, weight and height in Normal and Leprosy Patients. (Please refer to Appendix No. 1.)

TYPE	AGE	WEIGHT	HEIGHT
NORMAL	25.5±0.92 (21 to 30)	52 ± 1.89 (45 to 62)	163.80 ± 2.28 (150 to 175)
LEPROMATOUS	26.5±2.14 (21 to 35)	45.6±1.4 (42 to 51)	164.20 ± 1.64 (158 to 176)
MACULOANAESTHETIC	25.0±0.75 (22 to 29)	44.80±1.00 (41 to 51)	163.80±1.67 (150 to 168)

The persons who had undergone this trial were selected at random and their age, height and weight were noted as shown in Appendix No: 1.

The Normal persons were in the range of 21 to 30 years with the ranges for weight and height being 45 to 62 Kgs and 150 to 175 Cms respectively.

The Lepromatous were in the range of 21 to 35 years with the ranges of weight and height being 42 to 51 Kgs and 158 Cms to 176 Cms respectively.

Similarly were the range for Maculoanaesthetic Cases i.e. 22 to 29 years, 41 to 51 Kgs and 150 to 168 Cms.

Thus it is evident that the groups do not differ significantly from each other for age and height. However, the average weight of Leprosy patients was less than that of Normal although there was no significant difference.

Table No: 2. Ranges and averages for pressure and pulse rate of Normal and Leprosy persons in Basal Conditions.
(Please refer to Appendix No: 2.)

TYPE	SYSTOLIC	DIASTOLIC	PULSE PRESSURE	PULSE RATE.
NORMAL	113.4 $\pm$ 0.57 (105 to 125)	88.3 $\pm$ 0.99 (79 to 110)	25.1 $\pm$ 2.2 (15 to 36)	87.7 $\pm$ 4.4 (75 to 114)
LEPROMATOUS	102.2 $\pm$ 4.50 (80 to 120)	69.4 $\pm$ 4.4 (49 to 95)	32.8 $\pm$ 2.1 (22 to 42)	96.9 $\pm$ 4.1 (79 to 120)
MACULOANAESTHETIC	111.9 $\pm$ 4.16 (96 to 145)	79.7 $\pm$ 2.2 (71 to 92)	32.2 $\pm$ 3.6 (16 to 55)	103.2 $\pm$ 6.66 (68 to 130)

The blood pressure reading were in the normal range of 100 to 140 m.m. of Hg for Systolic and 60 to 100 for Diastolic.

The basal systolic, diastolic and pulse pressure did not differ significantly from each other as also was the pulse rate, when compared amongst the three groups. But the basal systolic and diastolic was found to be on the lower side of the normal in Leprosy groups, particularly in Lepromatous Leprosy.

All the following results are compared at the probability value of 95% or more.

VALSALVA'S MANOEUVRE.

Table No: 3. Average change in Blood pressure and Pulse Rate as a Result of Valsalva and in the Pulse Rate after the Valsalva. (Please Refer to Appendices Nos 3 to 5).

TYPE	SYSTOLIC	DIASTOLIC	PULSE PRESSURE	PULSE RATE	PULSE RATE AFTER MANOEUVRE.
N.	40.3±8.0 (23 to 95)	49.8±6.34 (20 to 91)	-10±2.3 (4 to 16)	10.5±5.65 (-17 to 44)	-10.4±3.39 (-3 to 24)
L.L.	21.9±4.7 (1 to 40)	32.6±4.1 (19 to 51)	-12.7±1.7 (-1 to -20)	10.9±8.2 (-15 to 62)	-7.6±1.7 (-20.5 to 9.5)
M.A.	20.2±4.27 (5 to 45)	34.8±4.96 (12 to 58)	-13.6±3.25 (-2 to 37)	2.8±4.06 (-25 to 18)	-2.8±3.04 (-16 to 82)

Note: N. denotes Normal Persons. L.L. denotes Lepromatous Persons
M.A. denotes Maculoanaesthetic Persons.

The sign (-) minus denotes shortening of pulse pressure and Bradycardia.

The sign (+) plus denotes widening of Pulse pressure and Tachycardia.

Normal Persons: In Normal persons the systolic and diastolic pressure rose during the Manoeuvre. In one case the rise was 95 and 91 m.m. of Hg respectively. The average change in systolic was 40.3 m.m. of Hg and that in diastolic was 49.8m.m. of Hg

The pulse pressure shortened and the pulse rate accelerated the average being -10 and 10.5 with ranges of 4 to 16 and -17 to 44 respectively.

Lepromatous Cases: In these cases the response was similar. The rise in systolic and diastolic was 21.9 and 32.6 m.m. of Hg respectively with a range of 1 to 40 in systolic and 19 to 51 in diastolic. The shortening of Pulse pressure was to the extent of 12.7 with the range of 1 to 20 m.m. of Hg.

There was no tachycardia during the Valsalva and no Bradycardia after the manoeuvre, except in one case. In this case pulse rate did shoot up by 62 beats per minute during the Valsalva.

Maculoanaesthetic Cases: The results were the same as in Lepromatous cases. The average change in systolic and diastolic was 20.2 and 34.8 m.m. of Hg with a range of 5 to 45 and 12 to 58 m.m. of Hg respectively.

The shortening of pulse pressure was to the extent of 13.6 m.m. of Hg on an average with a range of 2 to 37 m.m. of Hg

COMPARISON BETWEEN THE GROUPS.

1. Systolic Pressure: The rise in pressure was smaller in both the Leprosy groups than in the Normal and the two Leprosy groups do not differ from each other.
2. Diastolic Pressure: The results are similar to the changes in systolic pressure.

3. Pulse Pressure: The decrease in Pulse Pressure was more in Maculo-
anaesthetic, intermediate in L.L. and the least in Normal. The pulse
pressured did not differ significantly between the two Leprosy groups.
However, pulse pressure in Normal differ from that in either of the
Leprosy Groups.

4. Pulse Rate: The tachycardia produced did not differ from each
other amongst the three groups, during the Manoeuver. After the
Manoeuver there was a significant bradycardia in Normal Persons but
the two Leprosy groups did not show any Bradycardia as their pulse
rate were restored back to Normal.

Thus the pulse rate of Normals after the Manoeuver differed
from two Leprosy groups but these two groups did not differ between
themselves.

COLD PRESSOR TEST.

Table No: 4. Showing changes in systolic, diastolic, pulse pressure
and Pulse Rate in Normal and Leprosy Patients, due to
Cold Pressor Test. (Please refer to Appendices Nos 6 to 9-A)

TYPE	SYSTOLIC	DIASTOLIC	PULSE PRESSURE	PULSE RATE.
N.	43.4 $\pm$ 3.87 (22 to 64)	55.5 $\pm$ 3.92 (30 to 72)	12.1 $\pm$ 1.81 (3 to 20)	20.3 $\pm$ 8.42 (7 to 43)
L.L.	16.1 $\pm$ 3.28 (0 to 30)	17.7 $\pm$ 5.1 (-7 to 40)	-1.6 $\pm$ 4.6 (-20 to 25)	-5.5 $\pm$ 2.81 (-38 to 19)
M.A.	11.0 $\pm$ 5.18 (0 to 50)	16.3 $\pm$ 4.06 (-2 to 39)	-8.1 $\pm$ 5.77 (-39 to 30)	4.3 $\pm$ 4.52 (-11 to 41)

Table No: 5 Showing Mean Cold Sensitivity, Pain Threshold and Intolerance with their respective ranges.

TYPE	SENSITIVITY	THRESHOLD	INTOLERANCE
N.	Instantaneous (Few Seconds)	14.5±2.40 (5 to 25)	31.5±5.0 (18 to 60)
L.L.	9.5±2.32 (2 to 25)	34.5±7.15 (15 to 75)	296.5±7.4 (55 to 600)
M.A.	10.3±2.21 (3 to 25)	56.3±16.67 (10 to 120)	393±4.21 (135 to 600)

Normal Persons: In these persons there was rise in systolic, and diastolic pressures to the extent of 43.4 and 55.5 m.m.of Hg respectively. The ranges being 22 to 64 m.m.Hg and 30 to 72 m.m.of Hg.

The pulse pressure was decreased and the pulse rate accelerated by 12.1 and 19.6. The ranges being 3 to 20 and 0 to 43 respectively.

The sensitivity of cold was obviously instantaneous. The average pain threshold and pain intolerance was 14.5 Seconds and 31.5 Seconds with the ranges of 5 to 25 and 18 to 60 respectively.

The change was immediately restored to Normal, after the withdrawal of the hand from ice-cold water.

Lepromatous Cases: In these cases there was a rise in systolic and diastolic pressures of 16.1 and 17.7 m.m. of Hg as an average, with the ranges of 0 to 30 and -7 to 40 respectively.

The pulse pressure was decreased by only 2.7 m.m. of Hg with a very wide variation and thus statistically insignificant. The pulse rate also did not change to any significant extent. There were wide variations.

Further, the time sensitivity of Cold was 9.5 seconds on an average with a range of 2 to 25 seconds. The threshold and intolerance averaged to 34.5 seconds and 296.5 seconds respectively with a range of 15 to 75 and 55 to 600 seconds respectively.

Maculoanaesthetic Cases: In this group the systolic pressure did not rise to any significant extent so also was the change in pulse pressure although there was a variation of broadening and shortening of pulse pressure. The pulse rate also did not change although there were tachycardia as well as Bradycardia.

It was only the diastolic pressure which rose by 16.3m.m. of Hg on an average with a range of -2 to 39. Further, the average time for sensitivity was 10.3 seconds and that for threshold and intolerance were 56.3 and 393 seconds respectively. The ranges being 3 to 25 and 10 to 180 and 135 to 600 respectively.

COMPARISON AMONGST THE GROUPS.

Systolic: The rise produced was more in Normal persons as compared to Leprosy cases. But the rise was similar in two Leprosy groups.

Diastolic: The results were the same as for systolic pressure.

Pulse pressure: Here also the results were the same as in diastolic and systolic pressures obviously.

Pulse Rate: It did not show any difference for the change produced due to the test amongst the groups.

The Cold Sensitivity and Other parameters: The sensitivity, pain threshold and intolerance were different in Normals than in Leprosy groups. But the Leprosy groups did not differ between themselves.

EFFECT OF HOMATROPINE ON EYES.

Table No: 6 Showing Average size of the pupil and the ranges before and After the instillation of drug.

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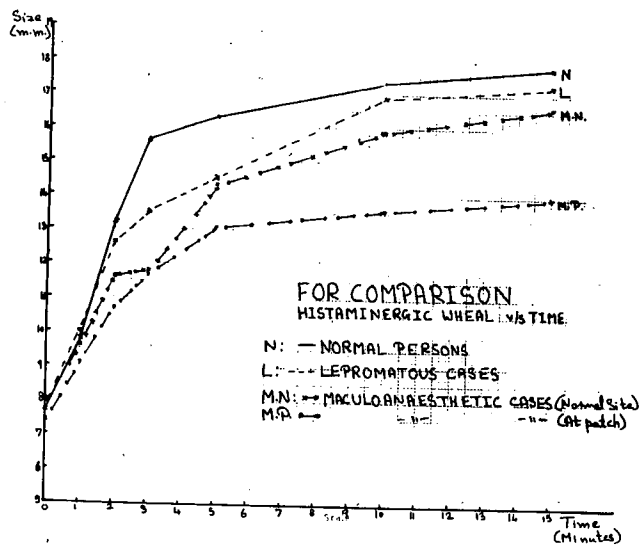
TYPE	BASAL READING	READING AT 30 MINUTES.
N.	2.05 ± 0.16 (1 to 3)	3.9 0.31 (3 to 6 m.m.)
E.L.	2.10 0.1 (2 to 3)	4.1 0.1 (3 to 6 m.m.)
M.A.	2.2 0.20 (1 to 3)	3.7 0.21 (3 to 5 m.m.)

Normal Persons: The average size of the pupil before Homatropine was $2.05 \text{ m.m.} \pm 0.16$. After the instillation of Homatropine the pupils dilated to 3.9 m.m. on an average at the end of 30 minutes after the instillation. The range of pupillary size before the instillation was 1 to 3 m.m. and it became 3 to 6 m.m. after the instillation. The average change in size was 1.8 m.m. with a range of 1 to 4 m.m.

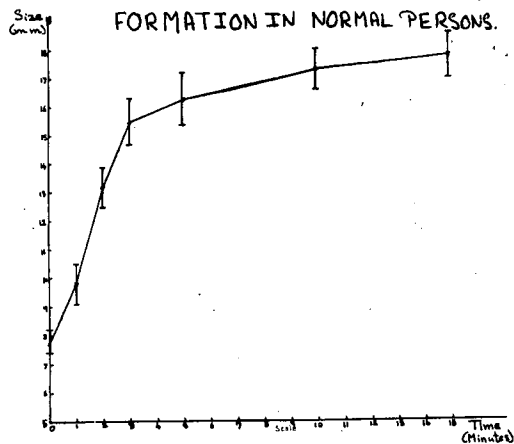
Lepromatous Cases: Here the average size of the pupil before Homatropine was $2.1 \text{ m.m.} \pm 0.1$. After the instillation of Homatropine the pupils dilated to 4.1 m.m. on an average at the end of 30 minutes. The range of pupillary size before the instillation was 2 to 3 m.m. and it became 3 to 6 m.m. after the instillation. The average change in size was 2 m.m. with a range of 1 to 4 m.m.

Maculoanaesthetic Cases: In these cases the average size of the pupil before Homatropine was $2.2 \text{ m.m.} \pm 0.20$. After the instillation of the drug they dilated to 3.7 m.m. on an average at the end of 30 minutes. The range of pupillary size before the instillation was 1 to 3 m.m. and it became 3 to 5 m.m. after the drug. The average change in size was 1.5 m.m. with a range of 0 to 3 m.m.

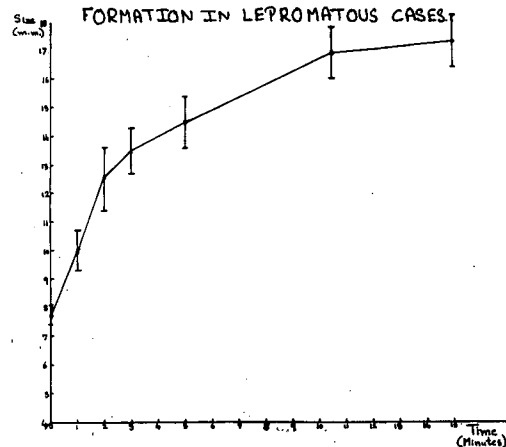
There was no difference between the right and the left pupillary size in any individual in any of the three groups.



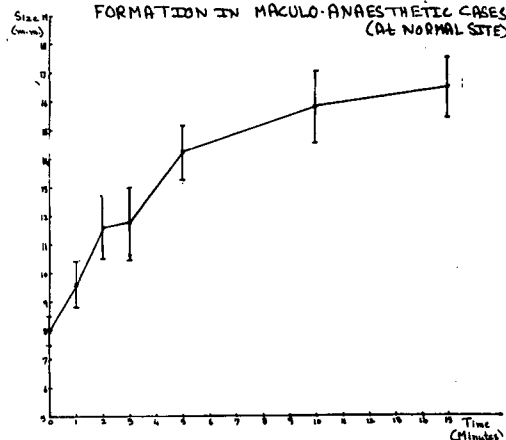
EFFECT OF HISTAMINE ON WHEEL FORMATION IN NORMAL PERSONS.



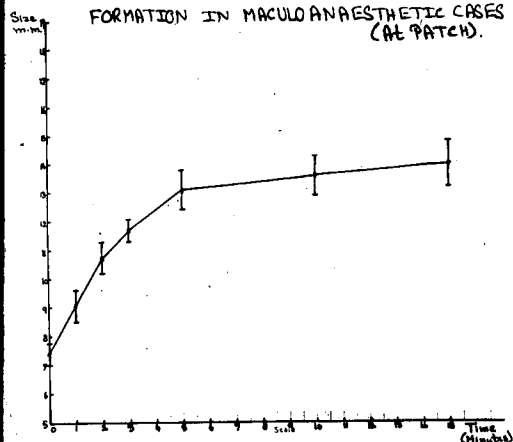
EFFECT OF HISTAMINE ON WHEEL FORMATION IN LEPROMATOUS CASES.



EFFECT OF HISTAMINE ON WHEEL FORMATION IN MACULO-ANÆSTHETIC CASES (At NORMAL SITE).



EFFECT OF HISTAMINE ON WHEEL FORMATION IN MACULO-ANÆSTHETIC CASES (At PATCH).



COMPARISON AMONGST THE GROUPS.

There was no difference either before and after the instillation of Homatropine amongst any of the groups when compared with each other.

HISTAMINE TRIPLE RESPONSE

Table No: 7 Showing average time for Maximum response and Average size of the Wheal. (Please Refer to Appendices Nos 11 to 15)

TYPE	AVERAGE TIME FOR MAXIMUM RESPONSE	AVERAGE SIZE OF THE WHEAL.
NORMAL	7.1 min $\pm$ 1.04 (2 to 15)	17.8 $\pm$ 0.77 m.m. (13 to 22)
LEPROMATOUS	10.1 min $\pm$ 1.37 (3 to 15)	17.3 $\pm$ 0.89 m.m. (13 to 22)
MACULOANAESTHETIC (NORMAL SITE)	9.7 $\pm$ 1.44 min. (2 to 15)	16.6 $\pm$ 1.09 m.m. (9 to 22)
MACULOANAESTHETIC (AT THE PATCH)	7.1 min $\pm$ 1.61 (1 to 15)	14.0 $\pm$ 0.8 m.m. (11 to 18)

Normal Persons: The net change in the size of the wheal is 10.1 m.m. In these persons 7.1 minutes was the average time for the formation of wheal to the maximum size. The average size of the wheal was 17.8 m.m. with a range of 13 to 22 m.m. The distribution of people along with time to give maximum response was discrete and only 4/10 people showed the maximum at 3 minutes, while the rest were distributed from a range of 2 to 15 minutes.

Lepromatous Persons: The net change in the size was 9.6m.m. The average time to attain maximum size was 10.1 minutes. The average size was 17.3 m.m. with a range of 13 to 22 m.m. Here 7/10 people showed maximum response at 10 minutes.

Maculoanaesthetic Persons: (Normal Site): The net change in the size was 8.6m.m. The average time for Maximum size was 9.7 minutes. The average size was 16.6m.m. Here 7/10 people showed maximum response at 10 minutes.

Maculoanaesthetic Persons (At the site of Patch) The net change in the size was 6.6. m.m. The average time for maximum size was 7.1 minutes. The average size of the wheal was 14m.m. with a range of 11 to 18 m.m. 6/10 people showed maximum response, at 5 minutes, while the rest were distributed discretely over the time period.

COMPARISON AMONGST THE GROUPS.

(Please refer to the graphs on the Opposite Page p.69)

Rate of Formation of Wheal: It can be seen from the graph that the wheal formation was faster in Normal, then in L.L. and in M.A. at Normal site. But it was least in the patch of M.A.

Colour of the Wheal : The colour was mahogany red in all the persons.

Size of the Wheal: It is evident from the graph and statistical

analysis that the size of the wheal differed from each other in all the groups when compared with each other. It is maximum in Normal Persons, Next to that is in L.L. The 3rd Rank was of M.A. at Normal site and the least was at patch of M.A. site.

SWEAT FUNCTION TEST.

(Please Refer to Appendix No 16)

Sweat Response was graded as nil to +4 depending upon the degree of sweating as usually seen. Here the No. of individuals of one type showing the same grades of response are grouped into one group at the given interval of time namely 5, 10, 15, and 30 minutes. Then the results are compared by Chi-Square test. The results are as following.

Normal Persons: All the persons sweated with in 5 minutes of the injection. The response was complete in 9/10 persons within 10 minutes. Only 3 persons sweated upto +3. Nobody sweated upto +4. There was no sweat in seven persons at the end of 30 minutes.

Lepromatous Persons: The secretion of sweat started only in seven patients within 5 minutes. The rest three did not sweat upto 10 minutes. One patient did not sweat at all upto 30 minutes. 3 Persons sweated upto +3 while only one sweated upto +4.

Maculoanaesthetic Persons (Normal Sites): The sweat occurred in 8/10 patients within 5 minutes after the injection. It reached its maximum only upto +2 within 10 minutes, only in two cases. At fifteen minutes 8/10 were with +1 sweat. At the end of 30 minutes there was no sweat in 4/10 cases. One person did not sweat at all.

Maculoanaesthetic Persons (At the site of Patch): The onset of sweat production was very slow. At five minutes only seven persons sweated upto +1. One patient did not sweat at all, upto thirty minutes. At the end of 10 and 15 minutes the maximum ~~size~~ reached was +2 in four patients. At 30 minutes 3 patients did not have any sweat at all.

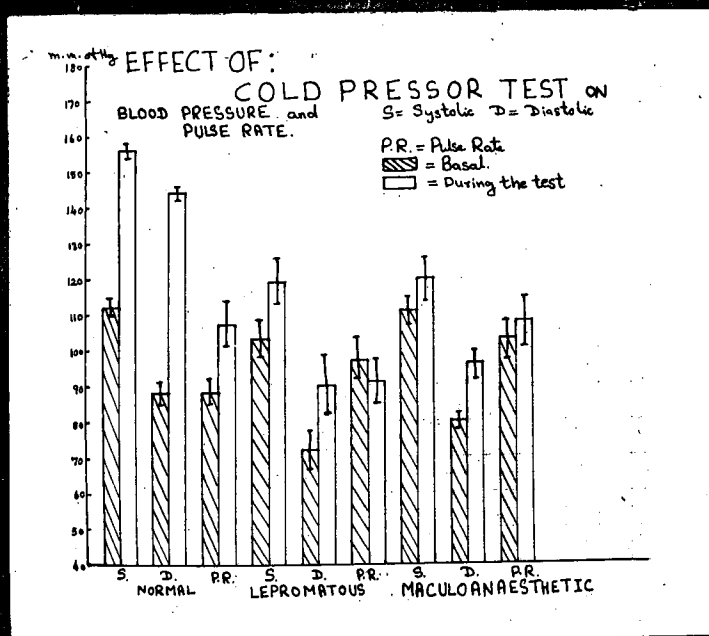
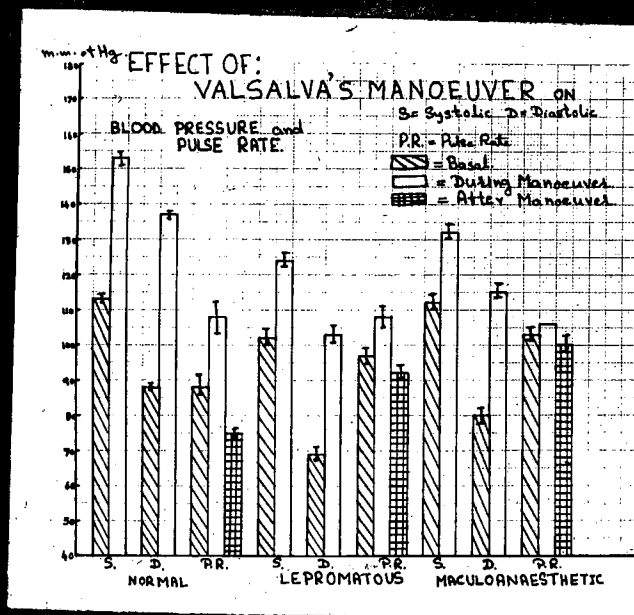
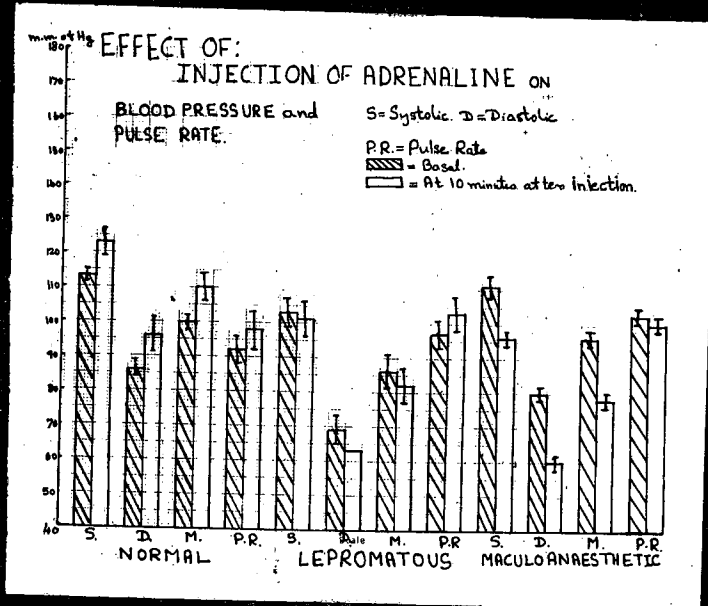
COMPARISON AMONGST THE GROUPS.

The degree of sweating did not differ in maculoanaesthetic cases at the two sites viz. Normal and Patch.

Similarly there was no difference between L.L. and Normal Persons.

But there was a significant difference as per following in other comparison.

The degree of sweating was most in Normal and Lepromatous,



Next was Maculoanaesthetic Cases at Normal Site and the least was at the site of Patch of Maculoanaesthetic Cases.

EFFECT OF ADRENALINE ON BLOOD PRESSURE.

(Please refer to Graphs on the Opposite page for Comparison of Effects of Injection of Adrenaline, Valsalva's Manoeuver and Cold Pressor Test on Blood Pressure and Pulse Rates.)

Normal Persons: The systolic pressure rose significantly higher at the end of 10 minutes but not after 20 minutes of the injection, to the extent of 10.2 m.m. of Hg with a range of -16 to +30 at 10 minutes, while at the end of 20 minutes the range was -10 to +20. But there was no change in diastolic pressure. Similar was the case with pulse pressure and mean pressure. The pulse rate also did not change.

Lepromatous Cases: Here there was no significant change at all in any of the parameters even at probability of 50%.

Maculoanaesthetic Cases: The systolic pressure fell significantly lower at 10 and 20 minutes after the injection. The fall produced was -15.8 and -13.8 respectively. Similarly was the decrease in diastolic which was to the extent of -20 m.m. of Hg and -12 m.m. Hg respectively. But what was more evident was feeling of giddiness

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produced by the drug Adrenaline in 4/10 patients in this group. Obviously the mean pressure was also decreased to the extent of - 17.3 and -7.6 m.m. of Hg. But there was no change in Pulse pressure and Heart Rate.

COMPARISON AMONGST THE GROUPS.

Systolic Pressure; The comparative results were the same at 10 and 20 minutes. In Normals there was a rise in Systolic pressure while in Lepromatous there was no change at all. In Maculoanaesthetic there was fall in pressure on the contrary.

Further, in Lepromatous 3/10 patients did not show any change at all at 10 and 20 minutes after the injection. While in Maculoanaesthetic 9/10 patients showed a definite fall below their basal readings, which is quite significant.

Diastolic Pressure: Here in Normal persons there was a rise which was not significant from rise in Lepromatous Cases. But in Maculoanaesthetic cases there was a fall in pressure and thus the results of Maculoanaesthetic differ from Lepromatous and Normal groups. This was the position at 10 as well as at 20 minutes.

Pulse Pressure: The pulse pressure changes differed from each other in that in Maculoanaesthetic there was a widening of pressure at 10 and 20 minutes while in Normal and Lepromatous there was

shortening. The shortening was not different at 10 minutes between Lepromatous and Normal but it was more of in Lepromatous at 20 minutes.

Mean Pressure: At 10 minutes there was a rise in mean pressure in Normal while in Lepromatous there was a small fall in it which was considerably different than the remarkable fall in Maculoanaesthetic.

While at 20 minutes in all the three groups there was a reduction in pressure which was not significantly different from each other amongst the groups.

Pulse Rate: The change in pulse rate did not differ in Normal and Lepromatous cases although both showed Tachycardia at 10 and 20 minutes. The tachycardia being more at 10 and lesser at 20 minutes. But the Maculoanaesthetic Cases showed Bradycardia at 10 and 20 minutes and thus the pulse rate differed from rest of the groups. Heart ^{rate} in this group differed very much from heart rate of Normal at 10 minutes but was not so at 20 minutes. When compared with Lepromatous the change produced was not significantly different at 10 minutes but it was significant at 20 minutes.

* APPENDICE *
* 101: 1 to 104 *
* PART 101: 73 to 104. *

APPENDIX No. 1 - Showing age, weight & height of the volunteers who have undergone this study.

NORMAL			LEPROMATOUS			MACULOANAESTHETIC		
Age	Weight	Height	Age	Weight	Height	Age	Weight	Height
25	45	165	24	42	162	29	45	168
25	47	150	25	51	176	24	41	168
24	48	170	28	48	170	25	43	165
21	45	160	22	47	163	24	48	165
30	62	160	29	45	158	29	47	162
24	58	175	24	43	164	25	43	150
24	58	170	25	42	162	22	42	166
28	55	165	21	43	162	25	46	168
30	53	165	32	49	165	25	51	164
24	49	158	35	46	160	22	42	162

Age : It is expressed in years as the number of completed years at the last birthday.
Weight; is expressed in Killograms and Height in Centimeters.

APPENDIX No. 2 - Basal Pressure and Pulse rate in Normal, Lepromatous and Macubanaesthetic Groups.

NORMAL				LEPROMATOUS				MACULOANAESTHETIC				
S	D	P. P.	P. R.	S	D	P. P.	P. R.	S	D	P. P.	P. R.	
110	80	30	107	90	60	30	79	110	80	30	94	
105	84	21	75	120	90	30	115	108	92	16	130	
120	90	30	76	120	79	41	103	96	70	26	100	
110	81	29	83	110	68	42	88	118	71	47	68	
115	79	36	90	88	59	29	94	110	78	32	125	
110	91	19	88	80	49	31	88	100	78	22	75	
111	79	32	75	105	80	25	94	110	80	30	107	
114	95	19	114	109	71	38	120	112	78	34	111	
125	110	15	94	90	68	22	100	110	80	30	97	
114	94	20	75	110	70	40	88	145	90	55	125	
MEAN	113.4	88.3	25.1	87.7	102.2	69.4	32.8	96.9	111.9	79.7	32.2	103.2
S.E.	± 0.57	± 0.99	± 2.2	± 4.4	± 4.5	± 4.4	± 2.1	± 4.1	± 4.16	± 2.20	± 3.60	± 6.60

NOTE: - S - denotes Systolic Pressure
P.P.-denotes Pulse Pressure

D - denotes Diastolic Pressure
P.R. - denotes Pulse Rate

APPENDIX No. 3 - Valsalva's Manoeuvre In Normal Persons

SYSTOLIC			DIASTOLIC			PULSE PRESSURE			PULSE RATE			
B	D.V.M.	A.V.M.	B	D.V.M.	A.V.M.	B	D.V.M.	A.V.M.	B	D.V.M.	A.V.M.	
110	140	110	80	126	80	30	14	30	107	90	88	
105	161	109	84	154	86	21	7	23	75	100	67	
120	145	120	90	130	90	30	15	30	76	120	69	
110	140	120	81	125	100	29	15	20	83	79	80	
115	210	120	79	170	70	36	40	50	90	131	75	
110	140	115	91	131	93	19	9	22	88	128	64	
111	155	120	79	140	82	32	15	38	75	83	66	
114	150	110	95	130	90	19	20	20	114	150	90	
125	148	123	110	130	105	15	18	18	94	114	84	
114	143	110	94	137	85	20	11	25	75	83	66	
MEAN	113.4	153.7	115.7	88.3	137.3	88.1	25.1	16.4	27.6	87.7	107.8	74.9
SE	± 0.57	± 2.10	± 2.0	± 0.99	± 1.40	± 3.3	± 2.2	± 2.9	± 3.10	± 4.4	± 7.73	± 1.55

NOTE: - "B" denotes Basal

"D.V.M." denotes During Valsalva's Manoeuvre

"A.V.M." denotes After Valsalva's Manoeuvre

APPENDIX No. 3-A - Change produced in Basal Parameters due to Valsalva's Manoeuvre in Systolic, Diastolic, pulse pressure and pulse rate in Normal Persons.

	SYSTOLIC	DIASTOLIC	PULSE PRESSURE	PULSE RATE	
				B-D.V.M.	B-A.V.M.
	30	46	- 16	- 17	- 19
	56	70	- 14	+ 25	- 8
	25	40	- 15	+ 44	- 7
	30	44	- 14	- 4	- 3
	95	91	+ 4	+ 41	- 15
	30	40	- 10	+ 40.5	- 24
	44	61	- 17	+ 8	- 9
	36	35	+ 1	+ 36	- 24
	23	20	+ 3	+ 20	- 10
	34	43	- 14	+ 8	- 9
MEAN	40.3	49.8	- 10	+ 10.5	- 10.4
S.E.	± 8	± 6.34	± 2.3	± 5.65	± 3.39

NOTE: - The sign (+) Plus denotes widening of pulse pressure and Tachycardia
 - The sign (-) Minus denotes shortening of Pulse Pressure and Bradycardia

APPENDIX No. 4 - Valsalva's Manoeuvre in Lepromatous Cases.

SYSTOLIC			DIASTOLIC			PULSE PRESSURE			PULSE RATE			
B	D.V.M.	A.V.M.	B	D.V.M.	A.V.M.	B	D.V.M.	A.V.M.	B	D.V.M.	A.V.M.	
90	129	90	60	100	60	30	29	30	79	75	79	
120	130	120	90	110	90	30	20	30	115	100	100	
120	158	110	79	130	65	41	28	45	103	107	100	
110	144	105	68	114	60	42	30	44	88	100	83	
88	100	90	59	81	60	29	19	30	94	100	88	
80	120	81	49	100	55	31	20	26	88	136	94	
105	130	110	80	120	80	25	10	30	94	115	88	
109	110	95	71	90	73	38	20	22	120	112	100	
90	100	90	68	90	63	22	10	27	100	83	94	
110	120	110	70	100	70	40	20	40	88	150	97	
MEAN	102.2	124.1	100.1	69.4	103.5	67.6	32.8	20.6	32.4	96.9	107.8	92.4
	± 4.5	± 5.8	± 3.94	± 4.4	± 4.8	± 3.40	± 2.1	± 2.2	± 2.46	± 4.1	± 7.1	± 2.37

NOTE: - - "B" denotes Basal
 - "D.V.M." denotes during Valsalva's Manoeuvre
 - "A.V.M." denotes after Valsalva's Manoeuvre

APPENDIX No. 4-A - Changes produced in Basal Parameters due to Valsalva's Manoeuvre in Lepromatous Cases.

	SYSTOLIC	DIASTOLIC	PULSE PRESSURE	PULSE RATE	
				B-D.V.M.	B-A.V.M.
	39	40	- 1	- 4	0
	10	20	- 10	- 15	- 15
	38	51	- 13	+ 4	- 3
	24	46	- 12	+ 12	- 5
	12	22	- 10	+ 6	- 6
	40	51	- 11	+ 48	+ 6
	35	25	- 20	+ 21	- 6
	1	19	- 18	- 8	- 20.5
	10	22	- 12	- 17	- 6
	10	30	- 20	+ 62	+ 9.5
MEAN	21.9	32.6	- 12.7	+ 10.9	- 7.6
S.E.	± 4.7	± 4.1	± 1.7	± 8.2	± 1.7

NOTE: - The sign (+) plus denotes widening of pulse pressure and Tachycardia.
The sign (-) minus denotes shortening of pulse pressure and Bradycardia.

APPENDIX No. 5 - Valsalva's Manoeuvre in Maculoanaesthetic Cases

SYSTOLIC			DIASTOLIC			PULSE PRESSURE			PULSE RATE			
B	D.V.M.	A.V.M.	B	D.V.M.	A.V.M.	B	D.V.M.	A.V.M.	B	D.V.M.	A.V.M.	
110	115	110	80	105	80	30	10	30	94	94	78	
108	121	110	92	111	90	16	10	20	130	112	115	
96	110	91	70	90	70	26	20	21	100	88	100	
118	130	110	71	120	78	47	10	32	68	75	85	
110	155	110	78	130	80	32	25	30	125	143	111	
100	110	100	78	90	78	22	20	22	75	88	97	
110	135	110	80	120	80	30	15	30	107	125	103	
112	140	110	78	121	70	34	19	30	111	85	107	
110	120	110	80	110	80	30	10	30	97	112	85	
145	185	140	90	148	90	55	47	50	125	136	125	
MEAN	111.9	132.1	110.1	79.7	114.5	79.6	32.2	18.6	29.5	103.2	105.8	100.7
SE	± 4.16	± 7.51	± 3.87	± 2.20	± 5.57	± 2.12	± 3.60	± 3.59	± 2.66	± 6.60	± 7.38	± 4.66

APPENDIX No. 5-A - Changes produced in Basal Parameters due to Valsalva's Manoeuvre in Maculoanaesthetic Cases.

	SYSTOLIC	DIASTOLIC	PULSE PRESSURE	PULSE RATE	
				B-D.V.M.	B-A.V.M.
	5	25	- 20	0	- 16
	13	19	- 6	- 17	- 15
	14	20	- 6	- 12	0
	12	49	- 37	+ 7	+ 17
	45	52	- 7	+ 18	- 14
	10	12	- 2	+ 13	+ 22
	25	40	- 15	+ 18	- 4
	28	43	- 15	+ 25	- 4
	10	30	- 20	+ 15	- 12
	40	58	- 8	+ 11	0
M E A N	20.2	34.8	- 13.6	+ 2.8	- 2.8
S E	± 4.27	± 4.96	± 3.25	± 4.06	± 3.04

NOTE: 1. The sign (+) plus denotes widening of pulse pressure and Tachycardia.
 2. The sign (-) minus denotes shortening of pulse pressure and Bradycardia.

APPENDIX No. 6 - COLD PRESSOR TEST - Cold Sensitivity in Leprosy Cases and Pain Threshold in Pain Intolerance in all the persons.

SENSITI-VITY		NORMAL		LEPROMATOUS		MACULOANAESTHETIC	
L. L.	M. A.	P. T.	P. I.	P. T.	P. I.	P. T.	P. I.
10	3	10	32	20	55	45	325
13	5	10	30	20	225	35	600
1	15	10	18	25	600	30	600
2	15	25	60	20	140	120	435
12	8	25	20	30	120	50	600
2	25	15	25	15	75	35	480
15	7	25	45	35	300	180	360
25	7	5	25	75	600	18	200
10	15	10	25	45	600	40	195
5	3	10	35	60	250	10	135
M E A N	9.5	10.3	14.5	31.5	34.5	56.3	393
	± 2.32	± 2.21	± 2.40	± 1.89	± 1.48	± 2.28	± 4.21

NOTE: - All the readings are in seconds.

L. L. - Lepromatous Cases

M. A. - Maculoanaesthetic Cases

P. I. - Pain Intolerance

P. T. - Pain Threshold

APPENDIX No. 7 - Cold Pressor Test - B. P. and Pulse Rate in Normal Persons.

SYSTOLIC		DIASTOLIC		PULSE PRESSURE		PULSE RATE		
BASAL	DURING TEST	BASAL	DURING TEST	BASAL	DURING TEST	BASAL	DURING TEST	
110	150	80	140	30	10	107	100	
100	164	84	156	16	8	75	100	
120	154	90	142	30	12	76	86	
110	150	81	140	29	10	83	88	
114	156	79	140	35	16	90	100	
110	150	91	142	19	8	88	125	
110	170	79	150	31	20	75	75	
108	160	95	150	13	10	114	145	
130	152	110	140	20	12	94	136	
110	150	94	138	16	12	75	118	
MEAN S.E.	112.2	155.6	88.3	143.8	23.9	11.8	87.7	107.3
	± 2.52	± 2.21	± 3.12	± 1.90	± 2.23	± 1.17	± 4.42	± 7.23

APPENDIX No. 7-A - Changes produced in Basal Parameters during Cold Pressor Test
(Normal Persons)

	SYSTOLIC	DIASTOLIC	PULSE PRESSURE	PULSE RATE
	40	60	20	- 7
	64	62	8	+ 25
	34	52	18	+ 10
	40	59	19	+ 5
	42	61	19	+ 10
	40	51	11	+ 37
	60	71	11	0
	52	55	3	+ 31
	22	30	8	+ 42
	40	44	4	+ 43
M E A N	43.4	55.5	12.1	+ 20 ¹ / ₃
S. E.	± 3.87	± 3.92	± 1.81	± 8.42

NOTE: - The sign (+) plus denotes Tachycardia.
The sign (-) minus denotes Bradycardia.

APPENDIX No. 8 - COLD PRESSOR TEST - B. P. and Pulse Rate in Lepromatous Cases

SYSTOLIC		DIASTOLIC		PULSE PRESSURE		PULSE RATE		
BASAL	DURING TEST	BASAL	DURING TEST	BASAL	DURING TEST	BASAL	DURING TEST	
90	120	60	100	30	20	79	83	
120	140	90	120	30	20	115	107	
120	138	79	72	41	66	103	93	
110	130	68	85	42	45	88	50	
88	100	60	60	28	40	94	83	
80	100	49	70	31	30	88	88	
110	140	95	130	15	10	94	100	
109	110	71	80	38	30	120	115	
90	90	68	70	22	20	100	88	
110	120	80	110	30	10	88	107	
M E A N S E.	102.7	118.8	72	89.7	30.7	29.1	96.9	91.4
	± 4.54	± 5.79	± 4.49	± 7.57	± 2.07	± 5.96	± 4.06	± 5.78

APPENDIX No. 8-A - Changes produced in Basal Parameters during Cold Pressor Test
(Lepromatous Cases)

	SYSTOLIC	DIASTOLIC	PULSE PRESSURE	PULSE RATE
	30	40	- 10	+ 4
	20	30	- 10	- 8
	18	- 7	+ 25	- 10
	20	17	+ 3	- 38
	12	0	+ 12	- 11
	20	21	- 1	0
	30	35	- 5	+ 6
	1	9	- 8	- 5
	0	2	- 2	- 12
	10	30	- 20	+ 19
M E A N	16.1	17.7	- 1.6	- 5.5
S E	± 3.28	± 5.1	± 4.6	± 2.81

NOTE: - 1. The sign (+) denotes widening of pulse pressure and Tachycardia.
2. The sign (-) denotes shortening of pulse pressure and Bradycardia
and fall in Diastolic pressure.

APPENDIX No. 9 - COLD PRESSOR TEST - B. P. and Pulse Rate in Maculoanaesthetic Cases.

SYSTOLIC		DIASTOLIC		PULSE PRESSURE		PULSE RATE		
BASAL	DURING TEST	BASAL	DURING TEST	BASAL	DURING TEST	BASAL	DURING TEST	
110	110	80	90	30	20	94	83	
108	100	92	90	16	10	130	125	
96	102	70	90	26	12	100	100	
118	118	71	110	47	8	68	83	
110	120	78	78	32	35	126	125	
100	130	78	110	22	20	75	79	
110	110	80	90	30	20	107	100	
112	118	78	92	34	26	111	115	
110	160	80	100	30	60	97	100	
140	140	90	110	55	30	125	166	
MEAN S.E.	111.4	120.8	79.7	96	32.2	24.1	103.3	107.6
	± 3.73	± 5.80	± 2.20	± 3.48	± 4.79	± 4.83	± 6.63	± 8.35

APPENDIX No. 9-A - Changes produced in Basal Parameters during Cold Pressor test.
(Macubanaesthetic Cases).

	SYSTOLIC	DIASTOLIC	PULSE PRESSURE	PULSE RATE
	0	10	- 10	- 11
	8	- 2	- 6	- 5
	6	20	- 14	0
	0	39	- 39	+ 15
	10	0	+ 3	- 1
	20	32	- 2	+ 4
	0	10	- 10	- 7
	6	14	- 8	+ 4
	50	20	+ 30	+ 3
	0	20	- 25	+ 41
<u>M</u> <u>E</u> <u>A</u> <u>N</u>	11.0	16.3	- 8.1	+ 4.3
<u>S</u> <u>E</u> <u>E</u>	± 5.18	± 4.06	± 5.77	± 4.52

NOTE: - 1. The sign (+) plus denotes widening of Pulse Pressure and Tachycardia.
2. The sign (-) minus denotes shortening of Pulse Pressure and Bradycardia
and fall/in Diastolic pressure.

APPENDIX No. 10 - Effect of Homatropine on Pupillary size in all the three groups.
(At the end of 30 Minutes).

NORMAL		LEPROMATOUS		MACULOANAESTHETIC		
BASAL	FINAL	BASAL	FINAL	BASAL	FINAL	
1	5	2	6	2	4	
2	3	2	4	2	4	
2	4	3	4	2	5	
2	3	2	3	3	4	
3	6	2	5	2	4	
2.5	4	2	5	2	3	
2	4	2	4	2	3	
2	4	2	3	3	4	
2	3	2	3	3	3	
2	3	2	4	1	3	
MEAN	2.05	3.9	2.1	4.1	2.2	3.7
S.E.	± 0.16	± 0.31	± 0.1	± 0.1	± 0.20	± 0.21

The final reading denotes the size of the pupil at the end of 30 minutes after the instillation of Homatropine in both the eyes. There is no difference between the pupillary diameter of both the eyes hence the average of the readings is taken in m.m.

APPENDIX No. 10-A - The increase in size of the pupil by Homatropine

	NORMAL	LEPROMATOUS	MACULOANAESTHETIC
	4	4	2
	1	2	2
	2	1	3
	1	1	1
	3	3	2
	1.5	3	1
	2	2	1
	2	1	1
	1	1	0
	1	2	2
M E A N	1.8	2.0	1.5
S E	± 0.056	± 0.059	± 0.046

Histamine triple response in Normal Persons

The size of the WEEAL EXPRESSED IN m.m.

	ZERO MINUTE	ONE MINUTE	TWO MINUTE	THREE MINUTE	FIVE MINUTE	TEN MIN.	FIFTEEN MINUTE
	8	9	11	12	13	16	<u>19</u>
	7	10	13	18	18	18	18
	8	8	16	16	18	18	18
	8	14	14	18	19	<u>20</u>	20
	8	10	10	<u>18</u>	18	18	18
	9	11	13	14	<u>18</u>	18	18
	7	11	<u>16</u>	16	16	16	16
	6	6	12	12	12	<u>16</u>	16
	7	7	11	<u>13</u>	13	13	13
	9	12	16	18	18	20	<u>22</u>
Mean:	7.7	9.8	13.2	15.5	16.13	17.3	17.8
S.E.: $\pm$	0.3	± 0.75	± 0.71	± 0.81	± 0.9	± 0.67	± 0.77

The figure which is underlined denotes the maximum size attained at the corresponding time.

The average time for maximum size is 9.1 minutes ± 1.04

6 /10 People showed maximum response by 5 minutes.

NOTE:- The readings of all the tables from table No. 11 to 15 are in millimeters.

Histamine triple response in

Lepromatous Cases.

The size of the WHEEL IS expressed in m.m.

	ZERO MINUTE	ONE MINUTE	TWO MINUTES	THREE MINUTES	FIVE MINUTES	TEN MINUTES	FIFTEEN MIN.
	8	9	9	13	13	<u>19</u>	17
	6	7	12	10	13	<u>14</u>	14
	7	8.5	12	12	12	14	<u>15</u>
	8	8	16	14	14	<u>17</u>	17
	8	14	<u>18</u>	<u>18</u>	21	<u>22</u>	22
	8	12	10	<u>18</u>	18	18	18
	7	9	13	12	14	16	<u>18</u>
	9	12	12	<u>13</u>	13	13	13
	8	10	13	13	13	18	<u>21</u>
	8	11	11	12	14	<u>18</u>	18
Mean:	7.7	10.0	12.6	13.5	14.5	16.9	17.3
S.E.: $\pm$	0.26	$\pm$ 0.69	$\pm$ 1.1	$\pm$ 0.82	$\pm$ 0.88	$\pm$ 0.86	$\pm$ 0.89

The figure which is underlined denotes the maximum size which ^{is} attained at corresponding time.

The average time for maximum size is 10.1. minutes $\pm$ 1.37

At 10 minutes 7/10 showed the maximum response.

Histamine Triple Response in Maculopaneesthetic Cases
(Normal Site) Size of the WHEAL is expressed in M.M.

	ZERO MIN.:	ONE MIN :	TWO MIN :	THREE MIN :	FIVE MIN. :	TEN MIN. :	FIFTEEN MINUTES
	8	10	11	11	<u>16</u>	16	16
	9	15	15	18	<u>20</u>	20	20
	12	13	20	20	20	<u>22</u>	22
	7	7	9	10	12	<u>16</u>	16
	8	10	12	14	14	<u>16</u>	16
	7	11	13	13	16	<u>18</u>	18
	8	9	11	12	14	14	<u>16</u>
	8	8	9	12	12	14	<u>15</u>
	7	7	<u>9</u>	9	9	9	9
	6	6	7	10	10	14	<u>18</u>
Mean:8	8.0	9.6	11.6	11.8	14.3	15.9	16.6
S.E.±	0.51	± 0.85	± 1.1	± 1.18	± 1.19	± 1.30	± 1.09

The figure which is underlined denotes the maximum size attained at the corresponding time.

The average time for maximum size is 9.7 minutes $\pm$ 1.44

At 10 minutes 7/10 people showed maximum response.

Histamine triple response in Maculoanaesthetic Cases
(At the site of Patch) size of the wheal expressed in m.m.

ZERO MINUTE : ONE MIN. : TWO MIN. : THREE MIN. : FIVE MIN. : TEN MIN. : FIFTEEN MIN.							
8	10	11	11	<u>18</u>	18	12	
7	<u>12</u>	12	12	12	12	12	
6	9	<u>12</u>	12	12	12	12	
6	6	9	10	<u>12</u>	12	12	
8	10	12	<u>14</u>	14	14	14	
7	11	13	<u>15</u>	<u>15</u>	<u>16</u>	<u>18</u>	
8	9	11	12	14	14	<u>16</u>	
8	8	9	12	12	<u>13</u>	13	
7	8	10	10	<u>11</u>	11	11	
8	8	8	11	11	<u>14</u>	14	
Mean:	7.4	9.1	10.7	11.7	13.1	13.6	14.0
S.E. $\pm$	0.27	$\pm$ 0.55	$\pm$ 0.52	$\pm$ 0.39	$\pm$ 0.69	$\pm$ 0.67	$\pm$ 0.80

The figure which is underlined denotes the maximum size attained at the corresponding time.

The average time for maximum size is 7.1 minutes $\pm$ 1.61

6/10 people showed maximum response upto 5 minutes.

8/10 people showed maximum response upto 10 minutes.

APPENDIX No. 15 - The net enlargement in the size of the wheal at the end of 30 minutes.

	NORMAL	LEPROMATOUS	MACULOANAESTHETIC (AT NORMAL SITE)	MACULOANAESTHETIC (AT THE SITE OF PATCH)
	11	9	8	10
	11	8	11	5
	10	8	10	6
	12	9	9	6
	10	14	8	6
	9	10	11	11
	9	11	8	8
	10	4	7	5
	6	13	2	4
	13	10	12	6
M E A N	10.1	9.6	8.6	6.6
S E	± 0.60	± 0.88	± 0.89	± 0.76

TYPE OF CASE	TIME (MINUTES)	0	+	++	+++	++++
NORMAL	5	0	7	3	0	0
	10	1	3	3	3	0
	15	2	2	4	2	0
	30	7	2	1	0	0
LEPROMATOUS	5	3	3	2	2	0
	10	3	0	4	3	0
	15	1	1	5	3	0
	30	1	4	3	1	1
MACULOANAESTHETIC (NORMAL SITE)	5	2	8	0	0	0
	10	1	7	2	0	0
	15	1	8	1	0	0
	30	4	6	0	0	0
MACULOANAESTHETIC (AT THE SITE OF P-ATCH)	5	3	7	0	0	0
	10	1	5	4	0	0
	15	1	5	4	0	0
	30	3	6	1	0	0

Effect of Adrenaline on B.P.& Pulse Rate in Normal Persons.

SYSTOLIC : DIASTOLIC : MEAN PRESSURE : PULSE PRESSURE : PULSE RATE [IN THAT ORDER]															
B : 10min : 20min :			B : 10min : 20min :			B : 10min : 20min :			B : 10min : 20min :			B : 10min : 20min :			
110	110	110	80	80	80	95	95	95	30	30	30	107	75	83	
110	110	110	80	80	80	95	95	95	30	30	30	75	68	60	
120	140	130	90	120	110	105	130	120	30	20	20	100	100	80	
110	120	110	80	100	80	95	115	95	30	20	30	93	125	125	
104	110	110	78	70	70	96	90	90	36	40	40	90	107	88	
110	130	130	90	110	110	100	120	120	20	20	20	88	125	110	
110	140	110	78	120	80	94	130	95	32	20	30	75	75	75	
108	110	108	90	82	90	99	101	99	18	18	18	114	107	112	
130	114	120	110	90	90	120	102	105	20	24	30	94	115	94	
110	140	110	88	100	88	99	120	99	22	40	22	83	83	83	
MEAN:	113.2	123.4	114.8	86.4	96.2	87.8	99.8	109.8	91.4	26.8	26.2	27.0	91.8	98	91
S.E.±	±	±	±	±	±	±	±	±	±	±	±	±	±	±	±
	2.16	4.11	4.69	3.09	5.40	7.28	2.48	4.74	4.40	1.96	2.66	2.11	4.0	6.71	5.77

Changes produced in Basal Parameters after the injection of
Adrenaline in Normal Persons.

SYSTOLIC :		DIASTOLIC :		PULSE PRESSURE :		MEAN PRESSURE :		PULSE RATE		
10min	20min	10min	20min	10min	20min	10min	20min	10min	20 min	
0	0	0	0	0	0	0	0	- 32	- 24	
0	0	0	0	0	0	0	0	- 7	- 15	
+ 20	+ 10	+ 30	+ 20	+ 10	- 10	+ 25	+ 15	0	- 20	
+ 10	0	+ 20	0	- 10	0	+ 20	0	+ 32	+ 32	
- 4	- 4	- 8	- 8	+ 4	+ 4	- 6	- 6	+ 17	- 2	
+ 20	+ 20	+ 20	+ 20	0	0	+ 20	+ 20	+ 37	+ 22	
+ 30	0	+ 42	+ 2	- 12	- 2	+ 36	+ 1	0	0	
+ 2	0	+ 2	0	0	0	+ 2	0	- 7	- 2	
- 16	- 10	- 20	- 20	+ 4	+ 10	+ 18	+ 17	+ 21	0	
+ 30	0	+ 12	+ 12	+ 18	0	+ 21	0	0	0	
MEAN:	+ 10.2	+ 1.6	+ 9.8	2.6	- 0.6	+ 0.2	+ 13.6	+ 4.7	+ 6.1	- 0.9
E.:	4.63	2.5	5.88	3.92	2.77	1.54	4.31	2.84	2.40	5.47

Note:- (1) The Sign (+) denotes increase in pressure and Tachycardia.

(2) The Sign (-) denotes decrease in pressure and Bradycardia.

Effect of Adrenaline on B.P. and Pulse Rate in Lepromatous Cases.

SYSTOLIC : DIASTOLIC : MEAN PRESSURE : PULSE PRESSURE : PULSE RATE [IN THAT ORDER]														
B : 10min : 20min			B : 10min : 20min			B : 10min : 20min			B : 10min : 20min			B : 10min : 20min		
90	100	90	60	70	60	75	85	75	30	30	30	79	75	68
120	120	120	90	100	100	105	110	105	30	20	30	115	100	100
120	122	110	80	70	60	100	96	85	40	52	50	104	100	104
110	98	110	68	50	60	89	74	85	42	52	50	88	125	125
88	90	90	59	60	60	74	75	75	29	30	30	94	125	125
80	80	80	49	30	50	65	55	65	31	50	30	88	94	88
110	110	110	80	80	80	95	95	95	30	30	30	94	115	100
110	90	90	70	60	60	90	70	70	40	30	30	120	100	115
90	80	80	68	60	60	79	70	70	22	20	20	100	94	88
110	120	110	70	50	70	90	85	90	40	70	40	88	100	100
102.8	101	99	69.4	63	66	86.2	82	82.	33.4	38.4	31.	97	102.8	101.3
4.56	5.14	4.58	3.75	5.98	4.47	3.99	4.95	4.24	2.09	5.23	5.57	4.07	4.8	5.57

Changes produced in Basal Parameters after the injection of
Adrenaline. (Lepromatous Cases)

SYSTOLIC : DIASTOLIC : PULSE PRESSURE : MEAN PRESSURE : PULSE RATE									
10min	20min	10min	20min	10min	20min	10min	20 min	10min	20 min
+ 10	0	+ 10	0	0	0	+ 10	0	- 4	- 11
0	0	+ 10	+ 10	- 10	0	+ 5	0	- 15	- 15
+ 2	- 10	- 10	- 20	+ 12	+ 10	- 4	- 15	- 4	+ 10
- 12	0	- 18	- 8	+ 10	+ 8	- 15	- 4	+ 37	+ 37
+ 2	+ 2	+ 1	+ 1	+ 1	+ 1	+ 1	+ 1	+ 31	+ 31
0	0	- 19	+ 1	+ 19	+ 1	- 10	0	+ 6	0
0	0	0	0	0	0	0	0	+ 21	+ 6
- 20	- 20	- 10	- 10	- 10	+ 10	- 20	- 20	- 20	- 5
- 10	- 10	- 8	- 8	- 2	+ 2	- 9	- 9	- 6	- 12
+ 10	0	- 20	0	+ 30	0	- 5	0	+ 12	+ 12
AN: -1.8	-3.8	-6.4	-3.4	+5.0	+2.4	-4.7	-4.7	+5.8	+5.3
E.: 3.01	2.25	3.54	1.30	4.02	1.51	2.88	2.34	5.36	5.7

NOTE: - (1) The Sign Plus (+) Denotes rise in pressure and Tachycardia.
(2) The Sign Minus (-) Denotes fall in pressure and Bradycardia.

SYSTOLIC			: DIASTOLIC		: MEAN PRESSURE		: PULSE PRESSURE			: PULSE RATE						
B : 10min : 20min			: B : 10min : 20min		: E : 10min : 20min		: B : 10min : 20min			: B : 10min : 20 min						
110	90	100	80	58	64	95	75	82	30	32	36	94	79	75		
108	100	100	92	70	90	100	85	95	16	30	10	130	107	125		
96	90	80	70	30	40	83	70	60	26	40	40	100	88	94		
118	84	96	72	52	76	95	68	86	46	32	20	68	78	71		
	112	110	78	70	70	94	91	90	32	42	40	125	136	107		
100	80	100	78	58	80	89	69	90	22	22	20	75	75	75		
110	90	90	80	60	60	95	75	75	30	30	30	107	115	107		
112	110	90	78	60	58	95	85	74	34	50	32	111	100	107		
110	90	100	80	50	70	95	70	85	30	40	30	97	94	83		
140	110	120	90	70	80	115	90	100	50	40	40	125	125	125		
MEAN: 111.4			95.6	98.6	79.8	59.8	68.8	95.6	77.8	83.7	31.6	35.8	29.8	103.2	99.7	- 96.9
S.E.: 3.73			3.66	3.48	2.16	2.50	4.47	2.59	2.86	3.60	3.21	2.54	3.16	6.6	6.61	6.40

Changes produced in Basal Parameters after the injection of Adrenaline.
(Maculoanaesthetic Cases)

SYSTOLIC		:	DIASTOLIC		:	PULSE PRESSURE		:	MEAN PRESSURE		:	PULSE RATE		
10min	20min	:	10min	20 Min	:	10 min	20 min	:	10 min	20 min	:	10 min	20 min	:
- 20	- 10	:	- 22	- 16	:	+ 2	+ 6	:	- 20	- 7	:	- 15	- 19	:
- 8	- 8	:	- 22	- 2	:	+ 14	- 6	:	- 15	- 5	:	+ 23	- 5	:
- 6	- 16	:	- 20	- 30	:	+ 14	+ 14	:	- 13	- 23	:	- 12	- 6	:
- 34	- 22	:	- 20	4	:	- 14	- 26	:	- 27	- 9	:	+ 10	+ 3	:
2	0	:	- 8	- 8	:	+ 10	+ 8	:	- 3	- 4	:	+ 11	- 18	:
- 20	0	:	- 20	2	:	0	- 2	:	- 20	21	:	0	0	:
- 20	- 20	:	- 20	- 20	:	0	0	:	- 20	- 20	:	+ 8	0	:
- 2	- 22	:	- 18	- 20	:	+ 16	- 2	:	- 10	- 19	:	- 11	- 4	:
- 20	- 10	:	- 30	- 20	:	+ 10	0	:	- 20	- 5	:	- 3	- 14	:
- 30	- 20	:	- 20	- 10	:	- 10	- 10	:	- 25	- 5	:	0	0	:
MEAN:	-15.8	:	-13.8	- 20	:	- 12	+ 4.2	:	+ 1.8	-17.3	:	- 7.6	-3.5	:
S.E.:	3.74	:	2.04	1.67	:	3.84	2.96	:	3.5	2.25	:	3.92	3.63	:

NOTE:- (1) The Sign plus (+) denotes rise in pressure and Tachycardia.

(2) The Sign minus (-)denotes fall in pressure and Bradycardia.

* D I S C U S S I O N *

Leprosy is a bacterial disease which causes neurological manifestations. So far research workers have studied the peripheral neuropathies produced by this disease. But the functional status of its autonomic counterpart still remains to be unexplored as also was the central nervous system's manifestations if any.

It appears from the literature review that the investigations of Autonomic System was done only in relation to local axon reflexes namely Histamine Triple Response and Sweat Function test. But a Comparative data of this mechanism of function has not been done with normal persons as is done in our study.

Leprosy is the only tropical disease which has got such a broad range of clinical manifestations depending upon which various types have been classified. So it was necessary to choose extremes of types of Leprosy namely L.L. (Lepromatous) and M.A. (Maculoanaesthetic) cases to evaluate the difference if any between them. The difference between the two ends of the spectrum of Leprosy. It is well known that M.A. cases are predominantly associated with sensory changes while L.L. cases are not so. But the evidence in our studies show that even in L.L. the sensation of Cold is affected.

Autonomic nerves pass along with spinal mixed nerves and hence as described in aims and objectives it is worth investigating autonomic functions with sensory functions by way of a test like cold pressor test.

In our studies we have followed the same order of performance of tests viz. 1. Valsalva's Manoeuver. 2. Cold Pressor Test.

3. Homatropine in Eyes. 4. Histamine Triple Response.

5. Sweat Function Test. 6. Injection of Adrenaline.

This order is followed throughout the study as the change in order may give different results. For, Example : If cold pressor test is followed by injection of adrenaline then perhaps the response to latter may not be consistent in all the groups and persons.

It is evident from the results that the basal blood pressure and body weight are low in Leprosy cases. This may be due to the disease process. As both systolic and diastolic pressures are low in Leprosy groups but within wider pulse pressure the cardiac output is normal. Secondly the heart rate did not differ from each other amongst the groups. The response to different test of sympathetic function of Leprosy group was rather feeble, which infers that the sympathetic system in Leprosy is affected.

The possibility of vagal hypotonicity is eliminated as had it been so the increased vagal tone, then the patient would have certainly hyper reacted to Valsalva's Manoeuver and Cold pressor test. Further, the response to adrenaline is practically negligible in L.L. and is of hypotensive type in M.A. suggest the sympathetic affection clearly.

In Valsalva's Manoeuvre one incidental finding in Normal group was a very haig rise in Systolic and Diastolic to the extent of 95 and 91 m.m. of Hg in an individual. Further, the same person has shown similar rise in Cold pressor test suggest his tendency to develop hypertension.

In both the Leprosy groups there is no change in pulse rate at all either during or after the manoeuver, thus clearly points out the deficiency or malfunctioning of baroreceptors. Further, the rise in systolic and diastolic pressure are lesser than normal suggests lack of vasomotor tone and dificient ionotropic activity of myocardium. In one M.A. case there is absolutely no change at all which clearly denotes the deficit.

It appears that both myocardium and the vasomotor tone have been involved, as if it is only one of them, then the compensatory mechanisms would have restored the pulse pressure within normal range but in this study it was evident that the systolic and diastolic pressures are low buttthe pulse pressure high.

Further, as mentioned in Handbook of Physiology(1965) and Campbell probably there is a lesion in the spinal cord in Leprosy group which is responsible for comparative non-responsiveness of autonomic system as in Tabes Dorsalis. As centrally as well as in hypothalamic region the autonomic system is normal as evidenced by

instillation of Homatropine in eyes and the casual measurement of arm and body temperature in the Leprosy patients, although the possibility can not be excluded as there is high incidence of Glaucoma in Leprosy.

The findings of prolonged P-R interval in Valsalva's Manoeuvre as shown by Hurst and Logue (1968) can neither be confirmed nor contraindicated due to small size of sample. But there is a definite Tachycardia in Normal as compared to none in Leprosy groups. This clearly points out the malfunctioning of central cardio-inhibitory and/or acceleratory mechanisms, along with the deficiency of myocardium as evidenced by smaller systolic rise in pressure. But the normal restoration of pressure changes after the manoeuvre suggests no abnormality with the mechanical part of thoracic cage related to manoeuvre.

In cold pressor test the obvious finding in M.A. was lack of sensitivity to cold and a very high threshold to pain and pain intolerance. But the results were also the same in L.L.

Another interesting fact was that in cases where there was high pain threshold and tolerance, there was a fall in diastolic pressure. This suggests that the sensitivity to arterioles and/or

capillaries due to direct action of Cold is not changed but it is only the reflex vasomotor tone that is altered and affected.

The smaller change in systolic and diastolic pressures with no or only little change in pulse rate once again is in favour of an evidence regarding the hypo-reactivity of symphathetic system which may be due to in this case to lesser release of adrenaline by adrenal medulla and lesser release of nor-adrenaline by post-ganglionic adrenergic nerve fibres.

Here also the cholinergic counterpart appears normal as in some cases there is a bradycardia and fall in diastolic pressure instead of reverse and the net change in groups being a little towards Tachycardia and rise in diastolic pressure.

The complete silence of pulse rate changes also suggest the hypo-activity of pacemakers and the sensitivity of change in temperature of myocardium is also decreased.

The cold sensitivity, threshold and intolerance shows that there is no difference between L.L. and M.A. as far as the sensation of Cold is concerned.

The above results naturally demands further investigations. The organs of Ruffini should also be checked using a hot pressor test.

Secondly the direct action of Cold on myocardium and pacemakers could be evaluated by designing a test in which a very cold water should be asked to drink and the changes in pulse rate ~~should~~ and blood pressure should be recorded.

Normal volunteers showed a remarkable rise of 43.4 and 55.5 m.m. of Hg in systolic and diastolic, this was greater than that in study reported by Hines and Brown (1933). In their study it was only 8.0m.m. in each. This may be due to the smaller difference in ambient temperature and the cold pressor temperature. As in our study there was ^{higher} gradient due to a higher ambient temperature.

It appears from the injection of adrenaline that it may not be the poor release of adrenaline or nor-adrenaline from respective sites in cold pressor test but it may be the lesser sensitivity or abnormality of Beta-1 and Alpha receptors with or without hyper-reactivity of Beat-2 receptors.

The injection of adrenaline did not produce any appreciable change in pulse rate in any one of the three groups including normal persons. But it did produce a rise in systolic in Normals, this suggests a dose of 200mcg was sufficient to produce at least a stimulation of myocardium though not of peripheral resistance. But what was more interesting is a remarkable fall in systolic as well as in diastolic in M.A. This shows a phenomenon which is something parallel to Dale's

Vasomotor reversal. It may be due to either lack of sensitivity of Alpha receptors as if a physiological alpha blockade or oversensitivity of Beta-2 receptors or both. Further, there may be hypo-activity of myocardium due to abnormal or hyposensitivity of Beta-1 receptors.

One of the most fascinating findings of the study was that 4/10 patients in M.A. group felt giddy due to adrenaline which is clearly as a result of remarkable fall of 18 and 20 m.m. of Hg in systolic and diastolic pressures respectively. This finding is of therapeutic significance and needs a greater evaluation. It would be rewarding to inject phenylephrine or nor-adrenaline and explore whether there is a rise which will be of course due to selective Alpha stimulation or no change at all which will suggest a Beta affection.

In L.L. there was no change in any of the parameters which of course may be due to ineffective dose or the malfunctioning of receptors. Response to adrenaline in L.L. cases as compared to that in M.A. clearly delineates the difference between the two forms of the same disease.

The evidence about the normal parasympathetic activity is produced by a absolutely normal response in all the three groups

to instillation of Homatropine. Not only the response was normal but even the initial size of the pupils were almost the same and without any after symptoms in any of the three groups.

Thus from the overall view of all the above tests it appears that it is the symphathetic system that is markedly affected. It is the symphathetic part which is hyporeactive to various stimuli. There appears to be no apparent reason for the selective affection of symphathetic except that the fibres of this system are more peripherally spread along with mixed spinal nerves. It is well known fact that in Leprosy the peripheral sensory nerves are affected hence it is the anatomical distribution which has affected symphathetic more than its counterpart.

So far much work has not been done on Histamine triple response test on dark skin people and nothing has been said about the wheal so formed. In our study the rate of formation of wheal was very slow in patches of M.A. as compared to rest of the three varieties. Further, the rate of formation of wheal and its size runs parallel.

Further as pointed out in Cold pressor test about the arteriolar dilatation it appears that the findings of Lewis(1927) that the arteriolar dilatation is reflected alone by the flare needs re-orientation. What is evident from our study is that it is also the

wheal which governed by the nerve fibres and not just the capillary dilatation only. Thus the size of the wheal should be the criterion of assessing the local axon reflex than the flare alone as it is a subjective index.

The colour of the wheal produced did not differ from group to group and it was mahogany red suggesting the active participation of arterioles. Had it been capillaries it would have certainly turned its colour to bluish tinge at least in Normals for in Normals the response was faster and the time of observation of the wheal is 15 minutes in each of the cases.

The lesser response to Histamine in M.A. cases at the site of patch could be due to the fact that the receptors are degenerated or that there is a partial fibrous barrier at the arteriolar walls, which prevents the transudate to come from the walls.

So in conclusion the local axon mechanism is markedly affected in M.A. cases at the site of patch, next to that is the normal look site in M.A. and least affection was that in L.L. Thus our findings are in conformity with that of Herbert H Gass that in Leprosy it is the peripheral nerve's twigs which are affected.

In 1971 H.K.Mathur studied the sweat function in Leprosy

cases but there were no normal persons as well as Lepromatous Cases in the same trial. In our study this error has been eliminated. From our study it can be inferred that the sweat is not at all affected in Lepromatous Cases. But it is remarkably affected in M.A. cases, as shown by several workers. But what is more interesting is that the sweat secretion is as deficient in patch of M.A. as in their counterparts. Thus it is not necessary to test sweat at the site of patch but even the testing at normal or apparently normal site can serve the purpose. Thus as far as sweat function goes it is the cholinergic sympathetic system that is affected.

It is noted that the formation of sweat is slow at the site of patch in M.A. cases than in any other groups, so also was the histaminergic wheal. Secondly the rate and amount of formation of sweat is least in M.A. cases at patch as also as the Histaminergic Wheal. It is also noted that in L.L. the sweat function is normal. All this evidence suggests that it is the nerve fibres and/or sweat glands that is affected as already pointed out by A.C. Parikh et.al. (1960).

Our findings differ from that of Felix Cinreas (1949) in that L.L. cases show normal responses than in later Author's study where it has shown that there is less response than Normal. Similarly the findings of Harry L. Arnold (1949) differs from us in that they have found equal importance in M.A. and L.L. cases.

One thing which is to be pointed out about the calibration of sweat. The method followed lacked sufficient accuracy. Instead a method designed by Dabholkar and Madhvanath (1977) may be followed although it is not yet completed. Here the sweat is collected on a piece of filter paper No 42 Whatman and sealed in a polyethylene sheet. The sample so formed is exposed to atomic reactor Apsara B.A.R.C. and the conversion of stable Na to radioactive Na is counted by selecting the requisite wave length and voltage in E.C.I.L. well type counter. A graph is plotted of a known concentration of Na and the sample value can thus be calculated. This method is undergoing a trial for its standardisation.

Further, our findings do agree with that of Yewalkar and Sanjana in that there is no recovery of sweat function inspite of treatment. As in our case it is about 8-12 years of therapy to which the patients were exposed. It was also noted that the other lesions of these patients have also decreased suggest that the patients were responsive to treatment to lesions other than the neurological.

In our studies we have eliminated the bias of circadian variation (Jean Timbal 1975) in sweat formation by conducting the trial during the day time. Secondly the effects of humidity and temperature are eliminated by conducting the trial at the same humidity and temperature.

If an overall study is done of the tables, it becomes evident that in Valsalva's Manoeuvre, Cold Pressor Test, and the injection of adrenaline there is a fairly high standard error which suggests a wide variation within the group, and reflects the smaller size of the sample. But all the results are expressed and explained on the basis of 95% probability or more eliminated the chances of erroneous interpretation but it certainly demands a trial on a sample of at least roughly 30 to 40 persons in each group.

* SUMMARY AND CONCLUSION. *

1. The disease called Leprosy is known since ages but the information about its autonomic functions is lacking so far.

2. That is why we undertook this problem with the aid of physiological and pharmacological parameters for exploration.

3. A comparative, open, controlled trial was undertaken under equal environmental conditions in Normal volunteers, and the two groups of Leprosy patients namely Lepromatous and Maculoanaesthetic types.

4. The parameters chosen were Valsalva's Manoeuvre, Cold Pressor test, Instillation of Homatropine in eyes, Intradermal injections of Histamine Acid Phosphate and Carbachol and Sub-cutaneous injection Adrenaline, ⁱⁿ every patients.
^

5. The heart rate was counted by the aid ^{of} E.C.G. machine for the sake of precision and the pupillary diameter was measured with the help of simple paper pupillometer. The size of the wheal was measured with the help of Vernier Calipers and the amount of Sweat was estimated by the Methods of N.K.Mathur et.al.

6. The results of the trial were evaluated for comparison by

the help of Student's 't' test and paired 't' for all the tests except Sweat function test, which was evaluated by Chi-Square test. All the results were compared at a probability value of 95%.

7. The results definitely show an impairment of autonomic functions in both the types of Leprosy. The results are remarkably different in case of effects of adrenaline injection in two of the Leprosy groups. Similar was the finding for Sweat function test and Histamine triphasic response.

8. The effects of Valsalva's Manoeuvre and Cold Pressor test were similar in both the Leprosy Groups.

9. The autonomic functions in Leprosy is perfectly normal as far as the effect of Homatropine on Sphincter pupillae is concerned.

10. In general the leprosy patients are hypo-reactive to the various 'autonomic' stimuli as compared to Normal persons.

11. Thus the above study gives us the evidence that in Leprosy there is a definite impairment of Autonomic functions.

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