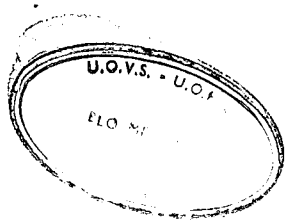

RADIONUCLIDE CISTERNOGRAPHY

IMAGING AND STUDY OF THE CEREBROSPINAL FLUID CIRCULATION

BY

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Dedicated to my wife Cecilia, and our children, for their inspiration and encouragement.

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1. INTRODUCTION

"THE EYE IS THE MOTHER OF THE BRAIN"

The terms "Cisternography" and the "Third Circulation" were coined by G. de Chiro in 1964 to describe the radionuclide imaging and cerebrospinal fluid (CSF) flow in the ventricular and cerebrospinal subarachnoid spaces[14, 17].

However, three hundred years ago Willis and Lower were the first to formulate a concept of the circulation of the CSF and to apply the new scientific methodology to its study[9].

Determination of CSF dynamics date back over sixty years to the use of dyes injected into the lumbar and ventricular subarachnoid spaces[8, 18, 35]. The injection of radiopharmaceuticals into the subarachnoid space to monitor CSF movement has been in use for almost twenty two years[7]. In the past decade there have been improvements in imaging devices and development of new radiopharmaceuticals with appropiate physical, chemical and biological properties[5, 19, 22, 32, 36, 39, 40, 41], and the versatility and importance of this diagnostic technique become apparent because of its investigative and clinical usefulness[3, 6].

The major stimulus for employing this diagnostic proce=

dure was its unique application to the study of hydrocephalus and the discovery that a number of neurological problems due to abnormalities of CSF flow, such as normal pressure hydrocephalus, are treatable[1, 2, 26]. Other uses of cisternography have become evident as recent developments recognized pathologic entities not previously forseen[11, 12, 20, 21, 23, 24, 28, 30, 31, 33, 37, 38].

This communication will discuss the general uses of CSF imaging (cisternography), detail experience with pediatric and adult patients employing different imaging devices and radiopharmaceuticals, relate investigations to determine tissue distribution, chemical and radiopharmaceutical toxicity, effective half life and radiation dosage. A classification of hydrocephalus based upon cisternography findings, clinical signs and symptoms will be presented as well as an attempt to quantify the amount of radioactivity within the cerebral cisterns and ventricular systems in order to document the time-course of radiopharmaceutical movement.

Throughout the centuries, the "Third Circulation" has been notoriously resistant to study. In contrast to the blood, the CSF occupies no clearly delineated physical compartment in which a circuit of flow can be readily observed or its motive force examined[17]. To obtain reliable information the CSF should be minimally

disturbed so as not to change the hydrodynamics under which it normally exists as a single-fluid system. Yet studies in man are essential, since morphologic as well as functional differences among species are so wide that human extrapolation from animal studies must be treated with the utmost caution[16].

Despite these difficulties we have learned from investi= gators since Cushing and Weed[13], that the CSF originates chiefly in the choroid plexuses, slowly circulates from the ventricular system into the subarachnoid spaces at the base of the brain and over the convexities, to be reabsorbed into the blood through the arachnoid villi (the Key and Retzius-Weed theory)[18](figure 1).

The evidence for a ventricular origin of the fluid, both physiological and pathological, is overwhelming and need not to be stressed, although CSF is probably also produced throughout the subarachnoid space[4, 15, 25]. Wherever the CSF originates, there is powerful evidence of a net directional flow[15, 16]. The motive force for this bulk movement has been variously postulated as due to (i) vascular pulsations, particularly from the richly vascularized choroid plexuses, a mechanism found in other systems involving continuous transport of water such as the kidney glomerulus, (ii) body movements, coughing, sneezing and straining and (iii) the vis a tergo emana= ting from the newly produced fluid[34]. Challenging con=

cepts, holding that simple diffusion is the principal factor in CSF kinetics seem unlikely in view of the fact that no movement can be demonstrated in dead animals[27].

The advent of radionuclide tracers has made it possible to study these questions safely in man. The cisternographic demonstration is clear-cut. When a radiopharmaceutical of sufficient molecular size - to prevent its local absorption - is injected intrathecally into human subjects, it can be observed to rise slowly, not in the spreading pattern of diffusion but as a bolus in a moving stream.

This can be visualized no matter how the patient is positioned, whether at rest or under exercising stress. The material normally reaches the basal cisterns in 1 - 3 hours, the frontal poles and sylvian fissures in 3 - 6 hours, the cerebral convexities by 12 hours and the sagittal sinus area by 24 hours[15, 22].

Following an intrathecal spinal injection, radioactivity is not normally detected in the ventricular system, reflecting the net bulk flow of CSF from the ventricles into the subarachnoid space, entering all the anatomic structures bathed by the CSF except the ventricles. Large injected volumes, and also in younger patients, has shown a faster flow of the radiopharmaceutical.

When the radionuclide is introduced directly into the lateral ventricles, it normally appears in the cisterna magna and basal cisterns within minutes, from where the movement of the radioactivity is similar to that obser= ved after an intrathecal injection in the lumbar area.

CSF fluid movement from the basal cisterns of the skull to the maximal resorption area in the parasagittal si= nuses is mainly through anterior communicating pathways. Flow of the CSF as depicted by radionuclide movement is both by a central and more superficial route to the pa= rasagittal region.

The central flow of radioactivity consists of two prin= cipal routes: one superiorly from the supracellar cis= tern to the hemispheric cistern medially and then upward to the parasagittal area, and a more inferior pathway from the basal cisterns to the quadrigeminal cistern by way of the ambient cisterns. From the quadrigeminal plate cistern the radionuclide passes to the posterior portion of the callosal cistern and again between the cerebral hemispheres in the interhemispheric cistern to the parasagittal region.

The lateral pathway of CSF flow is by way of the sylvian cisterns that occupy the space between the posterior sur= face of the frontal lobes and the anterior surface of the temporal lobes. From the sylvian cistern the radionuclide

flows out over the cerebral convexity to the parasagit= tal region. As the cisterns communicate freely they are visualized because of the radiopharmaceutical they contain[10, 16, 19].

The posterior pia-arachnoid limiting membrane which al= most always prevents free egress of air during pneumo= encephalography over the posterior and lateral aspects of the cerebellar hemispheres, does not appear to alter the movement of injected radioactivity. A small amount of radioactivity is seen sorrounding the cerebellum. However, temporary or transient cessation of movement of radioactivity in a small area is not easily detected.

It has been stated that cisternography does not provide the morphologic detail available from pneumoencephalo= graphy with its complicated maneuvers of introducing a gas into a hydraulic system. However, it should be noted that radionuclide cisternography often is more meaningful, because information is provided on physiolo= gical flow and function in addition to anatomic data. Injected radionuclides, reach every spot bathed by the CSF, which cannot always be said for injected air.

Thus a diagnostic challenge is set, to find areas of CSF obstruction, leakage, or advisable drainage, as radionuclide cisternography reflects:

a. The movement of CSF through the subarachnoid space.

b. Absorption of CSF from the cerebrospinal spaces into the vascular and extravascular spaces[6, 29].

c. Entry and exit of CSF into or from the ventricular system under pathologic circumstances.

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2. ANATOMY AND PHYSIOLOGY OF THE CEREBROSPINAL FLUID

A sound understanding of cisternography depends upon familiarity with both ventriculo-cisternal anatomy and cerebrospinal fluid physiology.

2.1 ANATOMY

Protection is provided for the delicate tissue structures of the central nervous system, firstly, by its being contained in bony cavities and secondly, by its being more or less suspended in a fluid cushion. This cushion is contained in the pia-arachnoid as all the interstices of its cobwebby structure are filled with a modified tissue fluid called cerebrospinal fluid[12].

Every segment from the rostral extreme to the caudal end harbours a portion of an interconnecting system of ventricles and spinal canal while the enveloping fluid-filled space forms the subarachnoid space. The internal system consists of the two lateral ventricles, their interventricular foramens (of Monro), the third ventricle, the cerebral (Sylvian) aqueduct, and the fourth ventricle. The external system consists of the subarachnoid spaces, including the dilated portions known as cisterns. Within the skull, the different regions of this space vary greatly in size, being small or absent over the summits of the cerebral convolutions and large where the brain does not follow closely the contour of the skull[1]. Communication between the two systems is established through the

lateral apertures of the fourth ventricle (foramens of LuschKa) and the medial foramen of the fourth ventricles (foramen of Magendie)[4].

Cerebrospinal fluid is formed mainly by the choroid plexuses, which are little structures, rich in capillaries that pro= ject into the lumens of the ventricles (mostly the lateral), though it may also be produced by diffusion through the ependymal and pial vessels[4]. Since CSF is produced more or less continuously, after circulating within the sub-arach= noid space, it must be absorbed at the same rate, lest in= creased intracranial pressure results. Thus, the CSF is absorbed into the blood stream by structures known as the arachnoid villi, which are button-like projections of the arachnoid into the venous sinuses of the dura mater[12].

2.1.1 INTERNAL SYSTEM

2.1.1.1 THE LATERAL VENTRICLES

The two lateral ventricles are irregular cavities situated one on each side, in the lower and medial parts of the cere= bral hemispheres. They are almost completely separated by the septum pellucidum, but each communicates with the 3rd ventricle and indirectly with each other through the inter= ventricular foramen. They are lined with ependyma and contain cerebrospinal fluid formed by the choroid plexuses.

Each lateral ventricle consists of (1) the anterior horn,

extending from the rostral extreme of the cavity to the interventricular foramen, (2) the body or central part, the remainder of the horizontal part below the corpus callosum, (3) the posterior horn, a short spur directed backwards from the junction of the body and (4) the inferior horn, sweeping broadly around the thalamus through the temporal lobe to the uncus. Of these, only the body and inferior horn contain the choroid plexus, which invaginates the ependyma into the cavity through the slit-like interval between the edge of the fornix and the upper surface of the thalamus. This ependymal invagination constitutes the choroid fissure.

The anterior horn is triangular in cross section. Its sloping roof is formed by the corpus callosum, its vertical medial wall by the septum pellucidum, its floor or ventrolateral wall by the bulging head of the caudate nucleus.

The body or central part is flattened from above downwards. Its roof is the continuation of the corpus callosum. The floor from lateral to medial is formed by the following structures: (1) the body of the caudate nucleus; (2) the stria terminalis and the terminal vein; (3) a thin strip of the superior surface of the thalamus; (4) the fornix. All these structures lie parallel and tend somewhat laterally as they are traced backward.

The posterior horn which curves backward and medially into the occipital lobe, is bounded, laterally by the tapetum.

Medially is a rounded elevation caused by the projection of the calcarine sulcus. Its development is variable, frequently asymmetrical, or it may be absent.

The inferior horn, the largest of the three, traverses the temporal lobe, forming in its course a curve round the posterior end of the thalamus. The convexity of the arch, projecting into it from below and medially, is formed by the hippocampus with its accompanying fornix. The roof is formed chiefly from the amygdaloid; the tail of the caudate which ends at the amygdaloid; and the fibrous mass of the medullary center of the temporal lobe. The collateral eminence is an elongated fissure on the lateral edge of the arch lying lateral to and paralled with the hippocampus. The medial edge of the arch is occupied by the choroid fissure and the choroid plexus, which bulges broadly into the ventricle.

2.1.1.2 THIRD VENTRICLE

The third ventricle which is a derivative of the primitive forebrain vesicle, is a medium cleft between the two thalami. It communicates posteriorly with the 4th ventricle through the cerebral aqueduct and anteriorly with the lateral ventricles through the interventricular foramina.

The ependymal roof presents a fold of pia mater named the tela choroidea of the 3rd ventricle from the inferior surface of which a pair of vascular fringed processes, the choroid plexuses of the 3rd ventricle, project downwards, one

on each side of the medium plane, and invaginate the epen= dymal roof into the ventricular cavity.

The floor descends ventrally and is formed mainly by struc= tures which belong to the hypothalamus. The hypophysis is attached to the apex of the infundibulum which is a down= ward prolongation of the ventricle.

The anterior boundary is inferiorly the lamina terminalis, which represents the cranial terminal of the primitive neural tube. At the junction of the roof with the anterior and lateral limits of the ventricle is the interventricular foramen, through which the third and the lateral ventricles communicate with one another.

The posterior boundary consists of the pineal body, the posterior commissure and the cerebral aqueduct.

Each lateral wall consists of an upper part formed by the medial surface of the anterior two-thirds of the thalamus and a lower formed by the hypothalamus and continuous with the grey matter of the ventricular floor.

2.1.1.3 THE FOURTH VENTRICLE

The fourth ventricle is a tent-shaped expansion of the cen= tral canal with a flat neural floor, a flat ependymal roof and no side walls, situated ventral to the cerebellum and dorsal to the pons and cranial half of the medulla.

It is widest where it is prolonged on to the side of the brain stem as the lateral processes. Rostrally, the ven= tricle narrows and its cross sectional shape changes. Here it has side walls, formed by the dorsal thrust of the resti= form body and brachium pontis.

In the midline of the caudal part of the roof of the fourth ventricle is a foramen, termed the medial aperture, through which the cavity of the ventricle communicates freely with the subarachnoid space. At the tips of the lateral proces= ses there is another pair of holes, ordinarily partly occu= pied by a tuft of the choroid plexus. These are the lateral apertures.

Occasionally one of the lateral recesses may fail to open into the subarachnoid space, but the medial aperture is constantly present.

The tela choroidea of the fourth ventricle is a double layer of pia mater which occupies the interval between the cerebel= lum and the lower part of the roof of the ventricle. In the tela choroidea are highly vascular fringes forming the cho= roid plexus of the fourth ventricle. This modified secretory epithelium presents a letter, T, with a double vertical limb.

In the midbrain there are many decussating fibers ventrally, while dorsally the roof is neural, not ependymal. These facts conspire to hinder the expansion of the central canal,

so as a result it is quite small in caliber. It is here termed the cerebral aqueduct through which it communicates with the third ventricle[16, 27] (figure 2).

2.1.2 THE EXTERNAL SYSTEM

The subarachnoid space is the interval between the arachnoid and pia mater. It contains the cerebrospinal fluid, the larger blood vessels of the brain, and is traversed by a network of delicate connective tissue trabeculae, which connect the arachnoid to the pia mater. They are in close contact on the summits of the cerebral gyri and separated by wide intervals at certain parts of the base of the brain. These are the subarachnoid cisterns which communicate freely with each other.

2.1.2.1 THE SUBARACHNOID CISTERNS

The cerebello-medullary cistern or cisterna magna is formed by the arachnoid bridging the interval between the medulla oblongata and the under surface of the cerebellum. The pontine cistern is an extensive space on the ventral surface of the pons, and is continuous behind with the cisterna magna and in front of the pons with the interpeduncular cistern. Both cisterns, pontine and magna continue below with the spinal subarachnoid space. The arachnoid is separated from the cerebral penducles and the structures in the interpenduncular fossa by the interpendencular cistern which contains the circulus arteriosus. The cistern of the lateral fossa contains the middle cerebral artery and is

formed in front of each temporal lobe by the arachnoid bridging the lateral sulcus. The cistern of the great cerebral vein (cisterna ambiens or superior cistern) occu= pies the space between the splenium of the corpus callosum and the superior surface of the cerebellum.

Other less prominent cisternae have been described, these include the prechiasmatic and postchiasmatic cisterns re= lated to the optic chiasma, the cistern of the lamina termi= nalis, and the supracallosal cistern, all of which become in a way extensions of the interpeduncular cistern.

A major lateral and superficial convolution of the cerebral cortex correspond to the areas of the Sylvian fissures that occupy the space between the posterior surface of the frontal lobes and the anterior surface of the temporal lobes (figure 3).

The spinal part of the subarachnoid space is a relatively wide interval, and is largest at the lower part of the ver= tebral canal, where the arachnoid encloses the nerves which form the cauda equina. Above it is continuous with the cranial subarachnoid space; below, it ends at the level of the lower border of the second sacral vertebra. It is par= tially divided by two septa, the subarachnoid septum and the ligamentum denticulatum.

The spinal subdural space is a potential space between the

dura mater and the arachnoid mater. It contains a film of serous fluid which moistens the apposed surfaces of the membranes. It does not communicate with the subarachnoid space.

The extradural space lies between the spinal dura mater and the periosteum and ligaments within the vertebral canal; it contains a quantity of loose fat, areolar tissue and a plexus of veins. This constitutes the epidural space which extends laterally for a short distance through the intervertebral foramina along the spinal nerves[27] (figure 4).

2.1.3 MICROSCOPIC STRUCTURE OF THE CHOROID PLEXUS AND ARACHNOID GRANULATIONS

As will be seen later, though some of the CSF is formed on the exterior of the brain, most of it is formed in the ven= tricles by the choroid plexuses which are the ideal struc= tures for the continuous production of fluid. The capil= laries in the highly vascular cores of the villi are fene= strated, a type that is found in other systems involving continuous transport of water such as the kidney glomerulus and peritubular capillaries of the cilliary body of the eye. Furthermore, within the nervous tissue there is not ana= logous structure that might be expected to secrete fluid into the extracellular spaces of the brain[24].

The part of the wall of the neural tube that becomes the roof of the third and fourth ventricles becomes very thin,

consisting of no more than a single layer of cuboidal cells that compromise the ependyma plus the vascular pia-arachnoid which covers it. In these areas the pia-arachnoid, pushing the ependyma ahead of it, invaginates into the ventricles to form the tufted choroid plexuses. A similar process occurs in the medial wall of the cerebral hemisphere along the line of attachment of the hemispheres to the hindpart (thalamus) of the forebrain, accounting for the development of the choroid plexuses of the lateral ventricles[12].

A choroid plexus has many leaflike processes that hang from the counterpart of a stem. Each contains an afferent and efferent vessel, an intervening capillary plexus, a small amount of flattened connective tissue and nerve fibres of still uncertain functional significance[5].

The capillaries, becoming tortuous produce elevations in the epithelium called villi, in this way creating a large surface area. The epithelium that covers the leaves and the villi of the choroid plexuses develops from the epen= dyma and is of a cuboidal type, called choroid plexus epi= thelium.

The choroid plexus is seen to be studded with microvilli which electron microscopy shows to be on the ventricular aspect of the ependymal cells, the basal aspect of which presents a series of invaginations. Ultrastructural stu= dies have shown that some ependymal cells posses cilia,

that tight junction exist between them, and that a distinct basement membrane separates them from the adjacent capilla= ries, some of them of the fenestrated type[30].

The blood supply of the choroid plexuses in the tela cho= roidea is derived from the single anterior and three to five posterior choroidal branches which anastomose to some extent. The capillaries drain into a rich venous plexus which is served by a single choroidal vein leaving the tela choroidea.

The choroid plexus goes through many changes during develop= ment which modify with time its vascular pattern. Degenera= tive changes are manifested by calcium deposits, termed con= centric bodies[12].

The cerebrospinal fluid drainage mechanism is provided by button-like projections of the arachnoid, called arachnoid or Pacchionian granulations, present in the vicinity of the superior sagittal, transverse and other venous sinuses. Arachnoid granulations are macroscopic enlargements or dis= tensions of minute projections of the arachnoid mater, termed arachnoid villi.

Each villus appears as a diverticulum of the subarachnoid space, penetrating into the interstices of the dura mater and fuses with the endothelial lining of one of the intra= dural venous sinus.

In so doing it pulls out a little stalk of arachnoid con= taining a diverticulum of the subarachnoid space[27].

2.2 PHYSIOLOGY

The central nervous system develops from a fluid-filled and fluid-surrounded neural tube. The adult retains this essen= tial feature, the internal cavity becoming the ventricles and spinal canal while the enveloping fluid-filled space becomes the subarachnoid space. The CSF is thus, a specia= lized cavity-filling fluid.

Historically through these channels, cerebrospinal fluid was conjectured to flow propelled by the pulsations of the blood vessels, perhaps "to and fro", or only in one direc= tion, many others envisioned these spaces as a microsewage disposal system emptying finally into the subarachnoid cess= pool where the digested residues of neuronal metabolism flowed sluggishly back into the blood stream. Some authors considered them the rivers of abundance down which streamed, from the cornucopia of the CSF, all the nutrients of the neurons. Still others saw them as high-ways of trade with loads of glucose consigned to the furnaces of neuronal me= tabolism passing garbage scows of refuse in the opposite direction. In any case there appeared to be a continuous pathway between the unique and mysterious liquor and the functional units of the CNS, giving rise to the concept that the CSF was indeed, the internal milieu[26].

In the 17th century inspired by the Harveian concepts of the circulation of the blood, Willis and Lower in their highly significant but generally unrecognized studies "Cerebri Anatomy: (1664) and "Tractutus de Corde" (1669), respectively, established the basis of CSF dynamics with their unequivocal principle that the intracranial "water fluid" secreted by the arteries into the ventricles is then absorbed into the venous system[3].

The basic concept has remained unchanged, through there is still some controversy over the exact mechanism of CSF pro= duction and absorption in both the normal state and hydro= cephalus. Recent physiological and anatomical studies have however supplied considerable data in these fields.

Mechanically, there is little doubt that the CSF serves as a fluid cushion damping down intracranial variations in pressure. Granting the need for such a damping device, there is some reason to believe that besides fulfilling this purely mechanical role, the presence of a circulating fluid in close relationship with the central nervous system (CNS) must certainly participate in the metabolic exchange of water and solutes.

If the nervous tissue is tobe protected from large fluctu= ations in blood concentration of solutes, such as electro= lytes, glucose or adrenaline the blood-brain barrier by it= self is insufficient unless backed by a similar barrier,

both qualitative and quantitative, between the blood and the CSF. Current available evidence demonstrates the con= tinuity of CSF and CNS parenchymal extra-cellular fluid (ECF)[2, 18]. Furthermore we may expect that the composition of ECF of the nervous tissue will necessarily be very simi= lar to that of the CSF by virtue of these exchanges between the two compartments. The composition of the CNS ECF with respect to Na, K and Cl is very similar to that of the CSF (Wallace and Brodie)[26] (table 1).

TABLE 1: ELECTROLYTE DISTRIBUTION IN THE FLUID COMPARTMENTS OF THE CENTRAL NERVOUS SYSTEM (IN mEq/L)

	Na	K	Cl
CSF	142	3,1	120
ECF	142	3,1	120
ICF	64	162	22,3
Vascular	135	3,1	106

Total H_2O = 78 ml/100 gr BRAIN

These facts and the low concentration of protein in the CSF indicate that the ECF of nervous tissue is in equilibrium with CSF and not serum. Obviously then, the fluid arising from the choroid plexus is not a simple filtrate from the capillaries, but a choroid secretion[11].

This is the contribution that a circulating, as apposed to a stagnant fluid may make in controlling the environment of

the neurones and glia. Thus, the escape of proteins from plasma into the brain must doubtless occur through "physio= logical leaks" in the blood-brain barrier. These would necessarily accumulate in a stagnant extra-cellular fluid since they could not get back into the blood vessels, the concentration gradient being unfavourable. However, by vir= tue of the high permeability of the ependyma and pia-glia, these proteins can diffuse into the CSF, and by virtue of the unrestricted flow through the arachnoid villi, they can be returned to the blood[7].

It is evident that by circulating, the CSF participates ac= tively in the metabolic homeostasis of the nervous tissue. This thesis will deal only with the mechanical implications of obstruction in certain pathological conditions by demon= strating with radionuclide cisternography the patterns of CSF flow, but a challenging field for further studies exists regarding the more complex cellular metabolic disturbances of the nervous tissue that may arise from the alteration of CSF dynamics.

2.2.1 CSF FORMATION

It is generally accepted that most, if not all of the CSF is produced within the ventricular system by a secretory process of the choroid plexuses.

The ventricular origin of CSF was established by the clas= sical studies of Dandy and Blackfan[10] who produced an experi=

mental hydrocephalus in dogs by plugging the aqueduct of Sylvius. When the choroid plexus of one lateral ventricle was removed and both foramina of Monro blocked, one ventri= cle dilated while the other collapsed. Bering[1], among others disputed this theory suggesting that ".... a special local force produced by the choroid plexus" was responsible for the ventricular enlargement and not the secreted fluid. But the most compelling demonstration is the difference in arte= rial and venous hematocrit in the choroid and the direct col= lection, detection and measurement of nascent fluid by a ven= triculocisternal perfusion technique[28].

The probable mechanism by which the choroid plexus secretes fluid is the following: The cuboidal epithelial cells of the choroid plexus secrete Na^+ ions, which develop a posi= tive charge in the CSF. This in turn pulls negatively charged ions into the CSF particullarly Cl^-, an excess of ions develops in the ventricular CSF. As a result osmotic pressure is highly elevated, 9 milliosmols more concentrated than in plasma and enough to excert an osmotic force of 160 mm Hg. This osmotic force moves large quantities of water and solutes through the choroidal membrane into the CSF[11].

When ^{24}Na is injected intravenously it appears first in the ventricular CSF[21], the same as $^{99m}TcO_4$ which readily concen= trates in the choroid plexuses, supporting the previous mechanism. More controversial has been the belief that CSF originates from an extrachoroidal source. Though diminished,

CSF production continues after choroid plexectomy or as an effect of drugs on total CSF production, as compared to that of an isolated choroid plexus. Davson[29] warns against at= tributing too much significance to experiments involving ex= tirpation of an organ, as there may be leakage of fluid from the capillaries in the scar. In spite of these objec= tions, alternative sources of CSF production can not be ruled out. The anatomical structures and mechanism respon= sible for extrachoroidal fluid formation remains unknown.

2.2.2 CSF CIRCULATION

There is in the adult about 140 ml of CSF of which about 20 ml are in the ventricles, 30 ml in the spinal subarach= noid space, which leaves about 90 ml for the cranial sub= arachnoid space. The rate of choroid secretion is estima= ted to be about 500 ml each day, which is about four times as much as the total volume of fluid in the entire cerebro= spinal cavity. The total intraventricular production of CSF has been measured by different methods, i.e. manometric, ventriculocisternal perfusion, and radioactive tracer turn= over, both in humans and in a variety of animals. All me= thods appear to give similar values in the same species, which for the adult healty human being corresponds to 0,4 ml/min[24].

After formation in the ventricular system there is a bulk movement of the CSF through the foramen of Magendie and the foramina of Luschka into the cisterna magna. It then flows

along the spinal subarachnoid space. Another pathway leaves around the brain stem to the pontine, interpenducular and supracellar cisterns, then upward into the quadrigeminal cistern. It then passes through the incisura which is the narrow portals formed by the reflexion of the falx cerebri and tentorium through which the brain stem passes. From here the CSF flows upward through the interhemispheric fis= sure and laterally through the Sylvian fissure and sulci of the cerebral cortex, finally to enter the venous circulation via the arachnoidal villi into the dural sinuses and to some minor extent, into spinal segmental veins (figure 5).

In addition to this slow, long-term net movements of about one mm/min, - on which the principal of cisternography is based - there are superimposed relatively large, short-term oscillatory movements of CSF created by transient changes in cranial blood pool volume in response to cardiac systole and changes in central venous pressure. These are respon= sible for most of the mixing and homogenization of CSF, with considerable clinical significance. Here the net migratory long-term turnover has little significance[9, 13, 14, 15, 17, 20, 23, 25].

2.3.2 CSF DRAINAGE

There is little doubt, and general agreement that the arach= noid protrusions into the dural venous system appear to be primarily responsible for the drainage of the CSF. Contro= versy exists, however, concerning the precise mechanism

of passage through these structures. It was originally thought that the CSF drained through the arachnoid by fil= tration of water and electrolytes as a fluid with a low os= motic pressure into the blood where the osmotic pressure is higher. But as there is a small amount of protein in the CSF this must also be eliminated, otherwise it would slowly accumulate and reach levels much higher than expec= ted in normal CSF. More so, the fact that plasma proteins are normally drained away and that the plasma proteins after injection into the subarachnoid space appear rapidly in the blood, make it very unlikely that the membranes separating the two fluids in the arachnoid villus are impermeable to protein; so this factor must be ruled out[6].

To explain the removal of large molecules, the presence of large pores or valves in the arachnoid granulations, has been postulated[22]. By electron-microscopic observations, however, the arachnoid villi were found to be covered by a non-fenestrated layer of highly permeable epithelial cells and no pores have been seen[29]. Another study suggested that proteins and other high molecular-weight substances are phagocytosed by leukocytes and thus eliminated from the CSF. The smooth rapid clearance of a high molecular-weight protein such as ^{131}I-labelled human serum albumin (RIHSA), appears to preclude phagocytosis as a mechanism[8].

It is important to remember that CSF absorption increases with increasing CSF pressure because of bulk flow into the

arachnoid villi. However, formation is relatively indepen= dent of CSF pressure. No CSF absorption occurs until CSF pressure excedes cerebral venous pressure at about 68 mm H_2O[11, 16, 22, 24].

In summary, there is good evidence that the CSF is almost entirely produced by the choroid plexuses distributed through all the ventricles, although a minor factor may well origi= nate from the brain parenchymal capillaries.

The circulation of CSF takes place as a slow migratory movement due to the pressure of the newly-formed fluid and resorption with superimposed transient movements due to changes in brain blood pool volume.

Drainage of CSF to venous blood occurs through the arach= noidal villi which act as one-way valves allowing flow only into the blood, this passage including proteins is probably by bulk flow through a highly permeable epithelial membrane[19].

Many aspects of CSF physiology remain obscure and unknown despite extensive experimental work, largely because the delicate balance of fluid dynamics is disturbed by the techniques used. The CSF is easily acessible for in vitro analysis, but inaccessible for sound meaningful in vivo physiological studies.

To a great extent, the rate and spatial distribution of the

CSF movements can be monitored and defined - without alter=ing the physiological condition of a single fluid system - by radionuclide cisternography.

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3. MATERIAL AND METHODS

3.1 INSTRUMENTATION

Biological and medical scientists have used great ingenuity in adapting many of the tools and techniques of the physical sciences to their complex problems. This interdependence of basic science, medicine and technology suggest that such ec= lecticism may well be a prophetic model of future advances in all fields of medicine. The technology of Nuclear Medi= cine offers a unique opportunity to asses the regional func= tion and structure of body organs by external monitoring.

Radionuclides, when matched to specific metabolic functions and physical characteristics of specific organs, concentrate in various regions in proportion to regional function. The time course of the spatial distribution of the tracer is then converted by means of scanners and cameras into two dimensional analog images which depict the regional tempo= ral concentrations in proportional shades of grey or colour. The images are a measure of the parameters "AREA", "COUNTS" quantities of measurement in nuclear medicine[53].

3.1.1 THE RADIONUCLIDE IMAGING PROCESS

Radionuclide imaging is a signal-to-noise process, where the signal, or counting rate from the abnormal region, is usual=

ly only slightly different from the noise, which includes the counting rate from the surrounding region as well as the statistical fluctuations of counting rate which occur in both, and which arise from the statistical nature of radioactive decay[46].

The spatial distribution of gamma-ray flux is sampled by the detection system which is essentially an information conversion and transfer device, which can be broken down into basic components: the collimator, the image converter and the display.

The collimator component samples the incident radiation, selecting the γ-rays from certain directions only, and allowing them to fall on the detector. The image converter responds to the γ-rays which have been screened by the collimator and transforms them into data which is capable of activating the display. The image converter consists of the detector component which converts the γ-rays into a more suitable form of data, such as the light scintillation from the γ-absorption in the crystal of the detector, and the data transfer component which transforms this data into one more suitable of activating the display.

The collimator and detector of an imaging device are the major factors determining the overall sensitivity and resolution of a device.

Sensitivity defines how many γ-ray events will be recorded from a known distribution of radioactivity, which is expressed as the ratio of the number of counts measured to the number of γ-ray photons emitted from a source. The scintillation detector is very sensitive, where the principal loss of sensitivity occurs in the collimator, which is necessary to obtain the desired spatial resolution.

The energy resolution defines the ability to recognize between γ-rays of different energies. This property allows radionuclides emitting different γ-ray energies to be distinguished.

The temporal resolution defines the ability of a system to distinguish time changes in radioactive distribution. A moving imaging detector or scanner has a poor temporal resolution. It can not detect fast time-lapse events as it takes a long time scanning an area of interest. A stationary imaging detector or gamma camera has a good temporal resolution and may portray dynamic events with time changes in the order of fractions of seconds provided enough counts are available.

Spatial resolution defines the geometrical ability to resolve the distribution of an isotope in the body, that is, the minimum separation of two points which can just be distinguished.

Unfortunately sensitivity and resolution are inversely pro-

portional, and design of an imaging device or choice of collimators is a practical compromise that should try to accurately image the actual distribution of the radionuclide within the organ being studied.

The availability of large crystals (which increased sensi= tivity but worsened resolution) led to the introduction of multihole focussing collimators. Such collimators used most= ly with scanners are provided with a large number of conical (circular or hexagonal in cross-section) bores whose axes meet at a certain distance from the collimator (focal length).

This arrangement multiplies the number of γ-rays coming from the smallest possible volume at a certain distance from the measuring head, increasing sensitivity, while in the focal plane, at least, the spatial resolution of the single hole is preserved. In contrast; the bores of most camera colli= mators, run parallel to each other.

While with the scanner the whole detector serves for produc= tion of an image element, in gamma scintigraphy an image ele= ment is produced by gamma absorption in only one part of the detector.[16, 17, 33, 46, 59]

The detector component of most imaging devices is based on the scintillation counter in which two principles are utilized: scintillation and photodetection.

Scintillation occurs when a suitable material such as sodium iodide crystals which has been activated by a trace of thal= lium (NaI (Tl)), absorb radioactive emissions such as γ-rays. An incoming γ-ray will often collide with an electron, knock= ing it out of its orbit around the nucleus of the atom. This electron will disturb other atoms in its path creating pairs of ions in proportion to the energy that was imparted to it, discharging part of its energy in the form of light photons, called scintillation.

However, this light flash is too dim to be seen by the un= aided eye. Thus, a sensitive photodetection system is coupled to the crystal that will detect, quantitate, record and dis= play this photons as electric voltage pulses; they are the photomultiplier tubes.

The data transfer component will present this information to the display in relation to the intensity and position of the original radioactive distribution.

Finally the display renders the data transferred to it, by the image converter, into a form which can be interpreted by the eye and brain of the observer as a recognizable pat= tern. This may be done in a digital mode in which the re= sults appear as a sequence of individual measurements or in the analog mode in which the display reproduces the results of a continuous measurement[3, 11, 59].

3.1.2 IMAGING DEVICES AND DATA ANALYSIS SYSTEMS

The first techniques used for localization of isotopes involved the estimation of radioactivity by counting with a hand-held Geiger counter at points marked on the patient's body. This was a fairly tedious, time-consuming, inefficient, and an often inaccurate procedure.

With the development of scintillation detectors, there was an increase in the sensitivity for measuring radioacitivity. However, these instruments, because of their sensitivity, required heavy shielding and collimation to get any degree of localization, and the weight of the system made hand-counting even more difficult than it was with the old Geiger counter.

In 1951 the first rectilinear scanner was designed by Benedict Cassen in which he used a simple method of display with a mechanical mark printer in which a stylus and ribbon moved over the paper in synchrony with the counter movement, a mark being stamped on the paper for every count, or more usually, whenever a preselected accumulation of counts were reached.

In 1952 Hal O. Anger introduced the first gamma camera which subsequently stimulated the development of multihole collimators, even larger sodium iodide crystals, the use of larger banks of improved detector phototubes, tomographic applications and highly sophisticated linkages with computers -

that has resulted in an explosion in new measurement techno= logy[52].

3.1.2.1 MOVING DETECTOR IMAGING DEVICES

In the moving detector device, position is conveyed by set= ting up a mechanical movement between the detection system and the subject and mechanically linking the position of the detector to the position of data recorded on the display. The most common scanning pattern is a rectilinear raster, consisting of to-and-fro motion on sequential adjacent lines, until the whole area of interest is systematically scanned.

A flow of innovations made remarkable changes to this basic concept. Heat sensitive paper was introduced, although at high counting rates burned areas tended to conglomerate. Colour coding was used as a simple way of telling at glance how the counting-rate varied from point to point. Photo re= cording is now widely used: a light source is moved over an X-ray film in synchrony with the counter movement, the source flashing once for every disintegration (figure 6).

Background suppresion and contrast enhancement; magnetic tape recording and playback; digital image processing; mul= tiple detectors for simultaneous scanning of different posi= tions; larger crystals (up to 20 cm in diameter); positron detection; opposed detectors; high speed scanners; minifi= cation; and an assorted array of focussing collimators for

different energies have provided a great versatility to radionuclide imaging[17, 18, 33, 58].

Rectilinear scanners offer a more planographic characteristic provided by the focussing collimator. For best response in cisternography (in sensitivity and/or resolution) a collimator with the lowest maximum energy should be selected. Ideally, though the finest resolution would be desired, to minimize the patient's dose the scan is normally count-limited, and a collimator should be chosen with a high sensitivity to give reasonably meaningful counts. Present rectilinear scanners have a choice selection of different energy collimators designed to maximize sensitivity without allowing excessive septal penetration.

One variation of this imaging system, used in part during this study, is the profile scanner, which proved to be a useful aid to quantitative cisternography (figure 7).

This is a Nuclear Enterprise whole body counter steel shielded room with two 12,7 x 10 cm crystal size opposing detectors moving in a longitudinal axis (SAAEB). The collimators of local design feature a 30 x 130 mm slit with a 100 mm focal length. To improve resolution a 8 mm thick septum is introduced in the centre of the slit providing two 11 x 130 mm slits. Data is recorded in a multichannel analyzer (Nuclear Data) which can be transferred via punch-tape to the x y plotter of a calculator (Hewlett Packard Model 30) for final

drafting of the scanned profiles.

3.1.2.2 STATIONARY DETECTOR IMAGING DEVICES (γ-CAMERAS)

The scintillation, Anger, or γ-camera is a stationary detec= tion system for continuously recording a planar projection of distribution volume of a γ-radiation emitting radionu= clide in vivo. In this way either a moving or a stationary label in a body organ can be pictured as an area of dots re= presenting the relative positions of all radiation events detected in the field of view for a given period of time.

The image converter of the Anger γ-camera consist of an array of photomultiplier tubes spaced a small distance away from the scintillation crystal so that their fields of view overlap. The output of these tubes is fed into electronic computer circuitry that is capable, by analysis of their outputs, of determining at which point beneath the array of phototubes each scintillation occurs, and of assigning to each event an x and y co-ordinate. When this determination of spatial location is made, at a speed of about 3 to 10 millionths of a second, it is then fed into the cathode-ray tube which responds to the x and y signals by displaying a point flash of light at the appropiate posi= tion on the oscilloscope screen.

This is recorded photographically, most frequently on Pola= roid or 35 mm film (referred to as a scan, though γ-cameras do not scan either mechanically or electrically to produce their

display) or it can be stored in video tape for dynamic stu= dies[3, 16, 58] (figure 8).

The primary advantage of the gamma camera is the ease with which various positions can be achieved in a relatively short time, limiting the problem of patient motion. This becomes indispensable when scanning infants and unco-opera= tive children, as well as with emotionally disturbed adult patients.

This higher speed is due to the fact that the detector is continuously sensitive to the entire field of view as a re= sult of a greater detection efficiency obtained from the various photo-multipliers, large crystals and the large collimators. The selection principles of collimators for the gamma camera are the same applied for rectilinear scan= ners.

The advantages and disadvantages of the rectilinear scanner and the gamma camera are minor and good quality cisterno= grams can be expected with either type of imaging device.

3.1.2.3 DATA ANALYSIS SYSTEMS - COMPUTERS

With adequate knowledge of the radionuclides, instruments and techniques used, the nuclear medicine specialist inter= pretes images subjectively on the basis of abnormal regional concentrations to diagnose a pathological condition.

Having perceived subtle variations among sites in a given image, he may then want to know further details about these variations. How large are they? Is the amount of activity significantly different in one region? What is the total radioactive count in area A as compared to area B? What are the rates of radionuclide accumulation or clearance in a specific site, how do they compare with each other, and how do they change over a period of time? To precisely what extent, in quantitative, non-subjective terms, do these counts and rates vary from normal?

Although remarkable in capacity for spatial resolution, the human eye and brain are notoriously poor in memory and abi= lity to quantify, precisely those attributes in which com= puters excel providing an answer to all the above questions and many more of diagnostic significance.

The digital computer can retrieve and process on call any portion of these data output by on-line scanners and cameras. It can quantify, combine, select, compare and display its answers in any of a wide variety of ways - tables, graphs or images. The method of display presents data in a form suitable for visual perception. The characteristics of the display such as brightness, contrast and size can be varied while the observer views the image. The ability to vary these characteristics aid in the subjective interpretation of the information in the image.

The image can also be analyzed quantitatively. This can be done in single or serial images. Single images provide the "counts" and "area" information. Serial images, in addition to counts and area, provide "temporal" information. Such quantitative analysis aid in the objective interpretation of the information of the image[53, 69].

The central processing unit at present being used for Nuclear Medicine at the National Hospital, Bloemfontein is a Zentron PDP-8 general purpose mini-computer (figure 9). This single-address, fixed-word-length, parallel-transfer computer uses 12-bit, two's complement arithmetic and includes standard features for indirect addressing, instruction skips and pro= grammed input/output device interrupts. High speed integrated circuits of the transistor - transistor logic (TTL) types are used throughout the central processing unit.

The basic capabilities of the computer system include: (i) digitization of analog data at the maximum rate provide by the γ-camera, and storage of 4 096 counts per element in a 64 x 64 matrix, (ii) data transfer to magnetic disk in single or multiple frames with a variable time base and (iii) display of digital images containing a maximum of 4 096 data points on a raster-type colour and monochrome cathode ray tubes[62].

3.2 RADIOPHARMACEUTICALS

The rapid development of Nuclear Medicine dates from the end

of the Second World War. In 1946, the June edition of "Science" quoted an announcement from the headquarters of the Manhattan Project in Washington which stated the pos= sibility of generally distributing radioactive substances[39].

Unstable radioactive isotopes such as those of radium and uranium, occur naturally. Their value was appreciated by early clinicians who used them to destroy cancerous lesions. However, the high radiation dose associated with them, ren= ders them unsuitable as diagnostic tracers. A broader range of diagnostically useful man-made isotopes have been produced for specific needs by bombarding target elements with sub- atomic particles. This was accomplished in the early 1930's by Ernest Lawrence with a cyclotron he developed in Berkeley, California. Very soon his brother John and Joseph Hamilton began working on the application of radio-isotopes as bio= chemical tracers, work which led to his obtaining the Nobel prize in 1943[71].

Nuclear Medicine began as an exotic toy for haematologists, when ^{32}P was used for the treatment of leukemia and polycy- themia vera and ^{59}Fe for the study of erythropoiesis, while endocrinologists used ^{131}I for thyroid studies. Radiolo= gists entered the field when imaging was made possible by the use of the newly developed rectilinear scanners and later the scintillation camera. Clinical pathologists soon became involved with the applications of <u>in vitro</u> studies[40].

Since that time its uses span the entire field of medicine and a significant part of the previously unexplored ter= ritory of nuclear medicine has been studied and charted. Nowadays, the use of radionuclides is accepted as an indis= pensable aid to the clinician in the functional and morpho= logic examination of the patient, and the growth of such applications expands exponentially.

The pharmacological and biochemical properties of a radio= active substance (radiopharmaceutical) ensure a high organ or tissue specificity and exact localization of the spatial distribution of radioactivity introduced into the human body compartments.

This requires radiochemical manipulation to incorporate radionuclides into physiologic substances that will distri= bute the signal to the specific organ, tissue or biologic system under examination, so that its detection and visuali= zation will reflect the function of those systems. When the labelled element is used in organic molecules, the radioche= mistry is clear-cut, and the potential for metabolic disco= very exciting. But it happens that the most useful radionu= clides, with suitable physical properties, are inorganic, and here the ingenuity of the radiopharmacologists is taxed to the utmost.

The so commonly used and popular Technetium-99m is an example. It is an unstable, fully artificial isotope of an element which

could not, therefore, have any applications in its own right as a natural component of any biologic system. But its physical properties of a short half-life, non-particulate low gamma energy (suitable for existing imaging instruments) and the ease of on-site elution or "milking" have made it a first class label, and radiopharmacologists have gone to great lengths to incorporate it into a wide range of medically useful chemical forms[71].

Based on the principle of compartment localization, assesment of CSF dynamics by means of radioactive materials introduced into the subarachnoid space have stimulated a energetic search for an "ideal" cisternographic agent, which has yet to be found.

Clearly there is no single appropiate tracer for investigating the CSF dynamics, as it consists of a heterogenous mixture of solute molecules (electrolytes, proteins, sugar, etc.) dissolved in a solvent (water). Each of these components have their own molecular properties and their own characteristic kinetics. It is a fundamental axiom in tracer kinetics, that the radionuclide should accurately mimic the behaviour of the molecule under study in the physical or biological system concerned[61].

Since any radiopharmaceutical, whether a normal consituent of the CSF or a foreign material can be used in tracer amounts

for cisternography, as long as it reflects primarily the CSF bulk flow, a wide variety of radiopharmaceuticals in colloidal and soluble forms have been proposed to study the spinal and cranial CSF spaces by external radiation detectors[21, 27, 30, 36, 37, 38, 47, 49, 63, 64, 65, 68, 72] (table 2). These agents have been evaluated in both animal experimental studies and in human clinical studies. Some were used only for comparative studies and not because they were potentially useful. Eventually only those few with optimal properties were selected for human cisternography.

3.2.1 BIOCHEMICAL CONSIDERATIONS

Edward G. Bell, et al[12], outlined the criteria for the selec= tion of radiopharmaceuticals suitable for cisternography:

a. Not metabolized in the CSF: The human CSF has enzy= matic activity and the resultant hydrolysis of labelled pro= teins to lower molecular weight peptides may disturb the quality of the images due to diffusion into the brain tissue. In certain pathologic conditions this proteinase activity can be markedly increased[60].

b. Lipid insoluble: To minimize diffusion of the agent into the lipid rich nervous tissue, the radiopharmaceutical should be lipid insoluble.

c. Rapid blood clearance: Once the radiopharmaceutical is reabsorbed into the blood stream via the arachnoid villi

TABLE 2

RATING OF AGENTS EVALUATED[12]

GOOD	FAIR	UNACCEPTABLE
^{99m}Tc-Inulin	^{99m}Tc-HSA	^{131}I-Indigo Carmine
^{99m}Tc-DTPA	^{99m}Tc-Iron Ascorbate	^{131}I-Hippuran
^{99m}Tc-EDTA	^{99m}Tc-S Sol	^{51}Cr-Hemoglobin
^{99m}Tc-Cysteine Complex	^{99m}Tc-Fe $(OH)_3$ Gel Sol	^{51}Cr-RBC
^{111}In-DTPA	^{99m}Tc-HSA Microspheres	^{133}Xe-Saline
	^{131}I-HSA	^{113m}In-Acetate
	^{51}Cr-Cl_3	^{99m}Tc-Pertechnetate
	^{113m}In-EDTA	
	^{171}Er-HEDTA	

it should be cleared from there as rapidly as possible. Chelating agents such as diethylenetriamine pentaacetic acid (DTPA) coupled to metal ions such as ^{111}In, or rare earth elements such as ^{169}Yb, form stable chelated compounds which are rapidly cleared from the plasma by way of glome= rular filtration[31, 38]. This allows injection of millicurie doses, while human serum albumin (HSA) is cleared from the plasma at a slower rate, thus with chelating agents better images are obtained with a lower radiation burden.

d. Main route of tracer egress via the arachnoid villi: Ideally only a minimal fraction of the total clearance should escape into the brain while the bulk of tracer preferentially carried to the Pachionian granulations for free egress from the CSF space.

e. High rate of molecular diffusion: If the tracer's molecule is too small transependymal diffusion could give a false estimate of CSF clearance. Albumin with a molecular weight of 70 000 truly reflects the bulk CSF flow, while smaller molecules like chelates (^{169}Yb-DTPA, molecular weight 603) are also useful cisternographic agents reflecting CSF flow as efficiently as protein labelled substances.

f. Non-irritating: Agents should (i) be adjusted to physiological osmolarity levels and (ii) have no potentially irritating particles which could lead to intracellular pha= gocytocis by the arachnoid cells. This could happen to col=

colloidal substances[64].

g. Non-reactive: All protein indicators such as albu= min or transferrin must manifest a very high specific acti= vity in order to avoid the danger of a meningeal reaction which tends to occur in the presence of a quantity of pro= tein in excess of 4 mg[5, 8, 55]. Chelating agents added to the CSF may sequestrate cations such as Ca^{++}. For this reason calcium should be added to the formula of these com= pounds[68].

h. Non-antigenic: While it has been suggested that glo= bulin contaminants of human serum albumin fractions may be immunogenic, none of the presently used agents appears to cause secondary immunogenic response, much less a primary one[12].

i. Non-pyrogenic: Sterility of intrathecal agents and its freedom from pyrogens, is much more critical than with preparations for intravenous use. Although no specific standards are laid down for these agents, it is known that the effect of pyrogens may be magnified up to 1 000 fold when injected intrathecally as compared with intravenously[19]. Special care should be taken in case of albumin preparations as they are more susceptible for microbial growth prior to injection.

j. Ease of sterilization: The radiopharmaceutical should

not show degradation after autoclaving. In this respect radionuclides with a long half-life such as ^{169}Yb, have an advantage over the short-lived ones, in that quality control can be carried out in great detail - even for large batches - by a radiopharmaceutical company, rather than immediately prior to use.

The selection of the agent of choice for cisternography is critically related to the duration of the study. As 48 and 72 hour studies provide valuable information related to alterations in reabsorption, ^{99m}Tc labelled compounds with their short half-life of 6 hours are not suitable. But should assessment of shunt patency, intraventricular obstruction, determination of CSF leakage, or spinal flow evaluation be aimed at, short-lived agents are most useful as they permit larger doses, higher specific activity, greater resolution and anatomical detail with the least radiation hazard[4].

The quality of scans with chelates is superior to that of albumin due to improved target to non-target ratio. The radioactive protein accumulates in the blood, whereas the radioactive chelate is excreted in the bladder after leaving the CSF[36, 37].

In the final instance one aims at a quality image with maximal diagnostic information obtained with minimal risk to the patient. These requirements are not met by ^{131}I-labeled human serum albumin[34, 61]. It was however used for the first

studies of this series, as it was the only available agent at the time.

^{99m}Tc-labeled agents are best suited for short term studies[20, 27, 63], while ^{169}Yb DTPA and ^{111}In-DTPA for the longer termed ones[30, 32, 37, 47, 49, 57, 68].

^{111}In-DTPA has most of the ideal properties which have been enumerated, especially in that the radiation dose is signi= ficantly less than with ^{169}Yb in situations where there is stasis around the cord and delay or blockage of CSF flow in= to the cranial subarachnoid space[1, 15, 42, 50, 51, 80]. The only problem with ^{111}In is its poor commercial availability. As it is a cyclotron produced radionuclide, with a half-life of 67 hours, such a facility should be at close reach. Some of the studies in this series were done with ^{111}In provided by the C.S.I.R. Cyclotron in Pretoria, and chelated with a commercial DTPA kit (CIS, INK-3). Unfortunately this radionuclide source was not always available.

For these reasons the bulk of the studies here presented were performed with ^{169}Yb-DTPA which proved the "ideal" radiopharmaceutical under the local circumstances. The ^{169}Yb-DTPA complex does not bind to plasma proteins and clears rapidly from the blood due to exchange with the ex= travascular space and excretion in the urine. The effective half life ($T_{\frac{1}{2}e}$) for ^{169}Yb in the subarachnoid space in pa= tients without spinal block or hydrocephalus is approximately

10 hours. As would be expected, the $T_{\frac{1}{2}b}$ for ^{169}Yb is greater in patients with hydrocephalus, since the CSF flow to the areas of greatest absorption is delayed[51].

3.2.2 PHYSICAL CONSIDERATIONS

Besides the biochemical properties of radiopharmaceuticals used in cisternography, there are physical properties of ideal γ-emitting radionuclides for imaging processes[46].

a. Plentiful γ-rays of an energy of 100 to 400 keV. If energy is too high, collimation tends to be inefficient. Lower energy collimators are more efficient in that they allow higher counting-rate by having thinner septa. If the energy is too low, it means increased radiation absorption in tissue so that deep-seated abnormalities are not so well detected.

b. Shortest half-life compatible with physiological phenomena. If half-life is too short, the test capabilities are spoiled by the radionuclide decay. If it is too long, radiation dose may increase to levels which are not satisfactory.

c. Minimum β-radiation. As the β-rays are not detected directly by the imaging devices, they only increase radiation dose to the patient and provide unwanted emergent radiation. The desired chemical agent should be easily bound to a pure low energy gamma emitting radionuclide with suit=

able photon yield for scanning.

Physical characteristics of the most commonly used radio= nuclides in cisternography are presented (table 3).

Iodine-131 is a fission product of uranium, the parent tel= lurium 131 which is first formed by the fission process un= dergoing beta decay. It is usually prepared by pile irra= diation of tellurium dioxide or extracted from irradiated uranium by steam distillation and then purified in a lengthy process[7]. It has a half-life of 8,08 days, and decays by multiple β and γ energies (figure 10).

Technetium-99m is produced as a result of the decay of molybdenum-99 (^{99}Mo). ^{99}Mo can be obtained as a fission product of uranium or by irradiating stable molybdenum with neutrons. The nucleus of ^{99m}Tc is in a metastable, energy-rich, excited state of ^{99m}Tc. The ^{99m}Tc emits this extra energy in the form of gamma quanta and thus de-excites to the ground state ^{99}Tc. In almost all these decay proces= ses gamma radiation with an energy of 140 keV is emmitted. The half-life of this disintegration process is 6 hours. ^{99}Mo-^{99m}Tc generators (half-life 67 hours) are commercially available. They are called "cows" and the elution procedure is known as "milking"[71] (figure 11).

Ytterbium-169 is a rare earth element of the lanthanide group that may be produced by thermal neutron bombardment of en=

TABLE 8

AGENTS PRESENTLY BEING UTILIZED FOR CISTERNOGRAPHY

RADIOPHARMACEUTICAL	HALF LIFE	ENERGY (keV)	INJECTED* ACTIVITY
^{131}I-HSA	8 d.	364	100 µCi
^{99m}Tc-DTPA and HSA	6 h.	140	1-4 mCi
^{169}Yb-DTPA	32 d.	177(60%) 198(60%)	1 mCi
^{111}In-DTPA	67 h.	173(89%) 247(94%)	250 µCi

* Average adult dose. Children and infants dose proportional to age and body mass.

riched stable Ytterbium-168 (^{168}Yb (n,) ^{169}Yb). The stable ^{168}Yb has a natural abundance of 0.135 with a high thermal neutron capture cross section of 11 000 barns. The gamma emissions range from 8 to 308 keV, the fractional abundance of the 177 keV and 198 keV gamma photons is relatively high (60 photons per 100 disintegrations) and the percentage of emissions of energy greater than these is low (10% for 308 keV). The physical half-life of 32 days is long, but in the chelated (^{169}Yb-DTPA) form biological elimination is rapid[68] (figure 12).

Indium-111 is usually manufactured in a cyclotron by irra= diating a target made of cadmium oxide containing 95% en= riched ^{111}Cd (^{111}Cd (p.n.) ^{111}In). The effective cross sec= tion is 50 mbarn at a proton energy of 10 MeV. ^{114}In, a contaminant with a long physical half-life, must be removed in the preparation process.

^{111}In decays by K-electron capture with a physical half-life of 67,5 hours (2,81 days). 99% of the disintegrations down to the stable state (^{111}Cd) result in the emission of two gamma-radiations in cascade[49] (figure 13).

3.2.3 DOSIMETRY

Radiation dose depends on the physical characteristics of the radionuclide, its biologic clearance, and its concentra= tion in the target tissue.

TABLE 4

COMPARATIVE MEAN ABSORBED RADIATION DOSES (RADS) TO SPINAL CORD FROM 1 mCi ADMINISTERED INTRATHECALLY

	DEPTH WITHIN CORD FROM SURFACE (cm)					
	0.0	.0001	.001	.01	.02	.04
^{169}Yb-DTPA	31.0	8.5	7.2	5.5	5.3	5.3
^{99m}Tc-DTPA	0.8	0.3	0.3	0.2	0.2	0.2
^{51}Cr-DTPA	1.4	0.7	0.7	0.7	0.7	0.7
^{113m}In-DTPA	1.2	0.4	0.4	0.4	0.3	0.2
^{67}Ga-DTPA	4.1	1.6	1.5	1.4	1.4	1.4
^{111}In-DTPA	5.3	2.7	2.6	2.5	2.5	2.5
^{131}I-HSA * (0.1 mCi)	16		14	9	6	
^{131}I-HSA** (0.1 mCi)	12			7	4	

* R.E. Johnston et al. Brit. J. Radiol.: 45: 444, 1972

** J.C. Harbert et al. J. Nucl. Med. : 11: 534, 1970

With a radionuclide of short half-life, the radiation dose to the patient is a function of the time radioactivity re= mains in the body. The rate of biological excretion of a radiopharmaceutical ($T_{\frac{1}{2}b}$) determines the radiation dose. For this reason, some radiopharmaceuticals with long-lived radionuclides can be safely employed in millicurie amounts. This is the case with ^{169}Yb-DTPA. As a whole, chelated com= plexes diffuse relatively slowly into the blood, but their clearance from blood is rapid[68].

One of the difficulties in calculating the absorbed dose is to assign a proper geometrical configuration to the CSF com= partments and CSF volumes, as well as the mass of the spine and brain. This has lead to different calculations by va= rious authors[15, 35, 51]. V. Brookeman, et al[15] presented comprehensive comparative data of mean absorbed radiation doses (Rads) to the spinal cord from 1 mCi, of different radiopharmaceuticals administred intrathecally (table 4).

D.A. Goodwin et al[30] made comparative whole body dosimetry calculation of CSF imaging radiopharmaceuticals (table 5).

For this study the South African Atomic Energy Board (G.P. de Beer) has calculated the internal dose to the spinal cord, brain, and skull for ^{131}I-HSA, ^{111}In-DTPA, ^{169}Yb-DTPA and ^{99m}Tc-DTPA with a computer program developed in their Depart= ment of Radiobiology (Table 6). The calculated doses are given as per µCi of injected activity. Also given are the in=

TABLE 5

COMPARATIVE WHOLE BODY DOSIMETRY OF CEREBROSPINAL FLUID AGENTS

COMPOUND	$T_{\frac{1}{2}e}$(hr)	ADMINISTERED ACTIVITY(μCi)	WHOLE BODY DOSE (RADS)		
			D_{γ}	D_{β}	D_{total}
^{131}RISA	120	100	0.068	0.102	0.170
^{99m}Tc albumin	6	2 000	0.025	0.007	0.032
^{111}In transferrin	67	500	0.212	0.053	0.265
^{111}In EDTA, DTPA	10	500	0.031	0.008	0.039
^{169}Yb DTPA	12	500	0.035	0.034	0.069
^{203}Pb EDTA	10	500	0.024	0.012	0.036

TABLE 6

ISOTOPE	SOURCE ORGAN AND INTEGRATED ACTIVITY A	TARGET ORGAN AND DOSE D RECEIVED
^{131}I	Spine A = 0,58 µCi.h	Spine D = 9 mrad
	Brain A = 14,53 µCi.h	Brain D = 5 mrad
		Skull D = 0,6 mrad
^{111}In	Spine A = 0,58 µCi.h	Spine D = 2 mrad
	Brain A = 13,06 µCi.h	Brain D = 2 mrad
		Skull D = 0,6 mrad
^{169}Yb	Spine A = 0,58 µCi.h	Spine D = 6 mrad
	Brain A = 15,07 µCi.h	Brain D = 4 mrad
		Skull D = 0,5 mrad
^{99m}Tc	Spine A = 0,55 µCi.h	Spine D = 0,8 mrad
	Brain A = 5,08 µCi.h	Brain D = 0,3 mrad
		Skull D = 0,09 mrad

tegrated activities. Because the doses are directly proportional to these , corrections can be made if assumptions appear to be non-realistic. These dose calculations were based on the following formula:

$$D(Rad) = \frac{\bar{A}}{m} \sum_i \Delta_i \phi_i$$

where

$\bar{A}$ = time integral

m = mass of organ

Δ_i = dose (μCi.h)

ϕ_i = type of rays absorbed in target organ

The radiation dose to the brain from ^{169}Yb-DTPA administered intrathecally has recently been questioned especially in cases of delayed clearance of the radiopharmaceutical in patients with hydrocephalus or spinal block[1, 15, 42, 50, 51, 61]. While Wagner et al[68] and 3M Company catalogue place the exposure in the range of 0,02 - 0,07 rad/mCi to the brain (Wagner) and 1,1 rad/mCi to the brain (3M) assuming normal renal function and normal resorption from the CSF, Barbizet, et al[6] claim that the radiation exposure to the brain can be as high as 1 500 rads. R.L. Morrin and F.H. de Land[50] conclude that in patients with delayed CSF flow the most conservative dosimetry assumptions yield surface CNS doses in the order of 30 rads (for 500 μCi of ^{169}Yb-DTPA), and that it is ..... "a safe radiopharmaceutical for cisternographic use and can be recom=

mended for these studies".

From the information on dosimetry quoted, it is clear that the most advantageous cisternographic radiopharmaceutical is ^{111}In-DTPA, which should be used when commercially available As the growing number of reports and personal experience of considerable quantities of retained ^{169}Yb does cast serious doubts upon the accuracy of published dosimetry studies, preference for ^{111}In should be strongly supported[34].

3.3 TECHNICAL CONSIDERATIONS

In order for radionuclide cisternography to be useful as a diagnostic procedure in the differential diagnosis of ab= normalities of CSF dynamics, instead of more invasive radio= logical examinations, meticulous attention to procedure detail is imperative. In general, it is technically easy and well tolerated, with few and minor complications[8, 43], but a care= fully established protocol should nevertheless be methodical= ly followed.

3.3.1 MATERIAL

3.3.1.1 LUMBAR PUNCTURE TRAY: Care should be taken that it is properly sterilized. A small gauge lumbar Dattner needle (No. 20 or 22) is recommended as it is less traumatic and prevents leaks leading to inefficient lumbar injection[23]. A good length is 8 cm. In small children standard 22 gauge injection needles 4 cm long, are easier to handle as there is

less soft tissue to traverse. A needle of larger diameter may be required in cases of meningitis to facilitate the flow of a more viscous CSF with high protein levels.

3.3.1.2 RADIOPHARMACEUTICALS

Radiopharmaceuticals used in cisternography have different biochemical and physical characteristics (label, half-life, molecular weight, energy, radiation dose, etc.) which in different clinical situations can be used advantageously[65, 67], but their choice should be weighed in relation to the proposed study, the type of imaging device, and most of all the availability of it[38].

^{131}I- Human Serum Albumin, was used for the first studies of this series, as had many other investigators for a long time, as it was the only available radiopharmaceutical for cisternography[2, 24, 25, 26, 28, 48, 56].

As with most protein indicators it must have a high specific activity to obviate the danger of an aseptic meningitis which occurs when protein is in excess of 3 - 4 mg. This limited the dose of ^{131}I-HSA to 100 μCi[10, 14].

The energy of ^{131}I (364 keV) is suitable for rectilinear scanning, and even though it is not optimal for the gamma camera, reasonable images can be obtained with it.

^{99m}Tc labeled Human Serum Albumin and DTPA with a pure gamma

emmission of 140 keV which is optimum for the gamma camera and suitable for the rectilinear scanner[20, 27, 63]. Larger doses can be used, between 1 - 4 mCi with the result of bet= ter images in a shorter time. However, its short half-life (6 hours) is not ideal for delayed studies.

^{169}Yb-DTPA, has a long physical half life of 32 days, coupled with a short effective half life of 9 - 13 hours[51] which al= lows delayed studies (24, 48, 72 hours) with a sufficiently large dose of 1 mCi[22, 68]. It emits photons with more than one γ radiation and is suitable for scanning with both a rectilinear scanner or gamma camera.

^{111}In-DTPA. Emits two pure gamma radiations in cascade. It has a 2,81 day half-life which is ideal for short and delayed studies. Lower doses can be injected (200 - 300 μCi) and still provide a good photon yield. All these fac= tors contribute to a low radiation dose[30, 37, 47, 49].

3.3.1.3 IMAGING DEVICES

During the time this study of CSF dynamics was developed, three different imaging devices were utilized, and the set= tings varied accordingly with the radionuclide being used:

Nuclear Chicago's Pho Dot II (La Paz, Bolivia). Crystal (NaI (Tl)) 3 x 2 in shielded by 2 in. of lead. Focussing collimator 19 hole with a focal length of 6,8 cm a relative count rate of 6 and ultimate resolution of 12 mm. Scan

speed 45 to 90 cm/min. Tap factor 4 to 8 depending on count= ing rate. K cpm varying from 10 to 100. Photo suppress set at 10%. Window 70 keV with centerline at 360 keV for ^{131}I, and 60 keV window with centerline at 190 keV for ^{169}Yb.

Ohio Nuclear Series 84 (Bloemfontein, R.S.A.). Dual 5 in crystal (NaI (Tl)). Focussing collimators Medium Energy to 370 keV 37 holes. Focal length 8,9 cm with a geometrical resolution radius of 15 mm, a geometrical plane source ef= ficiency of 24 x 10^{-3} cm^2, and a geometrical focus depth of 40 mm. Also, on occasions 163 hole 370 keV collimators were used with the same geometrical focal length, a geome= trical plane source efficiency of 4,4 x 10^{-3} cm^2 and a geo= metrical depth of focus of 18 mm. Line spacing $^1/16$ for head, $^1/8$ for spinal area. Ratio 5:1 for spinal area and 1:1 for head. Counting rates k cpm from 10 to 100 depend= ing on collimator. The speed varied from 200 to 600 cm/min depending on counting rate. Window setting of 60 keV with a centerline on 190 keV for ^{169}Yb. Enhance 10%. Both probes were used so that two opposing images could be per= formed at the same time (Figure 14).

Pho Gamma III Nuclear Chicago (Bloemfontein, R.S.A.). With a 12¼ x ½ in (NaI (Tl)) crystal, 19 photo multipliers. A low energy 250 keV, 4 000 hole parallel collimator was used for all radionuclides (^{169}Yb, ^{99m}Tc and ^{111}In).

10 k cpm were collected in 20 to 300 seconds according to

activity.

The isotope range was set at 140 keV for ^{99m}Tc, 190 keV for ^{169}Yb and 260 keV for ^{111}In with a preset window of 20% for the first two radionuclides and a 50% to get the two photopeaks of ^{111}In (247 keV and 173 keV) (figure 15).

3.3.1.4 SCINTIGRAPHIC SYSTEM PERFORMANCE

As radionuclides which emit photonswith more than one energy are being used for radionuclide cisternography, it is important to evaluate their scintigraphic system performance. This investigation was done at the Department of Biophysics, U.O.F.S. (National Hospital, Bloemfontein) for Ytterbium-169 and Indium-111[67].

When radionuclides with complex spectra are used (^{169}Yb, ^{111}In), the influence of the scattered high energy photons cause image resolution to deteriorate if low energy photons are selected. This is more marked if the high energy photons have a higher energy than the specified for the collimator, in which case septal attenuation breaks down and image resolution deteriorates even more.

To determine the photopeak of maximum performance the figure of merit proposed by Beck and Harper was used[66], which is a function of the plane sensitivity and geometrical resolution expressed in terms of the modulation transfer function (MTF)[54]. A Nuclear Chicago Pho Gamma III camera with

a 410 keV medium energy diverging collimator was used.

Ytterbium-169 (figure 12). The relative sensitivity ratios of 120 keV and 190 keV photons relative to 60 keV photons increased significantly with depth. At the surface the sensitivity of 120 keV photons was 27% of 60 keV photons and 52% at 12 cm. In the case of 190 keV the sensitivity was 34% at the surface and increased to 55% at 12 cm.

The figure of merit for the 190 keV photon energy is better than that for the other energies investigated at frequencies greater than 0,2 cycles/min. Therefore the geometrical resolution of 190 keV photons of ^{169}Yb is superior and recommended for cisternography.

Indium-111 (figure 13). The percentage of 247 keV photons was 69% at the surface and 62% at 12 cm as compared with 173 keV. With better geometrical resolution and higher figure of merit for a depth of 6 cm and frequencies greater than 0,2 cycles/min. the 247 keV photons provide better detail. However, with low count rates, better results are obtained with 173 keV.

It is possible to use two energy windows simultaneously to record images with photons at two different energies. This ensures higher sensitivity and shorter scanning sessions. The geometrical resolution of the combination, represented by the MTF, lies between those of the two individual photon

energies. The overall resolution of the combination proved to be much better than either the 173 keV or 247 keV images for the whole frequency range.

Even though this evaluation was performed with a 410 keV diverging collimator, and most, if not all the cisternograms done with the gamma camera were with a 250 keV parallel-hole collimator, the quality of the images was good, vali= dating the obtained data.

3.3.2 PROCEDURE

The most difficult part of the procedure lies in the per= formance of an adequate lumbar, cisternal or ventricular puncture, and efficient injection of the radiopharmaceuti= cal of choice. The success or failure of the procedure will depend to a great extent on the expierience gained by the injector, as well as other variables discussed below.

3.3.2.1 PATIENT MATERIAL

During a period of 4 years (1971 - 1975) 200 patients were evaluated by radionuclide cisternography for possible al= terations of cerebrospinal fluid flow. Of these, 100 were studied at the "Centro Medico de Diagnostico" (Medical Cen= tre) with the direct co-operation of the Department of Neuro= logy and Neurosurgery of the Medical Faculty of the Univer= sidad Mayor de San Andrés in La Paz, Bolivia (Head of Depart= ment: Prof. M. Michel). Patients were referred from the

General Hospital of Clinics as well as their medical records and neurological evaluation (1971 - 1972).

The remaining 100 patients studied were evaluated at the Radio-isotope facilities of the National Hospital, Bloemfontein. The patients came from the two teaching hospitals of the Medical Faculty of the University of the Orange Free State (Dean: Prof. F.P. Retief): National Hospital (European) and Pelonomi Hospital (Non-European) as well as the Oranje Hospital for Mental Diseases in Bloemfontein, Orange Free State, Republic of South Africa. The patients, their records and neurological evaluation were referred by the different departments of medicine and surgery (1973 - 1975).

3.3.2.2 PATIENT PREPARATION

Sedation should be used in the case of excited patients, most frequently 2 and 5 mg of Valium orally or 10 mg intravenously in the more serious cases. Five drops daily of Lugol's solution should be administered one day before and five after the test when using ^{131}I-HSA, to block thyroid uptake from free ^{131}I.

3.3.2.3 PUNCTURE

The selected radionuclide can be administered either via the lumbar or suboccipital (cisternal) route or can be injected directly into the ventricles. The patient is prepared for cisternography as in standard lumbar puncture

technique (or cisternal, or ventricular) as described by Brain and Walton[13].

The most frequent cause of failure of the technique is improper injection of the radiopharmaceutical into the epidural or subdural spaces, which has been reported in as high as 11 to 24% of the cases[70]. Imaging the spinal area 10 to 30 minutes after the injection demonstrates the distribution of activity and improper injection can usually be detected. When insatisfactorily injected, the study should be terminated and re-attempted after a suitable time lapse to allow radionuclide decay or biological removal[44]. Previous intrathecal punctures do not preclude subsequent cisternographic studies[45].

Suboccipital injection into the cisterna magna is an easy alternative route which can be used when the imaging of the lower spinal subarachnoid space is not relevant. It is time saving as the cephalic views can be started early and it is less likely to result in extra-arachnoid deposition of activity[70].

Following an intrathecal spinal injection, radioactivity is not normally detected in the ventricular system, thus a ventricular injection is usually only done in patients with suspected obstructive non-communicating hydrocephalus or to examine the efficiency or patency of a CSF diversionary shunt.

The following general points are emphasized: (i) The least possible manipulation is advisable and mannometric measurements and excessive barbotage should probably be avoided; (ii) a small gauge needle (20 to 22) and the least traumatic procedure is useful in preventing CSF leaks[23]; (iii) a standard injection-volume of less than one ml is recommended and the injection of air should be avoided in order to preserve the physiologic conditions of this single fluid system[41]; (iv) initial extraction of CSF does not necessarily guarantee a successful subarachnoid injection.

3.3.2.4 TIMING OF IMAGING

Regardless of the patient's position, radioactivity injected into the lumbar subarachnoid space, will normally pass cephaled to enter the basal cisterns. Here it accumulates before moving through the communicating pathways and over the cerebral cortex. It will not normally enter the fourth, third or lateral ventricles.

The spinal area is imaged 10 to 30 minutes following a lumbar injection. The initial images of the intracranial activity are obtained between 1 to 3 hours after introduction of the radionuclide, and almost immediately after cisternal injection. Early scans are important because ventricular filling almost always occurs early if at all. Such filling is generally obvious at this stage, but later may be obscured by tracer activity in the sylvian fissures.

Although the communicating pathways between the basal cis= terns and the more superior subarachnoid space over the cerebral convexity often can be seen on the initial examina= tion, they are most optimally visualized in these areas in the 4 to 6 hours study.

By 24 hours the distribution of radioactivity over the cere= bral cortex will usually demonstrate any non-uniformity or unilaterality and the superior sagittal sinus will show up as a localized area of increased activity that lies slightly inferior and conforms to the shape of the bony calvarium.

If this concentration of radioactivity is not present in the parasagittal area, delayed studies at 48, 72 hours or later, should be continued to document the changing pattern of CSF flow.

3.3.2.5 PATIENT POSITIONING

Specific projections are necessary to demonstrate certain anatomical features. Routinely, lateral, anterior and po= sterior views are obtained.

The lateral view is made with the patient lying supine and the head turned to one side (figure 16). In this projec= tion, the midsagittal plane of the cranium is parallel to the surface of the detector.

The anterior and posterior views are made with the cantomeathal

line perpendicular to the face of the imaging device (figure 17). This necessitates changing the patient's position for each view if a single probe detection device is employed, while two opposing views can be obtained simultaneously with a dual probe detector.

The radioactivity emanating from the CSF compartments will show optimally those anatomical structures in the focal plane of the imaging device. For example the major portion of the sylvian cisterns are anterior and better visualized in the anterior view. In obstructive communicating hydrocephalus, radioactivity usually enters the ventricles, and the superior portion of the activity in the lateral ventricle appears in the anterior view as a heart-shaped collection with a very active center, while in the posterior view it does not show radioactivity as concentrated in the focal plane, but show the temporal horns inferiorly as a "butterfly" configuration. In the lateral view the radiopharmaceutical in the lateral ventricle is seen as a reclining "C" configuration.

The optional vertex view is obtained with the patient in the prone position with the canthomeatal line closely parallel to the surface of the imaging device.

Another, useful view is the half axial view which simulates the radiographic Townes half axial projection. It is more easily accomplished with the gamma camera because the imaging

head can be easily angled. It is obtained by placing the face of the collimator in the frontal area at an angle of 30^{o} degrees caudal with the canthomeatal line (figure 18).

In cases of suspected rhinorrhea, placing the patient's head in a hanging position to enhance the gravitational nasal drip is very useful.

When evaluating the patency of a CSF diversionary shunt, the imaging device should be placed in the area of the distal extreme to determine the presence or absence of radioactivity.

Positional markers for alignment and orientation are an essential part of the procedure in most cases, and should be placed in each view by the physician responsible for the interpretation of the study.

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4. CLINICAL ASPECTS OF THE CEREBROSPINAL FLUID CIRCULATION

4.1 THE NORMAL INDIVIDUAL CSF DYNAMICS

In an age of sophisticated techniques and expert technicians, it is easy to be misled into accepting reports on special investigations at their face value - conflicting with clinical opinion. Obviously the outcome may be a more or less disastrous misdiagnosis. But how can a clinician avoid this danger when it is not possible to be an expert in the technical minutiae and potential failings of every investigative method? The only practicable answer is readiness to challenge diagnostic traps caused by misleading erroneous technical evidence or misinterpretation. For this it is necessary to establish the "normal" anatomical and physiological variants that may simulate disease.

Despite all the efforts of traditional medical education to regiment knowledge of health and disease in conveniently tidy systems (of anatomy, physiology or pathology), modern medicine is becoming more alive to reality. Truth demands recognition of every individual as genetically and environmentally unique. Anatomically, physiologically, biochemically, psychologically, individuals will differ from each other and, if no two people can ever be quite alike, no disease will be identical either. So much is virtually uncontestable, but difficulties arise when clinical practice requires clear-cut distinctions between normality and abnormality - which must often be based on incomplete evi=

dence. Since special investigations play an increasingly important role in acquisition of such evidence, the validity of their results must be rigorously and honestly examined. It is here where the normal variants may be grossly mis= leading when they cross the boundaries that clinical medi= cine must set between health and disease. Overdiagnosis of a normal variation as evidence of pathology may lead to needless and harmful therapy, rather than failure to recog= nize an actual abnormality. Some variations represent a phase of development and become eliminated in the course of maturation. It would be ideal to have clinical patterns that would fit Shakespeare's "Seven Ages of Men".

Radionuclide cisternography, based on anatomical and phy= siological principles of CSF flow as visualized by the ra= dio-activity in the subarachnoid space, can only be useful when the evaluation, management, and prognosis of its dis= turbances are analized in the context of these basic funda= mentals of clinical discrimination, and provide an answer to the following questions: Where is the tracer? How much tracer is in each CSF compartment? How long does it stay there[28].

4.1.1 ADULT CISTERNOGRAPHIC PATTERN

A radiopharmaceutical when injected intrathecally in the lumbar area by standard lumbar puncture technique, is graphi= cally depicted by scanning or scintigraphy as a smooth un= broken column of activity extending from the site of in=

jection to the basal cisterns, where it normally arives in less than 1 hour. If fills the basal cisterns on the 2 - 3 hour scan [77] (figure 19).

A faulty lumbar puncture delivering an insufficient amount of tracer into the spinal subarachnoid space deserves cau= tions interpretation ragarding CSF movement.

Both epidural and subdural injections will result in de= layed CSF movement. Epidural injections may be detected by imaging the area of injection, as the radionuclide will be temporarily confined to the lumbar region or may diffuse out into the soft tissues from where it will be removed by the blood stream. If the radiopharmaceutical is a chelated substance, it will show in the kidneys first and the bladder later (figure 20a).

Visualization of the nerve root sheaths in the shape of a "Christmas tree" is considered evidence of an epidural in= jection. Subdural injection may result in a parallel "rail= road track" patten of radioactivity[58] (figure 20b).

Once in the basal cisterns radioactivity will accumulate be= fore moving through the communicating pathways over the cere= bral cortex. From the cisterna magna radioactivity will flow in several cephalad directions, mainly: (i) a dorsomedial and superior route into the subarachnoid space investing the cerebellar hemispheres and brain stem, through the cisterna

quadrigemina, vena cerebri magna and callosi, to the medial and posterior aspects of the perihemispheric cerebri; and (ii) a ventral and major pathway, around the medulla and pons into the cisterna pontis, interpeduncularis, supracellar and prechiasmatic, from which it then passes through the Sylvian fissures and callosal cisterns to the lateral and frontal perihemispheric cerebri. The circulation finally ends at the level of the dural sinuses of the parasagittal region, where absorption occurs across the arachnoid villi [23, 39] (figure 5). The radionuclide appears to flow normally into all anatomical structures bathed by the CSF except the ven= tricles, probably reflecting the net CSF flow from them into the remainder of the CSF space [24].

When radioactivity is introduced directly into the ventricles, or by way of a suboccipital puncture, it normally appears in the basal cisterns in a few minutes (figure 21). From the basal cisterns movement of radioactivity is similar to the movement observed after intrathecal lumbar injection, except that from there a caudal movement can also be seen into the spinal subarachnoid space and subsequently reaching again the basal cisterns, confirming the directional CSF flow [22, 50, 55, 56, 57, 66, 71, 77] (figure 22).

At the time of the initial cisternographic imaging at 1 to 3 hours the various anatomic areas that can be separated in the lateral projections are the spinal cervical CSF canal, the cisterna magna, pontis, interpeduncularis and supracel=

lar. Although activity is also present in the quadrigeminal and ambient cisterns, multiple views (anterior, posterior and vertex) may be necessary to separate these structures from other areas of superimposed radioactivity[49] (figure 23, 2hr).

In 3 to 6 hours the radiopharmaceutical will be seen in the Sylvian fissures areas bilaterally as well as in the frontal portion of the longitudinal fissure. The Sylvian fissure area radioactivity overlaps the supracellar cistern in the lateral view. This and the quadrigeminal cistern in the posterior view have often been mistaken for lateral ventricular activity. Utilization of both a lateral and anterior view should minimize this error. Ventricular activity which is abnormal, will extend laterally and be more superior than the narrow band of radioactivity in the ambient cisterns.

At this stage the examination will normally show the more dorsal cisterns. There will also be beginning of diffuse movements of radioactivity over the cerebral cortex. The Sylvian fissure areas will be seen as extending dense bilateral bands in the anterior view. Radioactivity in the ambient and lamina terminalis cisterns will be noted anteriorly and posteriorly, but nearer the base than the convexity of the brain (figure 23, 6hr).

At 24 hours, the radiopharmaceutical is minimally present or absent from the basal cisterns, and is seen to be distributed over the cerebral hemispheres where it concentrates

as a band of increased radioactivity in the parasagittal region that lies below and conforms to the shape of the bony calvarium in the lateral view (figure 23, 24 hr).

Non-uniformity or uni-laterality of radioactivity over the cerebral cortex or lack of concentration in the parasagittal region should be regarded as abnormal[5].

Occasionally activity over the convexities will appear some= what irregular. This may be due to old scarring of the meninges with minimal local occlusion of the subarachnoid pathways. However, if there is no ventricular reflux and the rate of ascent is normal, the study as a whole should be considered as normal. If at 24 hours concentration of activity is not present in the sagittal area, delayed studies should be obtained at 48 to 72 hours to detect specific anatomic blocks of CSF movement[49, 50]. But it should also be kept in mind that radiopharmaceutical move= ment is slower in some elderly individuals who by all other criteria have no definable obstruction to CSF transit[47].

Only the larger CSF compartments will be clearly delineated by cisternography. Therefore cisterns of small volume which contain little CSF and a small amount of radioactivity, will be below the limits of spatial resolution of the present imaging devices and will not be identified as separate struc= tures. Examples of this, are the cisterna veli interposita and superior cerebellar cisterns.

The posterior pia-arachnoid membrane - a delicate structure - almost always prevents free egress of air during pneumoencephalography over the pericerebellar space, but does not appear to alter the movement of injected radioactivity as a small amount is seen occupying this space, even though anatomical resolution does not allow the identification of it anteriorly or posteriorly of the limiting membrane[49].

This implies that radionuclides, as they are "carried" by the CSF, will be able to pass narrow strictures that air may not. While this may be correct, it could also be quite misleading as has been suggested by another possibility[39], if in chronic communicating hydrocephalus periventricular transependymal migration of a radionuclide has been demonstrated[80], it could just as well be able to penetrate thin septa and narrow strictures giving the impression of an apparent unobstructed flow past the membrane.

Although the normal pattern is that of no ventricular filling and early clearance[40], some variants could rarely include transient appearance of radioactivity in the cerebral ventricles, preferential flow pattern to one side or other intracranially, and delay or acceleration in the progression of the labelled compound from the site of injection to the parasagittal region[55].

4.1.2 PEDIATRIC CISTERNOGRAPHIC PATTERN

The cisternographic pattern seen in children and in infants

is basically the same as that in adults, except the rate of ascent and clearance is much faster (figure 24). After intrathecal injection of a radionuclide into the lumbar area, activity appears in the cisterna magna within 5 to 10 minutes, probably forced upward by the large tracer bolus relative to the volume of ascent. By 30 to 60 minutes, the basal cis= terns have filled and radioactivity starts progressing to= wards the cerebral convexities. Often the cisterna magna is quite large and may not necessarily represent pathology if the remainder of the study is unremarkable. By 4 to 6 hours activity is at least halfway over the convexities, reaching them at approximately 12 hours. This resembles 24 hour distribution of the adults. At this stage, the tracer entirely surrounds the convexities and is beginning to clear from the basal cisterns. Delayed tracer clearance is con= sidered if cisternal and spinal activity persists at 24 hours, or if the ascending column of radioactivity has not advanced midway over the cerebral convexities by 12 hours[63].

4.2 THE PATHOLOGIC CSF DYNAMICS

Hydrocephalus as clinical entity needs constant redefinition and clarification of concept. This process of hydrocephalus, especially in adults, is superimposed on or secondary to an= tecedent brain disease or injury. Although hydrocephalus thus is not a primary disease entity, in its own right, it may be the critical factor in maintenance of symptomatology[29].

The fact that certain forms of hydrocephalus associated with

normal cerebrospinal fluid pressure may represent a treat= able form of dementia, is therefore of great clinical im= portance[2]. While in other situations the brain disease may be too far advanced, CSF pressure greatly elevated or the cerebral mass loss too great to permit a favourable clinical response to CSF shunting, which is also the case of arrested or compensated hydrocephalus where brain function loss may already have occurred and be irreversible[43].

Enlargement of the head, prominent scalp veins, enlargement and loss of pulsation of the fontanelle, turning down of the eyes (rising sun sign) are conspicuous symptoms in in= fantile hydrocephalus. Infantile hydrocephalus is thus usually diagnosed earlier than in adults[16]. This does not mean that the basic pathologic process in infants need neces= sarily be different from that of adults. The difference in the clinical picture which facilitate early detection in in= fants lies in the nature of the structures which produce re= sistance to increases in CSF pressure.

While hydrocephalus effects a lack of development in infants, it results in a loss of acquired capability in the adults with a panorama of neurological deficits and sociological implications, which can easily be reversed with CSF diver= sionary shunts if an early diagnosis is made.

The important role and indeed the necessity of radionuclide cisternography in selecting those patients that could bene=

fit from therapy stems from two sources. The first is the difficulty the clinician has in differentiating the signs and symptoms of normal pressure hydrocephalus from those of hydrocephalus ex-vacuo. The second is the equally difficult task which confronts the radiologist when he tries to differentiate the two by air studies[83].

4.2.1 CLASSIFICATION OF HYDROCEPHALUS

By determining the location of the radiopharmaceutical in the CSF compartments (Area), how much of it is located in each one of them (Counts) and how long it stays there (Time), with the pattern of normal radiopharmaceutical movement as a reference, the following categories of hydrocephalus can be recognized[11, 22, 40, 46, 50, 79].

4.2.1.1 Obstructive non-communicating (internal) hydrocephalus.

4.2.1.2 Obstructive communicating hydrocephalus (external)

(i) Overt obstructive

(ii) Occult obstructive (normal pressure) hydrocephalus.

4.2.1.3 Primary atrophic (ex-vacuo) communicating hydrocephalus.

(i) generalized

(ii) localized

4.2.1.1 OBSTRUCTIVE NON-COMMUNICATING (INTERNAL) HYDROCEPHALUS

Non-communicating hydrocephalus follows an obstruction to the circulation of the CSF either within the ventricles or

at the outlet from the fourth ventricle, which prevents free communication between the ventricles and the subarachnoid space[16, 90].

The interventricular aqueduct is a common site of obstruction and it may be occluded or narrowed by many disease entities. Classically, four processes have been distinguished: gliosis, stenosis, forking, and septum formation[76].

Gliosis of the aqueduct is probably the most common of the four. It may be acquired in utero or postnatally. It usually follows purulent or granulomatous leptomeningitis, chronic encephalitis, hemorrhage and in some cases it can be iatrogenically induced by intrathecal chemotherapy. In gliosis of the aqueduct, the original lumen is filled with nests of ependymal cells surrounded by fibrous astrocytes.

Stenosis is defined as a congenitally narrowed and deformed cerebral aqueduct. It is rare and difficult to recognize as the normal aqueduct varies in diameter and it is hard to tell how much narrowing is required before CSF flow becomes impaired. In man, stenosis may be genetic. In suckling hampsters, mumps virus will grow in ependymal cells producing a lesion similar to stenosis with hydrocephalus. It thus appears that infections early during embryogenic development may produce an imflamatory reaction leading to stenosis. Aqueductal stenosis has also been related experimentally to a lack or excess of vitamin A[16].

A communicating hydrocephalus may be converted secondarily into a non-communicating hydrocephalus when the aqueduct collapses or becomes atretic due to lack of CSF flow caused by a successful surgical bypass of the obstructed area.

Forking of the aqueduct is probably a developmental malformation usually associated with other malformations such as fusion of the corpora quadrigemina or oculomotor nuclea, or spina bifida. The aqueduct then usually consists of two channels with smaller branching blind channels[16].

The aqueduct may be occluded by a very thin septum. This is easily ruptured in autopsy handling and will them remain unrecognized, or it can be broken down while introducing an exploratory catheter which would cure a hydrocephalus[76].

The Dandy-Walker syndrome may also be a cause of non-communicating hydrocephalus. It is considered to be a cerebellar malformation with lack of development of the rombo-encephalic roof of the fourth ventricle with atresia of the foramina of Luschka and Magendie[41, 42].

In the Arnold-Chiari malformation abnormalities of the aqueduct are present so that there is also a component of non-communicating hydrocephalus[19, 86].

Radiopharmaceutical movement after lumbar injection in this form of hydrocephalus may be normal, as radioactivity is not

normally seen in the ventricular system[11, 40]. Failure to enter the ventricles because of an intraventricular block cannot be distinguished from normal, as increased CSF pressure in itself need not alter the pattern of flow, unless compression of the subarachnoid spaces is present with diminished upward flow of the tracer from the basal cisterns (figure 25).

Children with communicating hydrocephalus who undergo aqueductal closure after shunting often have a normal cisternographic pattern. In these cases a ventriculo-cisternal shunt can be useful in case a shunt revision should become necessary.

In obstructive non-communicating hydrocephalus ventricular injection of the radiopharmaceutical will be very informative as will be other radiographic techniques aimed at demonstrating the presence of dilated ventricles. Ventricles appear progressively enlarged, according to the extent and development of this type of hydrocephalus, do not drain into the subarachnoid space while radioactivity remains confined to the obstructed ventricles, until physical decay of the radionuclide (figure 26).

4.2.1.2 OBSTRUCTIVE COMMUNICATING HYDROCEPHALUS (EXTERNAL)

This form of hydrocephalus exists when there is either a disturbance in the formation, absorption of CSF, or an obstruction in its circulation in the subarachnoid space with

free communication between the ventricles and the subarach=noid space.

Increased production of CSF is a questionable entity, but may perhaps occur with papillomas of the choroid plexus[76]. Deficient absorption may be due to blockage of the arach=noid granulations by subarachnoid hemorrhage and rachnoidi=tis of obscure origin. Raised intracranial venous pressure due to compression of the venous sinuses by an intracranial tumour, or impediment to venous drainage, e.g. caused by dural sinus thrombosis extending into the tributary cortical veins occasionally produce hydrocephalus due to absorption deficit[35].

But in the great majority of the cases hydrocephalus results from obstruction to CSF flow. The block usually occurs in the region of the brain stem, at the incisura which is the narrowest part of the cranial subarachnoid space, over the cerebral convexities or around the superior sagittal sinus. The point of obstruction of CSF flow will be manifest by failure of normal movement past that point.

The most common cause of hydrocephalus is probably inflam=mation secondary to subarachnoid infections or hemorrhage. This may be in utero or later in life. Congenital malfor=mations and tumours probably occur next in order of fre=quency. In post-meningitic hydrocephalus the obstruction is usually produced by organization of exudate, fibrosis and adhesions[82]. Spontaneous, surgical or traumatic sub=

arachnoid hemorrhage may also produce adhesions in the sub= arachnoid space. Neoplastic infiltration and spread through the subarachnoid space, either primary or metastatic, can be extensive without altering CSF flow in many instances[76].

Laurence (1959)[16] in 100 consecutive pathologic examinations found that malformations were the sole cause of hydrocephalus in 14% of cases, but in association with infection and trauma, accounted for 46%. Inflammatory reactions due to infection or hemorrhage without malformation accounted for another 50% the remaining 4% being due to tumours. Thus, congenital and acquired factors contribute to hydrocephalus in infancy, and congenital factors may also contribute to adult hydrocephalus e.g. when arising from the Arnold-Chiari malformation.

The terms internal and external hydrocephalus which are often used, and placed here between brackets for reference purposes, are incompletely descriptive, since the ventricles are di= lated in all forms of hydrocephalus, both compensatory and hypertensive, and an increased volume of fluid in some parts of the subarachnoid space is common to both[16].

This type of hydrocephalus is divided into two subcategories:

(i) Overt obstructive communicating hydrocephalus

It is a form of hydrocephalus in which there is obstruction in the intracranial subarachnoid space with alterations of CSF flow accompanied by clinical and/or radiological mani= festations of increased CSF pressure (headache, vomiting,

cranial nerve pareses and papilloedema).

Cisternography will demonstrate the point of obstruction as an area of increased activity proximal to the lesion and failure of tracer movement past it. In some cases, no definite level of obstruction is identified, but it can be suspected if secondary or contralateral pathways of CSF flow contain increased activity.

Although in the majority of the cases the ventricles are enlarged, with evident early reflux into them there are grades of stasis of radioactivity inside the ventricular system which most likely represent stages of disturbance in CSF dynamics as the absorption defect and subsequent hydrocephalus does not follow an "all or none" rule. Hydrocephalus thus varies, from a complete block over cerebral convexities and filling of enlarged ventricles, to a partial obstruction of the subarachnoid space over one convexity and little or no ventricular filling. Front and Pening[73] observed that although about one third of the patients who suffered subarachnoid hemorrhage developed ventricular dilatation, only 10% had permant hydrocephalus (figure 27).

(ii) Occult obstructive (normal pressure) hydrocephalus

It is a paradox of modern medicine that the lengthening of the life span has resulted in a corresponding increase in the number of people who suffer some form of mental deficit due to the aging process. The longer people live, the less

ability they show to keep pace with their problems. When presented with an emotionally disturbed patient over the age of 50 who suffers personality changes, behavioural and intellectual impairment in the abscence of gross neurological signs, the general attitude has been to limit the differen= tial, diagnosis to psychosis and dementia of unknown etiology. The chronicity and hopelessness of his condition then confines the patient to a vegetative life in a mental institution.

The description of the syndrome of normal pressure hydro= cephalus (NPH) by Hakim and Adams[2. 36] in 1965, initiated a widespread renewal of interest in the diagnosis and neuro= surgical treatment of dementia.

Disturbed mental function is the most prominent symptom of NPH. This may vary from a mild apathy or mild loss of recent memory to severe psychomotor retardation, including akinetic mutism. The dementia develops at a rapid pace with daily fluctuations. The degree of apathy and lack of concentration is more striking than depression of cognitive ability.

Most patients with NPH are incontinent of both urine and faeces in the presence of normal or only moderately spastic sphincter tone[15].

Motor abnormality is a frequent component of this syndrome. Most often, a spastic gait, with increased deep tendon re=

flexes and extensor plantar sign is present. Typically the patient has great difficulty in starting to walk or standing up and shows a retropulsive tendency[56].

The CSF composition demonstrates nothing remarkable as far as cellular or chemical content is concerned. The pressure may be abnormally low or moderately elevated, but as the name implies, is most often in the range of normal[72]. It has also been noted that papilloedema is not a feature of this disease[48]. In this form of communicating hydrocephalus there is a decrease in brain substance which is mainly central (periventricular)[79].

The etiology of NPH is uncertain and probably multifactorial. The most frequent factors thought to contribute to its development are subarachnoid hemorrhage[3, 30, 37, 45, 74, 88], meningitis[57, 78, 82] and head injury[20, 31, 60] all of which may result in edema and fibrosis of the leptomeninges with interference to the normal CSF flow over the brain surfaces.

Normal pressure hydrocephalus should be considered in any patient with rapidly progressive dementia and the signs previously described, because NPH differs from other chronic organic brain syndromes in that it is potentially reversible and one of the rare forms of dementia that can be treated successfully by diversionary CSF shunts[72].

It is evident, therefore, that additional studies are required

in the diagnostic work-up of patients with progressive de= mentia in order to select those likely to benefit from a shunt. Diagnosis is validated by specific pneumoencephalagraphic (PEG) and radionuclide cisternographic findings. The con= dition basically results from a contraction of the subarach= noid space over the cerebral convexities with impairment of CSF flow towards the superior sagittal sinus. The cisterno= graphic pattern of NPH consists of delayed radiopharmaceuti= cal movement, abnormally early and persistent ventricular filling, failure of radiopharmaceutical to move over the surface of the brain convexities and to concentrate in the parasagittal region even on delayed studies. Radioactivity in the overfilled ventricles has a distinct "heart" configu= ration on the anterior view, a "butterfly" configuration on the posterior view and a reclined "C" shape on the lateral view[79] (figure 28).

4.2.1.3 PRIMARY ATROPHIC (EX-VACUO) COMMUNICATING HYDRO= CEPHALUS

This form of communicating hydrocephalus is characterized by a general or focal increase in the CSF volume in the ventricular system, basal cisterns or over the cerebral convexities, secondary to the shrinkage of brain substance. However, the principal pathway of CSF reabsorption is pre= served.

(i) Generalized

The reason for this abnormality may be multiple. The brain

is known to undergo atrophic change due to cerebrovascular arteriosclerotic disturbances associated with aging. Brain mass loss can be as much as 100 gr by 70 years of age: gyri become narrowed and sulci widened with an increase in the subarachnoid space surrounding the hemispheres. Dilatation of the ventricular system is also frequently observed, the dura becomes adherent to the underlying tissue, the pia thickens and becomes opaque. Even the arachnoid villi be= come fibrous and calcified causing delayed CSF absorption in the parasagittal region[89] (table 7).

Cisternography shows that the subarachnoid space is enlarged, as reflected by delayed movement of radiopharmaceutical through the subarachnoid spaces. If the ventricles are considerably enlarged, there may be an associated reflux of radioactivity into them. This will eventually fade after 24 hours and does not remain for longer periods as is frequent with NPH. For this reason, it is important to have late scans of these patients to demonstrate parasagittal activity. Flow of radioactivity over the cerebral convexities, however, is usually uniform and concentration of activity at the sites of absorption will eventually occur after a delay of 48 to 72 hours[59, 79] (figure 29).

(ii) Localized

Brain injury with focal loss of brain mass may result in porencephalic cysts communicating with the ventricular sys= tem, or manifest as focal enlargement of the subarachnoid space over the atrophic area. Porencephalic cysts may com=

TABLE 7

FINDINGS IN PATIENTS WITH HYDROCEPHALUS

DIAGNOSIS	CSF		PNEUMOENCEPHALOGRAPHY			CISTERNOGRAPHY	
	CHEMICAL DETERMINATION	PRESSURE	VENTRICULAR SIZE	CORTICAL SULCI	VENTRICULAR FILLING	FLOW OVER CEREBRAL CONVEXITIES	CONCENTRATION IN SAGITTAL AREA
1. Obstructive non-communicating hydrocephalus	Abnormal	Increased	Enlarged	Normal	Absent	Present	Present
2. Overt Obstructive communicating hydrocephalus	Normal or Abnormal	Increased	Enlarged	Normal or Abnormal	Present	Present or blocked at specific places	Present
3. Normal pressure hydrocephalus	Normal	Normal	Enlarged	Not visualized	Present	Absent or markedly reduced	Absent
4. Primary atrophic hydrocephalus	Normal	Low or Normal	Enlarged	Enlarged	Absent to Present	Present	Present though delayed

municate with the ventricles, with radionuclide entry into them as well as cyst. In such cases the porencepahlic cyst and ventricles will contain radioactivity when there is no evidence of obstructive communicating hydrocephalus. This may be due to the absorptive function of the cyst causing a reversal of the normal CSF flow pattern. The characteristic cisternographic pattern of porencephaly is thus increased focal accumulation of radioactivity[50] (figure 30).

4.2.2 BIOMECHANICS OF HYDROCEPHALUS

The description and widespread recognition of normal pressure hydrocephalus[2, 36] and the use of radionuclide cisternography has stimulated considerable interest in the dynamic physiopathology of impaired CSF circulation.

In most instances it has been impossible to distinguish the effects of the hydrocephalus from the disease which caused it such as meningitis, tumour, Arnold-Chiari malformations, etc. Only in conditions such as aqueductal stenosis, where little else is abnormal in the brain can one see hydrocephalus in its pure form where increased CSF pressure is responsible for progressive ventricular enlargement and the biomechanics of cerebral deterioration is clear-cut.

Attention has been attracted mostly to the infantile variety of hydrocephalus in which ventricular enlargement is followed by a corresponding and obvious head enlargement. Here the brain suffers lesser degrees of injury because the cranium

is permitted to expand and enlargement of the ventricles is due more to stretching than to wasting by hypoxia, which is the case in adult forms of hydrocephalus, where the brain is restricted to a limited space[1].

In order to understand the pressure changes that can accompany variations in CSF volume various theoretical and mechanical models have been developed[51].

The intracranial contents enclosed in a rigid skull are divided into three compartments: the brain tissue, the CSF and the vascular system. Since the sum of the three compartmental volumes remains constant an increase in the volume of one of them, necessitates a decrease in the volume of one or both of the other two compartments[70].

The CSF and venous systems behave as liquid circuits, while the brain tissue behaves like a viscoelastic solid. Thus the CSF and venous systems will transmit pressure as will any ordinary liquid system, while the viscoelastic brain tissue transmits forces and is thereby vulnerable to internal stresses.

A liquid at rest will transmit pressure equally in all directions while a solid transmits pressure in only one direction. Pressure is perpendicular force per unit area, while force is pressure multiplied by area. This means that for a given pressure the force will be increased when the area

over which the pressure acts is increased. The concept of force must then be considered in terms of pressure and area, as well as the medium trhough which it is transmitted[35].

$$F = P \times A$$

where F = Force

P = Pressure

A = Area

The main factor in maintaining intracranial pressure is the arteriolar - capillary blood pressure, a fact which becomes self-evident in shock, when the fall in CSF pres= sure corresponds to the fall in blood pressure. Variation in the cerebrovascular resistance offered by arteriolar constriction seems to be the main mechanism by which CSF pressure is modified. In addition, the venous pressure, which regulates to some extent the blood volume in the cranial cavity, and the mass of brain tissue itself and any pathologic element which it may contain, also influence the level of CSF pressure. Most likely at all times, there is a delicate balance between intracranial vascular volume, quantity of CSF, brain volume, and the force of arteriolar-capillary pressure[36] (figure 31a).

When intracranial disease interferes with CSF circulation between the ventricles and the arachnoid villi and the conditions which favour the development of hydrocephalus exist, the following events are observed.

Initially even though there is reduced absorption of CSF by the arachnoid villi, production is not diminished[6]. This subabsorption of CSF causes a slow and intermittent rise in pressure in both the ventricles and the subarachnoid space (figure 31b). At this time histologic changes take place with transformation of the ependymal cuboidal cells into flat non-ciliated cells, and enlargement of the extracellular space in the periventricular region suggesting edema. Permeability changes allow free transependymal movement of large molecules with CSF passing into the brain parenchyma by a process much more dynamic than simple diffusion [52].

The brain, being a viscoelastic substance resists these forces, but is somewhat compliant due to the presence of cerebral veins. The small periventricular cerebral veins and capillaries may collapse as their critical closing pressure is reached or their lumen is narrowed to such an extent that blood supply decreases, resulting in a combination of pressure and ischaemic damage initially localized to the periventricular white matter, with enlargement of the ventricles[10].

As the ventricles grow larger with rising pressure, flattening and destruction of ependymal cells occurs (figure 31c), increasing the loss of integrity of the ependymal layer and widening of the space between supporting cells which apparently facilitates transependymal movement[80, 81].

When the cause of the ventricular enlargement now disappeares and the CSF pressure returns to normal levels, the imbalance between the two opposing forces acting on the brain tissue will remain because of increased ventricular area. Thus, the neurological and mental symptoms are perpetuated in the face of normal CSF pressure (figure 31d).

This gradual fall in high CSF pressure, in the early stages of hydrocephalus, to normal or even low pressures, may thus coincide with the expansion of the ventricular system. Expressed in terms of pathophysiology any slightly elevated pressure in dilated ventricles will compress brain tissue more severely and impair its function to a greater extent than when the same pressure is applied to the walls of normal-sized ventricles. In other words, there might be a reciprocal relationship between ventricular pressure and surface[33].

Hakim[36] suggested that Pascal's law for fluids- where the force excerted by the fluid in the surrounding medium would be equal not to the pressure of the fluid but to the pressure times the area of surface on which if acts - might be applied. This he designated as the <u>hydraulic press effect</u> of hydrocephalus, thereby introducing into CSF hydrodynamics a totally new concept. Similar relationships are known to hold for fluids contained in elastic containers where low pressures in large containers will support heavier weights than those in small containers (the analogue of the truck tyre which is inflated with low pressure and bycicle tyres

with high pressure)[1]. In the same way, if two brains posses= sing different ventricular sizes are subjected to the same ventricular pressure, the larger one will exert a greater force on the cerebral tissue (figure 32).

4.2.3 OTHER CSF DISORDERS

The use of radiopharmaceuticals in delineating the CSF ca= vities is effective in diagnosing many disorders not neces= sarily accompanied by hydrocephalus. Some of these disorders are associated with localized occlusion of subarachnoid space. These can result from hematomas[30, 74], tumors[57], infarctions[3,37], abcesses, and adhesions following haemorrhage[68, 88], or me= ningitis[78, 82].

In this regard, a promising application of cisternography is the detection of tumors. Some of them show no abnormalities in angiographic studies, nor in the conventional brain scan= ning. It has been found, however, that cisternography fre= quently shows a localized blockage or contraction of the subarachnoid space above the tumour and this fact may lead to the diagnosis.

Case Demonstration (RI/979/75)

A 63-year-old man previously treated surgically and with radiotherapy for an adenocarcinoma of the right parotid gland, suddenly developed a right sidedhemiplegia. A left carotid angiogram (15.8.75) and a radionuclide brain scan (19.8.75) where negative. A cisternographic study (19.9.75)

showed a localized blockage of the subarachnoid space as an area devoid of radioactivity in the left parietal con= vexity. A brain scan performed 4 days later (23.9.75) demon= strated a space occupying lesion in the same area (figure 33).

Other clinical indications for cisternography include the assessment of CSF shunt function, diagnosis and follow-up of CSF leaks and localization of spinal block lesions.

4.2.3.1 ASSESSMENT OF EXTRACRANIAL NEUROSURGICAL CSF SHUNTS

The only way to restore a balance in hydrocephalus is to decrease the CSF pressure and convert the CSF system from a closed to an open system in order to create elasticity in it. Then the venous system will be able to return to its normal volume. This is attained by a surgical shunting procedure, which not only lowers the CSF pressure below normal but also opens the CSF system to the extracranial venous system (figure 34).

Once the shunt is established, the venous force pushes back the parenchyma against the now-lowered CSF system force and the once collapsed venous bed regains its free flow, correct= ing the hypoxia with a return to normal metabolism of the brain tissue and recovery of its proteins and lipids. Be= cause of its viscoelastic properties the brain tissue will return to its normal position and the ventricles return to normal size[35].

The treatment of hydrocephalus by establishing communication between the CSF pathways and vascular system was suggested by Gartner in 1895. Practical operative techniques had to wait the development of a check valve, which was engineered in 1956 by Spitz and Holter. This valve and others of the same type that soon followed had the inconvenience of not being sterilizable by autoclave, a tendency to block with high protein fluids and not adequately regulating the CSF pressure.

In 1964 Hakim invented an autoclavable, stainless steel valve using a spring device and a saphire ball which al= lowed control and a constant reduction of CSF pressure to any desired level, instead of simply draining fluid from the ventricles[1].

This was an important achievement, as there had been cases in which CSF pressure was lowered too far causing a rever= sal of the force imbalance with the venous pressure becoming larger than that of the CSF. Overcorrection of this kind led to engorgement of the veins, cerebral edema and decreased ventricle size. In children this problem may lead to micro= cephalus[35].

Contemporary therapy of hydrocephalus includes placement of a ventriculo-atrial or ventriculo-peritoneal shunt. The Nulsen-Spitz shunt with the subcutaneous Holter valve, and the Pudenz shunt with intravascular Heyer valve are the ven= triculo-vascular devices of choice while the Torkildsen

operation is still be preferred procedure for cisternal shunting[25, 44]. The dramatic clinical improvement in many patients operated on after a lengthy period of normal pres= sure hydrocephalus, with complete recovery once equilibrium has been restored between the venous and CSF system [8, 32, 45, 64], led to an over enthusiastic desire to cure any presenile demented patients with a simple shunting procedure. That was finding a cure for an incurable disease because uninten= tionally people had been losing sight of Hakim's original description of NPH[1, 38, 43].

With time NPH has been placed in perspective and cisterno= graphic changes have been identified with the best predic= tion of a shunt success. While hydrocephalus ex-vacuo may occasionally be associated with dementia, urinary incontinence and gait disturbance, a careful analysis of the cisternogra= phic pattern will generally suffice to separate the two con= ditions[62].

The understanding of rates of tracer movement and ventricular entry which are relevant to an adequate diagnosis should im= prove with quantitative analysis of CSF flow, as would a multi-institutional study concerning the usefulness of radio= nuclide cisternography in the evaluation of this disease spec= trum[38].

A variety of CSF shunts are in common use[44], they all con= sist of three basic components: a proximal (ventricular)

limb, a central reservoir or pump (flushing device) and a distal (systemic) limb. The proximal limb consists of a catheter which is inserted into the lateral ventricle through the skull. The reservoir is located under the skin in an accessible area of the scalp where it can be pumped to asses patency or can also be used to obtain CSF and pres= sure measurements by percutaneous injection. The distal limb catheter diverts CSF from the central reservoir into the heart or peritoneal cavity for reabsorption[75].

One of the major problems with this therapy is maintaining adequate shunt function. Malfunction can be due to mechani= cal failure of the shunt, occlusion of the shunt by debris, or the development of loculated spaces around the tip of one or both limbs. Usually a diagnosis of shunt patency and adequate CSF flow is easily made by clinical examination of the patient and inspection of the subcutaneous CSF reser= voir[84]. However, in doubtful cases an injection of a small dose of a radiopharmaceutical (1 mCi or less of ^{99m}Tc DTPA) into the ventricular system or the shunt reservoir, will suf= fice in determining the CSF shunt patency, as radioactivity should be visualized in both limbs of the device (figure 35). Any obstruction will show an interrupted flow pattern. Even more, this flow through the shunt can be assessed by quanti= tative methods which have also proved to be reliable means of identifying patients with <u>arrested</u> hydrocephalus[34, 44, 84, 75].

4.2.3.2 DIAGNOSIS AND FOLLOW-UP OF CSF LEAKS

Localization of leakages in cases of CSF rinorrhea and/or otorrhea of traumatic origin, spontaneous, or congenital[85], is a difficult diagnostic problem where various procedures have proved disappointing.

The use of dyes and fluorescent substances is not very reliable in the localization of external CSF fistulae and, in addition, may be dangerous[28]. Plain x-rays provide little information, except in major obvious lesions. Cotton pledgets located in the walls and roof of the nasopharinx and external auditory canal fail to give anatomical infor= mation about the place of the leakage[65, 67].

The most common sites of CSF leakage are: through the fron= tal sinus, the lamina cribosa, the sphenoid sinus via the sella, and the petrous bone via the middle ear and eustachian tube[26].

Radionuclide cisternography is a reliable, informative, simple and innocuous method for localizing the site of leakage in cases of CSF external fistulae. The procedure is the same followed for cisternography. The radiopharmaceutical, usually a short lived radionuclide (2 to 3 mCi of ^{99m}Tc-DTPA), - as no delayed studies are necessary - can be introduced directly into the basal cisterns via a suboccipital injection. It is advisable to scan the patient's head in a position that will facilitate the "drip" through the fistulous track.

This procedure localizes the meningeal-bony break or the fistulous path. Such information cannot be obtained by any other method. Radionuclide cisternography can be repeated safely in order to follow-up cases after surgery.

Case Demonstration (CMD/C 13 and 92)

Two patients with postraumatic CSF leaks are presented. The first patient had right side otorrhea which was later repaired by a surgical plastic procedure (figures 36a and b). The other patient had rinorrhea which was treated conservatively with antibiotics to avoid the ever present danger of meningitis (figure 37).

4.2.3.3 LOCALIZATION OF SPINAL BLOCK LESIONS

Radionuclide myelography has been used as an occasional, aid in the localization of spinal block lesions. It is the oldest application of CSF scanning introduced by Bauer and Yuhl[12] in 1953. They showed its potential usefulness in cases in which the introduction of irritating foreign contrast media would be contraindicated. It is interesting that in large Russian neurosurgical centers, radionuclide myelography is the procedure of choice in confirming disc herniations, although it has been primarily used to localize complete spinal block lesions[61].

The procedure is the same as for cisternography and scans of the spinal canal are obtained during the first hour after

intrathecal injection.

The block can be complete, with no activity distal to the le= sion, or partial with delayed, irregular or incomplete pas= sage of the radiopharmaceutical to the basal cisterns. The most frequent causes for blockage are primary or metastatic tumors, medullary angioma, intramedullary ependimona, ab= cess or degenerative vertebral changes of different etiology[27]. Surgical, traumatic or spontaneous fistuale due to tear of the dura can be shown as extravasation of radioactivity. Collections such as in myelomeningocoele appear as sacular areas of increased activity.

Case Demonstration (RI/839/74): A 50 year old man presented with severe iron deficiency anemia, pain in the neck and lumbar area. The CSF spinal scan showed an activity void at the level of C3-6 with partial block and delayed flow to the basal cisterns, from where the cisternographic pattern was normal. The radiological report was that of osteoarth= ritis in the midcervical spine with degenerative disc lesions at C3/4, C4/5, C5/6 with anterior and posterior osteophyte formation (figure 38).

4.3 COMPLICATIONS OF CISTERNOGRAPHY

Isolated case reports of aseptic or chemical meningitis fol= lowing intrathecal administration of radiopharmaceuticals for cisternography have appeared in the literature[4, 9, 10, 53, 69].

The reported reactions have been of the same general type, with high fever of short duration, neck stiffness, increase of cell count and of protein in the CSF. Sugar almost always remained normal; cultures and the standard rabbit pyrogen tests have always been negative. Complete recovery within a few days has been the rule. No objective neurological signs have been reported.

Most of the cases have been associated with the use of ^{131}I-human serum albumin[9, 14, 53, 69], in a few cases the radiopharmaceutical was ^{99m}Tc-albumin[10] and in two cases the agent was ^{111}In-DTPA.[4]

The incidence of this complication has varied between 3%[69] and 27%[9]. In the series presented for this thesis, there were only 3 cases of meningeal irritation.

In two cases (CMD/C 12 and 17) where ^{131}I-HSA was used the clinical picture was similar to that described above, while in the third, a very labile woman (RI/726/75) where ^{169}Yb-DTPA was injected the only positive signs were neck stiffness and headache for 6 days.

This low incidence can be related to the fact that in only a small number of patients ^{131}I-HSA was used, while the bulk, were studied with chelated radiopharmaceuticals (^{169}Yb-DTPA, ^{111}In-DTPA, ^{99m}Tc-DTPA).

The pathogenesis of the meningeal reaction is uncertain. The clinical course and CSF culture exclude bacterial etiology. However, as noted by others[14] the human subarachnoid space may be much more sensitive to pyrogens than the standard culture or pyrogen tests, and the use of the Limulus test as a more sensitive method has been proposed[21]. Contamination by trace quantities of irritant chemicals used to clean pharmaceutical vials and skin might have resulted in chemical irritation. Finally, an accompanying pneumoencephalogram has shown to have increased the incidence of a febrile course[9].

Another possible complication of cisternography is the retention of the radiopharmaceutical in the subarachnoid space in the eventuallity of block or poor reabsorption, becoming a radiation hazard to the patient.

Case Demonstration (RI/76/75)

A 16-year-old girl presented severe and persistent headache with other symptoms that suggested a focal epilepsy. The cisternogram performed with 1 mCi of ^{169}Yb-DTPA, showed a delayed CSF flow towards the cerebral convexity. She was scanned every week for 4 weeks, and then, there was still enough radioactivity intracranially to produce a satisfactory image (figure 39). Even though the radiation dose this girl received was not calculated, it is presumed, it was very high.

4.4 QUANTITATIVE CISTERNOGRAPHY

As experience with cisternography increases, newer uses for this diagnostic modality will be found. Results to date suggest that the time course of the passage of the various radiopharmaceuticals through the cerebral cisterns and ventricular cavities during cisternography is important in differential diagnosis. These observations were previously made by subjective interpretation of serial scan images. Visual interpretation of images is adequate for anatomical determinations but quantification of the time course of radioactivity by this method is hazardous. A method to quantify the amount of radioactivity within the cerebral cisterns in serial scan images obtained at various time intervals after intrathecal injection of an appropiate radiopharmaceutical should improve the clinical value of this technique[18].

In assessing the value of CSF diversionary shunts, it appears that patients with stasis of the radiopharmaceutical in the lateral ventricles receive the greatest benefit. To determine "stasis", images were obtained at 4, 24, 48 and 72 hours. The diagnosis of "stasis" depends upon identification and quantification of continued radioactivity in the lateral ventricles, basal cisterns and superior sagittal sinus. This may also lead to more accurate determination of CSF flow and stasis, and allow comparison of various patient populations.

An image display and analysis system to quantify cisterno= graphic studies has been employed for this purpose. The image display and analysis (IDA) system consists of a television screen terminal command generator coupled with a PDP-8 mini-computer and colour and black and white tele= vision display monitors (figure 9). Scans are recorded simul= taneously in the conventional manner and transferred directly on-line to the IDA disc storage system. The relative amounts of radioactivity present within the cerebral cisterns and/or ventricular cavities at various time intervals after injec= tion (generally 4, 24 and 48 hours) are measured using a joy-stick to delineate the area of interest (figure 40). These data are expressed as percent of activity, and curves expressing the amount of radiopharmaceutical within the spaces and the time course of its passage through the cisternal and ventricular pathway are derived. The amount of radiopharma= ceutical present within the ventricles is compared with that in the basal cisterns and superior sagittal sinus.

This technique provides objective quantification of cisterno= graphic abnormalities, e.g. intraventricular stasis, and de= layed as well as decreased reabsorption.

As this system has only recently been available for quanti= tative cisternography, no statistical evaluation of diffe= rent patient populations is presented but rather three typi= cal selected cases. In a normal individual (figure 41) acti= vity clears rapidly from the basal cisterns and soon reaches

the superior sagittal sinus from where it is cleared to a great extent by 24 hours. The activity in the ventricles is small, due mostly to overlying structures which contain the radiopharmaceutical. A case of NPH (figure 42) where there was significant activity in the lateral ventricles and a patient with cerebrovascular arteriosclerotic disease (figure 43) where very little activity reached the superior sagittal sinus in a delayed 72-hour study are also shown.

With the same purpose in mind, that is to correlate the scan's qualitative anatomical information with a more meaningful time course passage of the radiopharmaceutical through the CSF space, profile scans and total body counts at different time intervals where performed in a whole body counter[17, 54] (figure 7).

Patients were scanned at 2 mm/sec with two opposing detec= tors in the longitudinal sagittal axis in the supine posi= tion from the mons pubis to the cranial vault at 30 minutes, 4, 24, and 48 hours and occasionally 72 hours after intra= thecal lumbar injection of an appropiate radiopharmaceutical. Data was recorded separately on a multichannel analizer from where it was transferred via punch tape to a calculator plot= ter where the profile was delineated and expressed in counts accumulated in the area circumscribed by the profile. For each case the same radiopharmaceutical and the same dose were injected.

As with the previous method, only a limited number of patients have been studied by this procedure and two selected cases are presented: the same normal and cerebrovascular arteriosclerotic patient demonstrated above.

In the normal individual (figure 44) the activity can be seen rising from the lumbar area towards the head (4 hours); from there activity is cleared by the blood and excreted by the urinary tract, appearing in the bladder at the same time that activity is cleared from the head (24 and 48 hours).

In the patient with primary atrophic hydrocephalus (figure 45) due to arteriosclerosis a considerable amount of activity remains in the head after 72 hours without being reabsorbed into the blood (the scale factor for this patient is double that of the normal).

The profile scan and total body counts have added information on the complex behaviour of CSF in pathologic conditions. The cumbersome multiple blood sampling for the study of transfer of a radiopharmaceutical from CSF to plasma is obviated[7, 13, 87] and the profile curve can be easily quantitated at any desired segment. The further extension of these studies to other clinical conditions involving abnormalities of CSF fluid dynamics would seem worthwhile, and the value of the methods described in this thesis and their limitations, could be further explored.

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5. RESULTS AND DISCUSSION

For the purpose of this study 200 patients with neurological disease were evaluated by radionuclide cisternographic proce= dures (tables 8, 9). The patients were arranged into eight groups according to the suspected pathologic conditions for which the examination was performed (tables 10, 11).

5.1 NORMAL (Table 8, no. 3, 4, 10, 11, 19, 20, 23, 25, 28, 29, 30, 34, 36, 41, 43, 46, 49, 58, 66, 76, 77, 84, 85, 94, 98, 101, 103, 104, 105, 110, 116, 123, 125, 126, 130, 137, 140, 143, 147, 148, 151, 157, 158, 160, 163, 166, 169, 171, 175, 176, 181, 182, 183, 186, 189, 190, 195 and 200).

58 individuals demonstrated a composite visual picture which could be accepted as being within the range of normal[10, 14] (figure 22, 24). Of these 11 had presented with head injury; 11 suffered epilepsy; 7 had TB meningitis; 8 has degenera= tive neurological disease of which 5 were spino-cerebellar degenerations (3 in one family); 4 were investigated for suspected brain tumour or metastases. The remaining 12 in= dividuals with normal cisternograms were investigated after lumbar punctures performed for unexplained headache and other diverse minor conditions.

5.2 FAILURE AND INCOMPLETE (Table 8, no. 1, 32, 40, 48, 50, 60, 62, 71, 106, 107, 119, 142, 153, 156, 174 and 177).

4 studies were not completed, and in 12 instances attempts to introduce the radiopharmaceutical into the subarachnoid space

failed[4, 15] (figure 20).

5.3 OBSTRUCTIVE NON-COMMUNICATING HYDROCEPHALUS (Table 8, no. 8, 44, 78, 80, 81, 82, 97, 111, 120, 155, 173, 179 and 187).

All 13 patients in this group were children under 12 years of age with congenital malformations, 7 of which had the Arnold Chiari syndrome clinically and radiologically con= firmed. Ten of them were evaluated with ventricular injec= tion of the radiopharmaceutical which demonstrated large ventricles without clearance of the tracer due to obstruc= tion of the ventriculo-cisternal communicating pathways[16, 17, 18] (figure 26). Two had ventricles so large that they compressed the subarachnoid space against the cranium (fi= gure 25).

5.4 OBSTRUCTIVE COMMUNICATING HYDROCEPHALUS (Table 8, no. 5, 6, 7, 11, 12, 13, 14, 15, 24, 33, 39, 42, 47, 52, 54, 56, 63, 64, 67, 72, 73, 74, 89, 90, 92, 99, 100, 109, 114, 118, 121, 131, 135, 139, 144, 167, 172, 171 and 198).

This group consisted of 40 patients who showed a wide spec= trum of abnormal CSF flow patterns ranging from delayed flow to the convexities due to partial or total obstruction of the subarachnoid space (figures 27, 33), to different degrees of ventricular reflux, and enlargement. Cisternography demon= strated the point of obstruction as an area of increased acti= vity proximal to the lesion and failure of tracer movement past it[6] (figure 27).

These alterations most likely represent stages of distur= bance of CSF dynamics which if progressive lead to perma= nent obstructive hydrocephalus. Most of them probably re= cover with restoration of normal CSF flow with a compensa= tion[19]. One half of the patients in this group (20) owed their disturbances to infectious processes: 16 had resi= dual sequelae of TB meningitis which probably produce me= ningeal scarring as cause of altered CSF flow[23], 2 patients had non-TB meningitis and in 2 the diagnosis was encephalitis of uncertain origin.

Of the 16 patients with alterations in CSF flow due to TB meningitis, 13 were referred from the Isolation wards at Pelonomi Hospital for black patients in Bloemfontein. Three patients had a history of epilepsy which could have been as= sociated with trauma, and 4 had severe head injury. The rest of the patients had tumors(2),intracranial hemorrhage (4), cysts (1), cerebrovascular disturbances (1), cerebellar de= generative processes (4) and dementia (1).

Demonstration Case (CMD/C 72)

A 16-year-old girl sustained severe head injury after fal= ling from a horse. There was initial improvement followed by deterioration of conciousness and appearance of right hemiparesis. A left carotid angiogram revealed an avascular area over the convexity of the left hemisphere. She was im= mediately operated and a subdural clot was removed through a posterior-frontal burr-hole.

Immediately after the operation there was satisfactory improvement followed by two weeks of intermittent impairment of conciousness with normal CSF pressure. A short remission followed removal of CSF which suggested the possibility of a post-traumatic obstructive communicating hydrocephalus. A radionuclide cisternogram revealed moderate ventricular enlargement with early ventricular reflux which cleared after 30 hours. There was impaired tracer flow towards the convexity with a large void of activity in the left lateral communicating pathway.

A ventriculo-atrial shunt with a Holter valve was done 4 weeks after the head injury and a progressive and dramatic recovery followed until the patient was finally discharged fit to resume normal schooling.

5.5 NORMAL PRESSURE HYDROCEPHALUS (Table 8, no. 27, 53, 55, 68, 87, 91, 95, 117, 132, 135, 138, 145, 152, 154, 161, 164, 165, 160, 178, 188 and 193).

Of the 21 patients in this group, the majority complained of intellectual deterioration, ataxic gait, occasional to frequent urinary incontinence, and, at times headache. CSF pressure was normal in all except 2 patients in whom it was not recorded. Many of the patients were suspected of having presenile dementia, and the examination was undertaken to differentiate between normal pressure hydrocephalus and cerebral atrophy.

The radionuclide cisternogram was considered diagnostic if

most or all of the tracer injected into the lumbar subarachnoid space entered the cerebral ventricles with little, if any, flow over the cerebral convexities[8, 12, 13, 20].

Ten patients underwent extranial CSF diversionary shunting with varying degrees of improvement of their neurological deficits (table 12). Of the ten patients operated on, 8 showed marked improvement.

Case Demonstration (CMD/C 38)

At the time of her admission to hospital a 57-year-old housewife showed severe memory loss, disorientation, agitation, depression, wide base spastic ataxia and occasional urinary incontinence. These symptoms started 3 years previously with progressive deterioration.

A ^{131}I-HSA cisternogram revealed early ventricular reflux with stasis and lack of flow over the convexities (figure 28). CSF pressure was normal. She underwent ventriculo-atrial shunting with a Holter valve and within days started improving. She was finally discharged, and her mental faculties returned to normal, although she retained a mild residual gait disturbance.

5.6 PRIMARY ATROPHIC COMMUNICATING HYDROCEPHALUS (Table no. 9, 31, 70, 75, 83, 88, 93, 96, 115, 124, 127, 128, 159, 162, 170, 197 and 199).

The 17 patients in this group were older individuals with

longstanding intellectual deficit. Their cisternographic evaluation showed varying degrees of ventricular reflux with delayed flow towards the convexities and patent, enlarged CSF pathways[9] (figure 29).

5.7 POREncephaly (Table 8, no. 2, 21, 59, 42, 184 and 194).

The 6 patients examined had been previously evaluated clinically and by air encephalography. Upon cisternography they showed abnormal, slowly-clearing collections of tracer at the site of cysts[22] (figure 30).

5.8 CSF LEAKS (Table 8, no. 65, 113, 122, 185 and 192).

Six patients suspected of having post-traumatic CSF rhinorrhea (5) and otorrhea (1) comprised this group. The cisternogram was considered abnormal if radioactive material could be demonstrated on the scan outside the subarachnoid space[5] (figure 36, 37).

5.9 DETERMINATION OF SHUNT PATENCY (Table 8, no. 37, 38, 45, 51, 69, 79, 102, 108, 134, 136, 141, 146 and 150).

When the extracranial diversionary CSF shunt is functioning properly, radioactive material injected into the ventricles, in the subarachnoid space or into the valve will appear in the distal limb of the shunt catheter. Non-appearance of isotope indicates that the shunt is not patent[3, 7, 11, 21, 24].

Thirteen patients with extracranial CSF shunts were examined. 7 patients were children with obstructive non-communicating hydrocephalus, and 4 had NPH. Seven of the shunts were functioning and 5 were blocked. The latter 5 cases had their shunts revised.

Radionuclide cisternography is considered the most expedient and valuable examination for determining the patency of shunts[1].

5.10 SPINAL LESIONS (Table 8, no. 16, 18, 22, 26, 35, 57, 61, 86, 149, 180 and 196).

A total of 11 patients showed abnormalities of CSF flow in the spinal canal. Five had disc pathology, 2 had tuberculous vertebral disease and the rest had alterations of diverse etiology In all cases the cisternographic pattern showed a partial block with a segmental void of radioactivity but subsequent flow distal to the lesion[2] (figure 38).

TABLE 8

PATIENTS DATA

NO.	PATIENT	AGE	SEX	RACE	CLINICAL FEATURES	CISTERNOGRAPHY FINDINGS	SHUNT FOLLOW-UP	FINAL DIAGNOSIS
1	JK 68/74	30	M	B	Muscle Atrophy. Normal CSF. Tuberculosis Meningitis	Epidural inj.		FV
2	EM 61/74	12	M	B	Paralysis L arm. Small L hand & foot. Hirsutism	FC.		P
3	JS 120/74	35	M	B	Tuberculosis Meningitis	Normal		N
4	MA 119/74	27	M	B	Tuberculosis Meningitis	Normal		N
5	AvN 508/74	30	F	W	?	VR. S. BP.		OC
6	SL 165/74	21	M	B	Tuberculosis Meningitis	VR		OC
7	SL 166/74	33	F	B	Tuberculosis Meningitis. Back pain	VR		OC
8	AM 190/74	20	M	B	Hydrocephalus. Ataxia	LV. S.		ONC
9	IvB 549/74	52	F	W	Pre-senile dementia	DF.		PA
10	GB 601/74	31	M	W	Cerebral Cyst	Normal		N
11	ES 234/74	3	F	B	Tuberculosis Meningitis	VR		OC
12	EM 236/74	3	M	B	Tuberculosis Meningitis	VR. S.		OC
13	WM 233/74	1	M	B	Tuberculosis Meningitis	BT		OC
14	SM 232/74	4	M	B	Tuberculosis Meningitis	FC. BP.		OC
15	MK 231/74	1	F	B	Tuberculosis Meningitis	VR.		OC

NO.	PATIENT	AGE	SEX	RACE	CLINICAL FEATURES	CISTERNOGRAPHY FINDINGS	SHUNT FOLLOW-UP	FINAL DIAGNOSIS
16	JW 482/74	72	M	W	Back pain.	BP. L5-S1		N
17	JW 482/74	72	M	W	Back pain.	Normal		N
18	EK 329/74	28	M	B	Transverse myelitis traumatic. L leg atrophy.	BP L4-S1		S
19	EK 329/74	28	M	B	Transverse myelitis traumatic. L leg atrophy.	Normal		N
20	SM 333/74	54	M	B	Chorea	Normal		N
21	WL 352/74	25	F	C	?	FC. VR. S.		P
22	SV 839/74	40	M	W	Disc pathology. Cervical pain.	BP C3-6		S
23	SV 839/74	40	M	W	Disc pathology. Cervical pain.	Normal		N
24	JR 791/74	39	M	W	Temporal lobe epilepsy	BP		OC
25	AS 1030/74	60	M	W	Hodgkins Disease	Normal		N
26	FS 1083/74	70	M	W	Disc pathology. Low back pain. Dementia	BP		S
27	FS 1083/74	70	M	W	Disc pathology. Low back pain. Dementia	VR. S.		NPH
28	BB 1080/74	15	M	W	Epilepsy	Normal		N
29	AP 556/74	60	F	B	Spastic paraplegia. Tuberculosis Meningitis.	Normal		N
30	AP 72/75	61	F	B	Tuberculosis Meningitis	Normal		M
31	SvB 125/75	45	F	W	Degenerative sclerosis	DF		PA
32	SM 104/75	6m	M	B	?	Incomplete		FV

NO.	PATIENT	AGE	SEX	RACE	CLINICAL FEATURES	CISTERNOGRAPHY FINDINGS	SHUNT FOLLOW-UP	FINAL DIAGNOSIS
33	EK 103/74	2	F	B	Tuberculosis Meningitis	BP.S.		OC
34	KvN 31/75	2	M	C	Subdural haematoma	Normal		N
35	IB 303/75	49	M	W	Myelomatosis	Normal		S
36	EM 123/75	1	M	B	?	Normal		N
37	CT 492/73	4m	F	B	Hydrocephalus with shunt. Congenital.	DF	VP	SH
38	FP 491/73	16	F	B	Hydrocephalus with shunt. Congenital.	Normal	VP	SH
39	SN 145/74	16	M	B	Tuberculosis Meningitis	BP		OC
40	BN 71/75	70	M	W	Dementia	Epidural inj.		FV
41	SR 41/75	21	F	B	Tuberculosis Meningitis	Normal		N
42	JK 76/75	17	F	W	Headache. Epilepsy.	DF		OC
43	PM 109/75	34	F	B	Cushing's Syndrome.	Normal		N
44	EP 470/75	7d	F	W	Arnold Chiari malformation	BT S LV		ONC
45	EP 470/75	8d	F	W	Shunt evaluation	Normal	VP	SH
46	JT 152/75	50	M	B	Tuberculosis Meningitis	DF to Normal		N
47	MC 454/75	24	F	W	Headache. Epilepsy.	DF		OC
48	AF 486/75	19	F	W	Encephalitis	Epidural inj.		FV
49	AF 486/75	19	F	W	Encephalitis	Normal		N

NO.	PATIENT	AGE	SEX	RACE	CLINICAL FEATURES	CISTERNOGRAPHY FINDINGS	SHUNT FOLLOW-UP	FINAL DIAGNOSIS
50	FM 184/75		F	B	?	Epidural inj.		FU
51	JC 505/75	1m	F	W	Non-communicating hydrocephalus. Shunt.	Normal	VP	SH
52	EvZ 295/75	34	M	W	Encephalitis	DF. BP.		OC
53	'GvB 514/75	62	M	W	?	LV.VR.S.DF.		NPH
54	DP 515/75	48	M	W	Subdural haematoma?	BP		OC
55	LL 181/75	40	F	B	Brain atrophy	VR.S.LV.		NPH
56	JB 442/75	50	M	W	Infectious cerebellar disruption.	DF. BP.		OC
57	AP 588/75	38	F	W	Carcinoma Thyroid. Spinal Metastasis	BP T-12		S
58	AP 588/75	38	F	W	Carcinoma Thyroid. Spinal Metastasis	Normal		N
59	CM 244/75	16	F	B	Porencephaly. R hemiplegia.	FC		P
60	CC 726/75	26	F	W	Brain tumor. Complication Cisternography.	Subdural inj.		FU
61	PR 265/75	4	M	B	Tuberculosis Meningitis	BP T3 & L3		S
62	JM 227/75	21	M	B	Cerebellar ataxia.	Epidural inj.		FU
63	JM 227/75	21	M	B	Cerebellar ataxia.	DF.		OC
64	JM 253/75	26	M	B	Meningitis vs. Encephalitis	DF.		OC
65	FS 315/75	40	M	B	Trauma	Rhinorrhea		LR
66	AS 880/75	19	F	W	?	Normal		N

NO.	PATIENT	AGE	SEX	RACE	CLINICAL FEATURES	CISTERNOGRAPHY FINDINGS	SHUNT FOLLOW-UP	FINAL DIAGNOSIS
67	AS 28/75	65	M	W	Normal Pressure Hydrocephalus	DF.BP.VR.		OC
68	DF 949/75	69	M	W	Trauma. Dementia. NPH?	DF.BT.		NPH
69	EL 950/75	4	F	W	Hydrocephalus. Congenital. Shunt evaluation.	BP.DF.	VP	SH
70	SvM 942/75	76	M	W	Dementia	DF		PA
71	RT 376/75	16	M	B	Tuberculosis Meningitis. Bromide-PT: 1,04	Epidural inj.		FU
72	ZM 375/75	28	M	B	Tuberculosis Meningitis.	BP		OC
73	JV 979/75	63	M	W	Brain tumor	BP		OC
74	JvM 964/75	53	M	W	Brain tumor	BP		OC
75	PM 429/75	47	M	B	NPH?	DF		PA
76	HS 1197/75	15	M	W	Familiar spinocerebellar degeneration	Normal		N
77	CC 21/75	42	F	W	Spinocerebeller degeneration	Normal		N
78	SM 444/75	1m	M	B	Arnold Chiari malformation. Shunt evaluation.	LV		ONC
79	SM 444/75	1m	M	B	Arnold Chiari malformation. Shunt evaluation.	Normal	VP	SH
80	ID 445/75	1m	M	B	Arnold Chiari malformation.	LV.S.		ONC
81	EP 447/75	1m	F	B	Arnold Chiari malformation.	LV.S.		ONC
82	JL 446/75	1m	M	B	Arnold Chiari malformation.	LV.S.		ONC
83	CL 1115/75	68	M	W	NPH?	DF		PA

NO.	PATIENT	AGE	SEX	RACE	CLINICAL FEATURES	CISTERNOGRAPHY FINDINGS	SHUNT FOLLOW-UP	FINAL DIAGNOSIS
84	CS 1188/75	18	M	W	Familiar spinocerebellar degeneration	DF		N
85	MS 1189/75	25	F	W	Familiar spinocerebellar degeneration	Normal		N
86	HL 498/75	28	M	C	L arm paresia. Cervical lesion?	BP C8		S
87	CS 1176/75	56	F	W	Carcinoma mamma. Metastasis.	DF.VR.S.		NPH
88	JG 1235/75	60	F	W	Anxiety neurosis. NPH?	DF		PA
89	EK 522/75	3	F	B	Tuberculosis Meningitis	VR. DF.		OC
90	QW 523/75	1	M	C	Tuberculosis Meningitis	VR. DF.		OC
91	MP 1273/75	78	F	W	Dementia, ataxia, urinary incontinence	VR.S.DF.BT.	VA	NPH
92	AM 524/75	45	M	B	Tuberculosis Meningitis	DF		OC
93	ML 1271/75	56	M	W	Spinocerebellar degeneration	DF		PA
94	JK 1298/75	61	M	W	Cerebellar atrophy	BP to Normal		N
95	AvW 1246/75	63	F	W	Dementia	VR. DF.		NPH
96	BC 1302/75	57	M	W	Dementia	DF.		PA
97	DF 1322/75	8m	M	W	Hydrocephalus, congenital	LV. BT		ONC
98	MS 1299/75	26	F	W	Headache	Normal		N
99	EvN 1331/75	50	F	W	Cerebellar atrophy	DF. BP		OC
100	ES 547/75	50	F	B	Dementia	DF. BP		OC

NO.	PATIENT	AGE	SEX	RACE	CLINICAL FEATURES	CISTERNOGRAPHY FINDINGS	SHUNT FOLLOW-UP	FINAL DIAGNOSIS
101	DC C1	32	M	LA	Epilepsy	Normal		N
102	MG C2	64	F	LA	NPH. Shunt evaluation. Progr. Dementia	NPH	VA F,I	SH
103	DM C3	49	M	LA	Brain tumor	Normal		N
104	MQ C4	37	M	LA	Epilepsy	Normal		N
105	MC C5	30	M	LA	Brain atrophy	Normal		N
106	DF C6	24	M	LA	Head injury	Incomplete		FU
107	AY C7	18	F	LA	Epilepsy	Epidural inj.		FU
108	NQ C8	63	M	LA	Dementia, gait disturbance, intellectual slowing	LV, VR, S	VA - I	SH
109	PN C9	4	M	LA	Herpes encephalitis	VR, S	VA - NI	OC
110	AR C10	34	F	LA	Tuberculosis Meningitis	Normal		N
111	RR C11	10d	M	LA	Large head, congenital hydrocephalus	LV, S		ONC
112	FI C12	17	M	LA	Spastic gait, Complication meningitis	FC		P
113	DE C13	21	M	LA	Head trauma R side, otorrhagia	Otorrhea	VA - F	OC
114	BZ C14	16	F	LA	Previous trauma, headache, tremor. Leptomenigeal cyst	VR.S.DF	VA - F	OC
115	LK C15	58	M	LA	Urinary incontinence, tremor	VR. DF		PA
116	NZ C16	32	M	LA	Head trauma. Complication meningitis	Normal		N
117	HO C17	67	M	LA	Dementia, incontinence feas. Bilateral Bakinsky	VR.S.BP	VA - F	NPH

NO.	PATIENT	AGE	SEX	RACE	CLINICAL FEATURES	CISTERNOGRAPHY FINDINGS	SHUNT FOLLOW-UP	FINAL DIAGNOSIS
118	JC C18	21	M	LA	Arteriovenous malformation. Bleeding at surgery.	LV, VR	VA - NI	OC
119	ID C19	62	M	LA	Epilepsy	Incomplete		FU
120	RS C20	1m	M	LA	Dandy-Walker cyst	FC, LV, S		ONC
121	VP C21	31	F	LA	Head injury, spastic gait, mental impairment	BT	VA - Died	OC
122	WG C22	3	M	LA	Trauma	Rhinorrhea		LK
123	RS C23	69	M	LA	Carcinoma prostrate, metastasis in skull	Normal		N
124	AD C24	62	F	LA	Mental deterioration	DF		PA
125	ZI C25	25	M	LA	Trauma	Normal		N
126	SD C26	32	M	LA	Epilepsy	Normal		N
127	QA C27	61	F	LA	Loss of memory, arteriosclerosis	DF, VR		PA
128	LC C28	54	M	LA	Irregular behavior, irritability	DF		PA
129	MP C29	21	F	LA	Stab wound in back	Spinal leak		LK
130	MQ C30	6	M	LA	Enlarged head	Normal		N
131	DK C31	27	M	LA	Head trauma. Unconcious. Urinary incontinence	VR. BP	VA - I	OC
132	MD C32	61	M	LA	Dementia, ataxia, intellect. deterioration. NPH	VR.S.DF	VA - I, F	NPH
133	PZ C33	53	F	LA	Surgery for ependymoma. Dementia, irritability	LV, VR	VA - I	NPH
134	JI C34	2	F	LA	Hydrocephalus for evaluation of shunt	Not patent		SH

NO.	PATIENT	AGE	SEX	RACE	CLINICAL FEATURES	CISTERNOGRAPHY FINDINGS	SHUNT FOLLOW-UP	FINAL DIAGNOSIS
135	FA C35	33	F	LA	Tuberculosis Meningitis	DF, BP		OC
136	SN C36	62	M	LA	Previously shunted NPH, deteriorating	Not patent		SH
137	DM C37	7	M	LA	Encephalitis	Normal		N
138	ND C38	57	F	LA	Dementia, gait disturbance, incontinent. NPH	VR.DF.S	VA - 1	NPH
139	LA C39	6	M	LA	Tuberculosis Meningitis	BP		OC
140	MY C40	27	M	LA	Head trauma	Normal		N
141	TO C41	60	F	LA	NPH. Previously shunted, evaluation	Patent		SH
142	PR C42	3	M	LA	Convulsions, vomiting	Epidural inj.		FU
143	AL C43	32	M	LA	Head trauma	Normal		N
144	MC C44	18	M	LA	Spinocerebellar degeneration	DF, BP. S		OC
145	NQ C45	68	M	LA	Loss of memory, ataxia, incontinence. NPH	VR.S.	LP - F	NPH
146	NA C46	1	M	LA	Hydrocephalus. Ventriculoperitoneal shunt	Patent		SH
147	PL C47	12	F	LA	Head trauma	Normal		N
148	SP C48	26	M	LA	Epilepsy	Normal		N
149	SE C49	48	F	LA	Low back pain. Disc pathology	BP L 4,5		S
150	FV C50	2	F	LA	Hydrocephalus for shunt evaluation	Patent		SH
151	MO C51	47	M	LA	Head trauma	Normal		N

NO.	PATIENT	AGE	SEX	RACE	CLINICAL FEATURES	CISTERNOGRAPHY FINDINGS	SHUNT FOLLOW-UP	FINAL DIAGNOSIS
152	SF C52	58	M	LA	Irritability, occasional urinary incontinence	UR.S.DF		NPH
153	VP C53	47	M	LA	Brain Tumor?	-		FU
154	HP C54	62	M	LA	Irresponsible behavior, ataxia, incontinent once. NPH	VR.S.	LP - I	NPH
155	BL C55	3m	F	LA	Enlarged head. Obstructive non-comm. Hydrocephalus	LV.S.		ONC
156	CW C56	31	M	LA	Head injury. Patient to surgery	_		FU
157	NO C57	17	F	LA	Epilepsy	Normal		N
158	NC C58	23	M	LA	Brain atrophy	Normal		N
159	OC C59	57	F	LA	Mutism	DF		PA
160	PF C60	61	M	LA	Brain abcess?	Normal		N
161	FD C61	58	M	LA	Mild, progressive dementia, occasional incont.	LV. VR. S.		NPH
162	CF C62	72	M	LA	Senility	DF		PA
163	SS C63	31	F	LA	Head trauma	Normal		N
164	YH C64	54	M	LA	Dementia	LV.VR.S.BP		NPH
165	DS C65	63	M	LA	Head trauma triggering dementia, ataxia	VR.S.BP.		NPH
166	JV C66	15	F	LA	Epilepsy	Normal		N
167	RS C67	26	M	LA	Tuberculosis Meningitis	BP.DF		OC
168	CT C68	66	M	LA	Paranoid, disorientation, incontinent, headache	VR.S.DF	VA - I	NPH

NO.	PATIENT	AGE	SEX	RACE	CLINICAL FEATURES	CISTERNOGRAPHY FINDINGS	SHUNT FOLLOW-UP	FINAL DIAGNOSIS
169	HG C69	16	M	LA	Familiar spinocerebellar degeneration	Normal		N
170	HO C70	58	F	LA	Spastic gait, incoherent speech	DF.VR		PA
171	EM C71	14	M	LA	Head trauma	Normal		N
172	MP C72	16	F	LA	Head injury, unconcious, incontinent	LV.VR.S.DF	VA - I	OC
173	RB C73	1	F	LA	Arnold Chiari malformation	LV.S.		ONC
174	JG C74	25	M	LA	?	Epidural inj.		FU
175	MM C75	1	M	LA	Large head	Normal		N
176	EA C76	5	M	LA	Battered child	Normal		N
177	HP C77	?	M	LA	Head trauma (Died)	Subdural inj.		FV
178	LA C78	67	M	LA	Alcoholism. Mild but progressive dementia	LV.VR	VA - NI	NPH
179	DG C79	3	M	LA	Arnold Chiari malformation	LV.S		ONC
180	MS C80	17	M	LA	Tuberculosis Meningitis, Scoliosis	BP T4-6		S
181	DR C81	35	F	LA	Epilepsy	Normal		N
182	FR C82	43	M	LA	Epilepsy	Normal		N
183	JK C83	7m	M	LA	Delayed growth, apparent large head	Normal		N
184	IS C84	8	F	LA	X-rays diagnosed porencephaly	FC		P
185	JA C85	13	M	LA	Head trauma	Rhinorrhea		LK

NO.	PATIENT	AGE	SEX	RACE	CLINICAL FEATURES	CISTERNOGRAPHY FINDINGS	SHUNT FOLLOW-UP	FINAL DIAGNOSIS
186	MI C86	23	M	LA	Epilepsy	Normal		N
187	MR C87	6m	F	LA	Hydrocephalus congenital	LV.S		ONC
188	JC C88	57	M	LA	Dementia	LV.VR.S.BP		NPH
189	MD C89	18	F	LA	Head trauma	Normal		N
190	LP C90	23	M	LA	Epilepsy	Normal		N
191	RP C91	15	M	LA	Head trauma	BP		OC
192	AG C92	23	M	LA	Head trauma L temporal. Epistaxis an rhinorrhea	Rhinorrhea		LK
193	JM C93	52	M	LA	Head trauma Alcoholism. Syphilis. Ataxia. Dementia	VR.S.BP		NPH
194	JA C94	25	M	LA	Hemiplegia	FC		P
195	ZC C95	19	F	LA	Head trauma	Normal		N
196	DQ C96	45	M	LA	Low back pain. Disc pathology	BP		S
197	AS C97	58	M	LA	Dementia	DF.S		PA
198	EB C98	8	F	LA	H. influenza meningitis. Large head, oligophrenia	LV, VR	VP -	OC
199	FM C99	64	M	LA	Tremor, occasional urinary incontinence	DF		PA
200	MH C100	37	F	LA	Dementia	Normal		N

ABBREVIATIONS: TABLE 8

RACE:

B = Black
W = White
C = Coloured
LA = Latinamerican

CISTERNOGRAPHY DIAGNOSIS:

N = Normal
ONC = Obstructive non-communicating hydrocephalus
OC = Obstructive communicating hydrocephalus
NPH = Normal pressure hydrocephalus
PA = Primary atrophic hydrocephalus (Generalized)
P = Porencephaly
LK = CSF leaks
S = Spinal block
SH = Shunt evaluation
FU = Failure, unsatisfactory

SHUNT FOLLOW-UP:

VA = Ventriculo-atrial shunt
VP = Ventriculo-peritoneal shunt
LP = Lumbo-peritoneal shunt
I = Improved
F = Fair
NI = No improvement

CISTERNOGRAPHY FINDINGS:

VR = Ventricular reflux
S = Stasis
DF = Delayed flow
BT = Total block
BP = Partial block
LV = Large ventricles
FC = Focal collection (Localized pooling)

TABLE 9

PATIENT DISTRIBUTION

LOCATION:	Total cases studied (200)
La Paz	100
Bloemfontein	100

SEX:	Male	Female
La Paz	67	33
Bloemfontein	61	39
TOTAL	128	72
% OF TOTAL	64	36

AGE:	Children*	Adults
La Paz	20	80
Bloemfontein	25	75
TOTAL	45	155
% OF TOTAL	22,5	77,5

MEAN AGE (YEARS):	Male	Female	
La Paz	34	31	33
Bloemfontein	33	29	31
	33	30	32

AGE RANGE:	7 days to 78 years

RACE:	White	Coloured	Black	Latin American
La Paz	-	-	-	100
Bloemfontein	51	4	45	-

* 12 years and under

TABLE 10

SUMMARY OF RADIONUCLIDE CISTERNOGRAPHY STUDIES

	LA PAZ	BLOEMFONTEIN	TOTAL CASES	% OF TOTAL
Normal	33	25	58	29,0
Obstructive non-communicating hydrocephalus	6	7	13	6,5
Obstructive communicating hydrocephalus	12	28	40	20,0
Normal pressure hydrocephalus	14	7	21	10,5
Primary atrophic communicating hydrocephalus (Generalized)	9	8	17	8,5
Porencephaly	3	3	6	8,5
CSF leaks	5	1	6	3,0
Spinal block	3	8	11	5,5
Shunt evaluation	7	5	12	6,0
Failure and incomplete	8	8	16	8,0
TOTAL CASES	100	100	200	100

TABLE 11

ETIOLOGICAL FACTORS

	LA PAZ	BLOEMFONTEIN	TOTAL CASES	% OF TOTAL
Infection	8	27	35	17,5
Trauma	26	3	29	14,5
Tumor	5	7	12	6,0
Congenital	8	15	23	11,5
Epilepsy	12	4	16	8,0
Dementia	13	9	22	11,0
Degenerative	4	9	13	6,5
Multiple	23	19	42	21,0
Equivocal	1	7	8	4,0
TOTAL CASES	100	100	200	100

TABLE 12

RESPONSE TO SHUNT (15 CASES)

EXCELLENT	FAIR	NO IMPROVEMENT	TOTAL
8 53%	4 27%	3 20%	15 100%

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6. SUMMARY

Radionuclide cisternography performed in 200 selected patients with neurological disease has proved to be a simple and relatively safe procedure, with minimal disturbing side effects, which can provide useful information about cerebrospinal fluid (CSF) flow and dynamics.

Following the subarachnoid or ventricular injection of an appropiate radiopharmaceutical, the tracer flows with the CSF and demonstrates the pathways of circulation under normal and abnormal conditions with virtually no disruption of the existing CSF physiology.

The eventual distribution of the tracer is complex. The range of normal varies from rapid ascent with early absorption of the radiopharmaceutical to slower ascent and absorption, frequently with laterilization of flow to one or other side intracranially and occasionally with transient ventricular reflux.

In pathological states the cisternographic picture varies according to the underlying disease. It may lack the ability to establish the precise anatomical features available from air encephalography. However ventricular dilatation, the communication (or lack of it) of the ventricles with the subarachnoid space, and the delay or lack of absorption are only satisfactorily demonstrated by radionuclide cisternography. Repeated examinations may be readily performed to show progression of the disease or the results of surgical treatment.

The abnormal flow pattern in patients with normal pressure hydrocephalus proved to be the most important criterion in their selection for extracranial neurosurgical CSF shunting. When properly selected, these patients often respond to sur= gical treatment. The routine use of radionuclide cisterno= graphy in the examination of patients with suspected presenile dementia and compensated hydrocephalus results in a low yield of operable patients. When operation is contraindicated conservative management of the patient is then instituted and unnecessary surgical intervention avoided.

Radionuclide cisternography gained wide acceptance in the evaluation of shunt patency. The test is fast and safe in the presence of extracranial diversionary CSF shunts. The rapid flow into the cerebral ventricles and the fast disap= pearance of the radioactive tracer, as well as the relative size of the ventricular system, are valuable indexes for the determination of patency and efficaccy of the shunt. Another important use of radionuclide cisternography is the investi= gation of CSF leaks and CSF spinal flow obstruction. It may demonstrate the existence and site of CSF leakage or block and offer valuable assistance to the neurosurgeon.

Radionuclide cisternographic images are usually interpreted subjectively on the basis of abnormal regional and temporal concentrations of radiopharmaceuticals in the CSF space. The evaluation of images can be improved by the use of quantita= tive computerized digital scanning, increasing the sensitivity

and value of the measurements.

The further extension of these studies involving abnormalities of cerebrospinal fluid dynamics would seem worthwhile, and the value of the methods described in this thesis and their limitations, remain a potential and challenging field for further exploration.

OPSOMMING

Radionuklied-sisternografie is by 200 geselekteerde pasiënte met neurologiese aandoenings uitgevoer. Dit is gevind om 'n eenvoudige en veilige ondersoekprosedure te wees - 'n tegniek met minimale komplikasies, wat nuttige inligting betreffende serebrospinale vloeistof (S.S.V.)-vloei en -dinamika verskaf. Na die subaragnoiedale of ventrikulêre inspuiting van 'n ge= skikte radiofarmaseutiese materiaal, volg die merker die S.S.V.-vloeibaan. Sonder versteuring van S.S.V.-fisiologie kan die vloeipatroon by normale of abnormale toestande dan be= studeer word. Die uiteindelike verspreiding van die radio- aktiewe merker word bepaal deur komplekse faktore sekondêr tot die patologiese en patofisiologiese aard van die beson= dere siektetoestand.

Die normale patroon van isotoopvloei na spinale inspuiting wissel van persoon tot persoon. Daar mag vinnige styging van merker met verspreiding oor die serebrale hemisfere, en snelle absorpsie wees, of relatief vertraagde vloei en absorpsie - selfs met 'n mate van intrakraniale isotoop-la= teralisering. Soms word kortstondige ventrikulêre refluks- vulling selfs opgemerk.

Die skerpomlynde anatomiese afbeelding van S.S.V.-ruimtes by lugenkefalografie verkry, ontbreek kwalitatief by radionuklied- sisternografie. Andersynds word ventrikulêre uitsetting met refluks, S.S.V.-verbindings tussen die ventrikels en die sub= aragnoiedale ruimte as geheel, asook vertraagde of gebrekkige

S.S.V.-absorpsie slegs met sisternografie bevredigend ge=demonstreer. Herhaalde ondersoeke kan voorts uitgevoer word om die verloop van 'n siektetoestand of die gevolg van chi=rurgiese behandeling te beoordeel.

Die abnormale S.S.V.-vloeipatroon kenmerkend van normale druk-hidrokefalus, was een van die nuttigste kliniese toepassings van sisternografie - veral by die sorgvuldige selektering van pasiënte geskik vir ekstrakraniale neuro-chirurgiese aftakkings=prosedures. Hierdie terapeutiese ingreep lei dan dikwels tot omkering van die siekteproses en verbetering van simptome. Al=hoewel die roetine gebruik van radionuklied-sisternografie by die ondersoek van vermoedelike preseniele demensie en gekom=penseerde hidrokefalus gelei het tot 'n lae opbrengs van pa=siënte geskik vir vermelde operasie, is 'n negatiewe bevind=ing tog nuttige bevestiging dat konserwatiewe terapie ingestel en chirurgiese ingrepe vermy moet word.

Radionuklied-sisternografie is ook van groot waarde by die doeltreffendheidsbeoordeling van aftakkingsprosedures. So 'n ondersoek kan vinnig en veilig uitgevoer word deur iso=toop in die ventrikel te plaas. Die opruimingsnelheid vanuit die serebrale ventrikels, asook die relatiewe grootte van die ventrikulêre sisteem is waardevolle aanduidings van die doeltreffendheid van die ekstrakraniale aftakking.

Ander waardevolle gebruike van radionuklied-sisternografie sluit in die ondersoek van S.S.V.-lekkasie en obstruksie van

spinale S.S.V.-vloei. Dit het unieke waarde by die presiese anatomiese lokalisering van areas van S.S.V.-lekkasie.

Die nut van sisternografie, op die basis van subjektiewe beoordeling van abnormale vloeipatrone of regionale konsentrasie van radio-farmaseutiese stowwe in die S.S.V.-ruimte, kan aangevul word deur gebruik te maak van kwantitatiewe gereke=nariseerde digitale flikkergrafie.

Die verdere uitbreiding van hierdie studies waardeur abnormaliteite van S.S.V.-vloei atroumaties beoordeel word, bied vele toekomsmoontlikhede op die gebied van kliniese gebruik en navorsing.

APPENDIX

FIGURES AND LEGENDS

Figure 1: Drawing of the concept of CSF circulation. The CSF originates mainly in the choroidal plexuses; circulates from the ventricular system into the subarachnoid space, proceeding toward the con= vexity of the brain to be reabsorbed in the supe= rior longitudinal sinus by the Pacchionian granu= lations (Copied from Di Chiro (1.17).

Figure 2: Drawing of the internal CSF system which consists of the choroid plexus, the lateral, third and fourth ventricles with their communicating path= ways and apertures.

Figure 3: Drawing of the external CSF system with the major cisterns, the superior sagittal sinus and the Pacchionian granulations.

Figure 4: Drawing of the frontal section of dural cul-de-sac showing relationship of spinal cord to major intraspinal spaces (Copied from Larson (3.45).

Figure 5: Drawing and schematic diagram of CSF circulation.

Figure 6: Schematic representation of a moving detector imaging device, the rectilinear scanner (Nuclear Chicago Pho Dot).

Figure 7: Picture of a longitudinal profile scanner with its two 12,7 x 10 cm crystal size opposing detec= tors (National Hospital, Bloemfontein)

Figure 8: Schematic representation of the scintillation γ camera depicting the radionuclide imaging pro= cess (Reproduced from Mallard 3.46).

Figure 9: Picture of Zentron's PDP-8 data analysis and display ssytem central processing unit. (Na= tional Hospital, Bloemfontein).

Figure 10: Energy spectrum and decay scheme of Iodine-131.

Figure 11: Energy spectrum and decay scheme of Technetium-99m.

Figure 12: Energy spectrum and decay scheme of Ytterbium-169.

Figure 13: Energy spectrum and decay scheme of Indium-111.

Figure 14: Picture of Ohio Nuclear Series 84 dual 12,7 cm crystal size opposing detectors scanner (National Hospital, Bloemfontein).

Figure 15: Pho/Gamma III Scintillation Camera System and simplified block diagram (Nuclear Chicago).

Figure 16: Position for the lateral view.

Figure 17: Position for the anterior and posterior views.

Figure 18: Position for the vertex and half axial views.

Figure 19: Posterior view scan of successful lumbar injection, extending as a smooth unbroken column of radioactivity from the site of injection in the spinal lumbar area to the basal cisterns.

Figure 20: Posterior views of the lumbar area after unsuccessful injections: (a) Epidural injection in the shape of a "Christmas tree" and (b) Subdural injection with diffused radioactivity in the kidneys. No radioactivity in the intracranial CSF space.

Figure 21: Ventricular injection in a normal individual radioactivity is seen in the ventricles and in the basal cisterns.

Figure 22: Cisternal injection with radioactivity in the basal cisterns, moving towards the convexity of the brain and spinal canal caudally, confirming the directional CSF flow.

Figure 23: Normal adult cisternographic pattern at: 2 hours where the basal cisterns contain radiopharmaceutical, no ventricular activity present; 6 hours with radiopharmaceutical in pathways of CSF flow peripherally and centrally; 24 hours with radiopharmaceutical concentrated in parasagittal region without significant radioactivity in basal cisterns.

Figure 24: Normal pediatric cisternogram which is basically the same as in adults except that the rate of ascent and clearance is much faster. Note that by 4 hours the activity is completely over the convexities.

Figure 25: Cisternogram in a child with obstructive non-communicating hydrocephalus where the enlarged ventricles have pushed the brain against the cranial wall to sufficiently block the subarachnoid space. The cap of activity outlines the cranial margins.

Figure 26: Cisternogram of a child with obstructive non-communicating hydrocephalus where radiopharmaceutical injected directly into the ventricles shows them enlarged and 24 hours later radioactivity still remains confined to the ventricular system.

Figure 27: Cisternogram of a patient with obstructive communicating hydrocephalus. Delayed flow and obstruction in the left lateral pathway (anterior view) and "cold" area in the left parietal region (Left lateral view) with transient ventricular reflux.

Figure 28: Cisternogram in patient with normal pressure hydrocephalus: Entry and marked retention of radiopharmaceutical in lateral ventricles without flow towards cerebral convexity.

Figure 29: Cisternogram in patient with generalized primary atrophic communicating hydrocephalus (ex-vacuo) due to cerebrovascular anteriosclerotic disease. Slow flow to convexities with uniform concentration seen on delayed study (72 hours).

Figure 30: Cisternogram in patient with large porencephalic cyst which appears as area of increased radioactive pooling.

Figure 31: Biomechanics of hydrocephalus: (a) the brain is surrounded by a CSF space which communicates with the ventricles and is enclosed in a rigid cranium. In equilibrium the CSF pressure is balanced against the cerebral venous pressure. (b) when a CSF block develops, continued CSF production raises CSF pressure and the ventricles begin to dilate, (c) with increased pressure, cerebral hypoxia develops resulting in periventricular loss of brain tissue, there is a fall in CSF pressure but not to equilibrium, and (d) the ventricles are greatly dilated, the CSF pressure has returned to normal, but hydraulic press effect perpetuated imbalance (Modified from Hakim 4.35).

Figure 32: Hydraulic press effect in hydrocephalus. The force excerted on ventricular wall A_2 is greater because of greater surface area. (Copied from Hakim 4.35).

Figure 33: Case demonstration (RI/979/75). Cisternogram and brain scans of patient with metastatic tumor in the brain. First brain scan is negative, cisternogram shows a block in left parietal region, second brain scan is positive showing space occupying lesion in left parietal region.

Figure 34: Schematic drawing of an extracranial CSF diversionary shunt.

Figure 35: Patient with non-communicating hydrocephalus. Shunt patency evaluation: radioactivity over distal tip of a ventriculo peritoneal shunt.

Figure 36: Cisternogram in patient with right side otorrhea (a) before and (b) after surgical repair.

Figure 37: Cisternogram in patient with rhinorrhea.

Figure 38: Case demonstration (RI/839/74). Patient with degenerative disc lesions in cervical spine, showing a partial spinal block at the level of C3-6.

Figure 39: Case demonstration (RI/76/75). A 16-year-old patient with poor radiopharmaceutical clearance following a cisternogram. Radioactivity is still present 28 days after injection.

Figure 40: Schematic representation of area selection for quantitative computerized cisternographic digi= tal scanning in basal cisterns, ventricles and superior sagittal sinus.

Figure 41: Graph of quantitative radiopharmaceutical move= ment in areas of interest in normal individual.

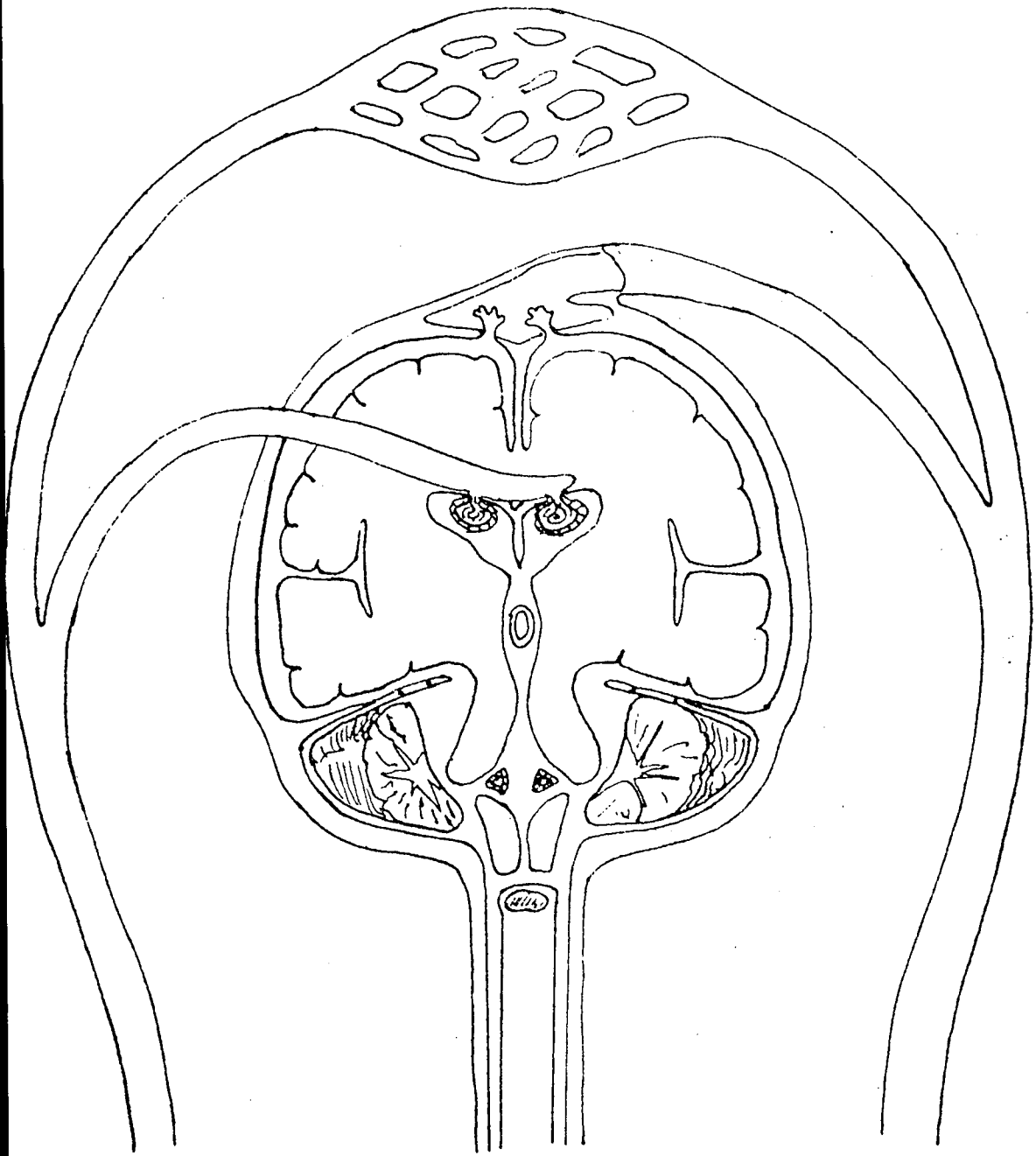
Figure 42: Graph of quantitative radiopharmaceutical move= ment in areas of interest in patient with nor= mal pressure hydrocephalus. Notice increased activity in ventricles with no activity in the superior sagittal sinus.

Figure 43: Graph of quantitative radiopharmaceutical move= ment in areas of interest in patient with gene= ralized primary atrophic hydrocephalus. Notice the delayed radioactivity flow towards the supe= rior sagittal sinus.

Figure 44: Profile scan of normal individual (a) 30 minutes, (b) 4 hours, (c) 24 hours and (d) 48 hours after intrathecal lumbar injection of radiopharmaceuti= cal.

Figure 45: Profile scan of patient with generalized primary atrophic hydrocephalus (a) 30 minutes, (b) 4 hours, (c) 24 hours, (d) 48 hours and (e) 72 hours after intrathecal lumbar injection of radiopharmaceuti= cal. Notice the delayed flow with retention of radioactivity intracranically.

FIGURE 1



CAROTID
ARTERY

JUGULAR
VEIN

FIGURE 2

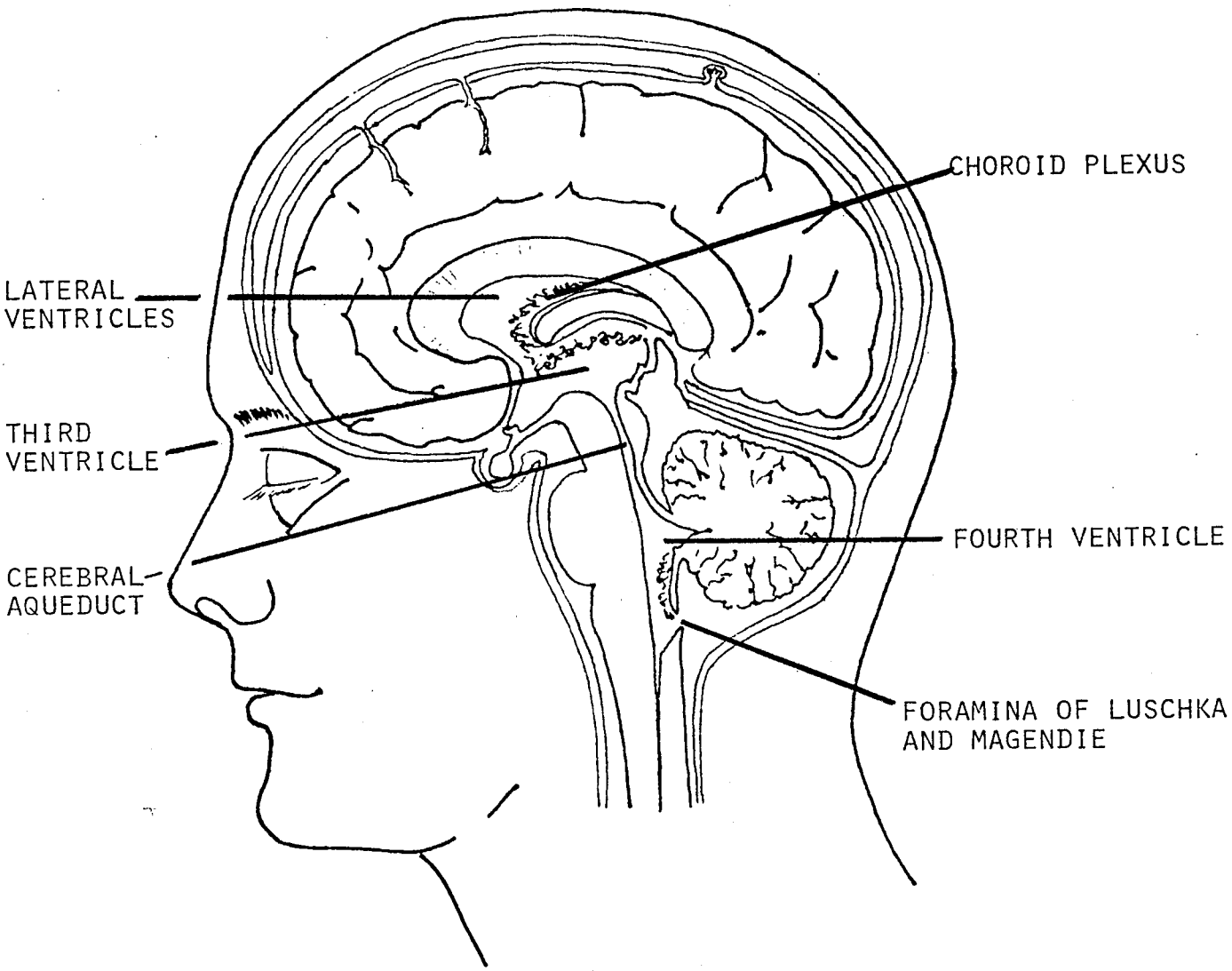

CHOROID PLEXUS
LATERAL VENTRICLES
THIRD VENTRICLE
CEREBRAL AQUEDUCT
FOURTH VENTRICLE
FORAMINA OF LUSCHKA AND MAGENDIE

FIGURE 3

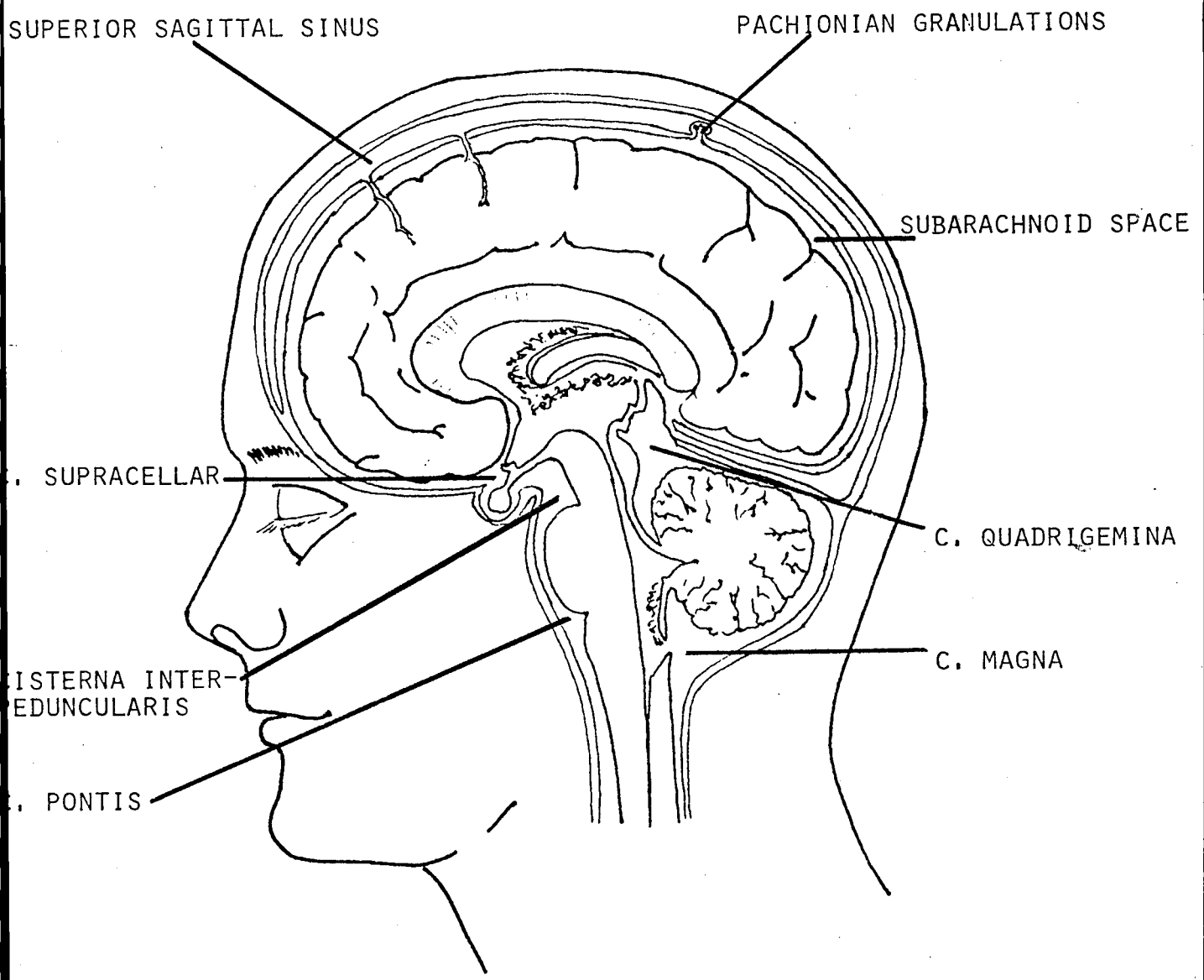

SUPERIOR SAGITTAL SINUS
PACHIONIAN GRANULATIONS
SUBARACHNOID SPACE
. SUPRACELLAR
C. QUADRIGEMINA
C. MAGNA
ISTERNA INTER-
EDUNCULARIS
. PONTIS

FIGURE 4

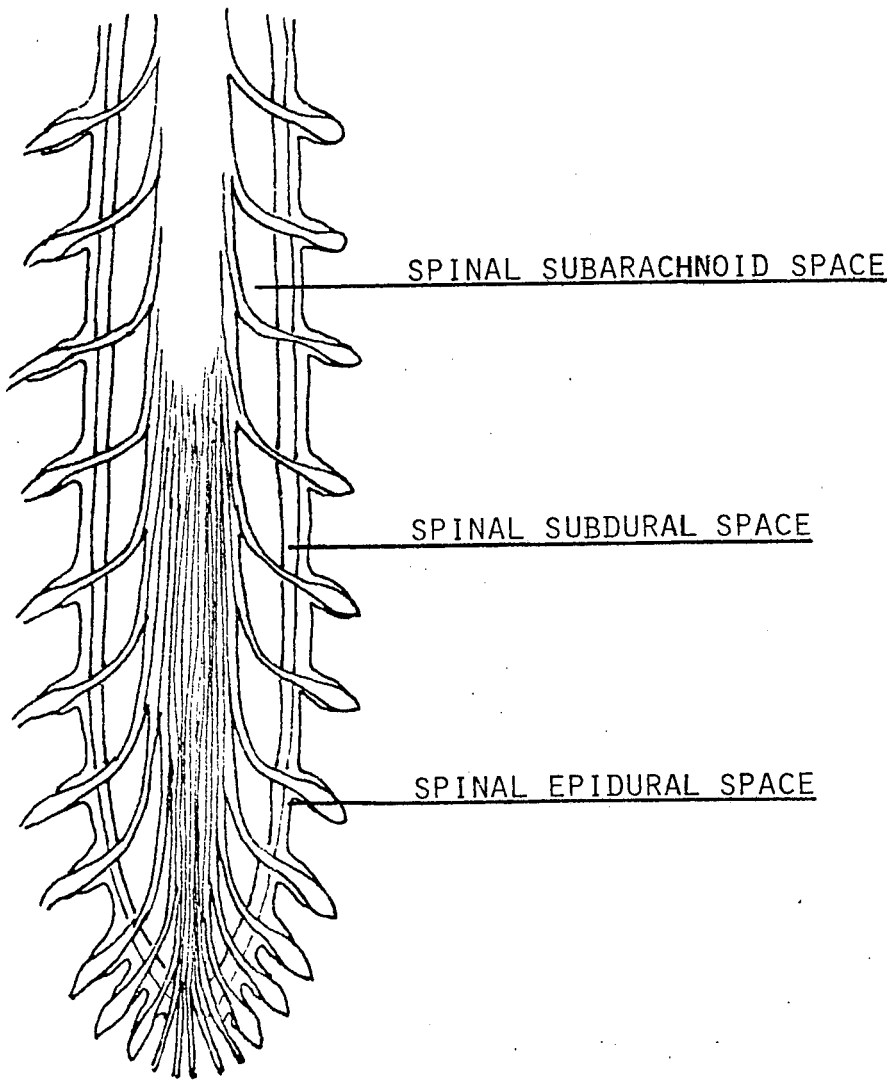

SPINAL SUBARACHNOID SPACE
SPINAL SUBDURAL SPACE
SPINAL EPIDURAL SPACE

FIGURE 5

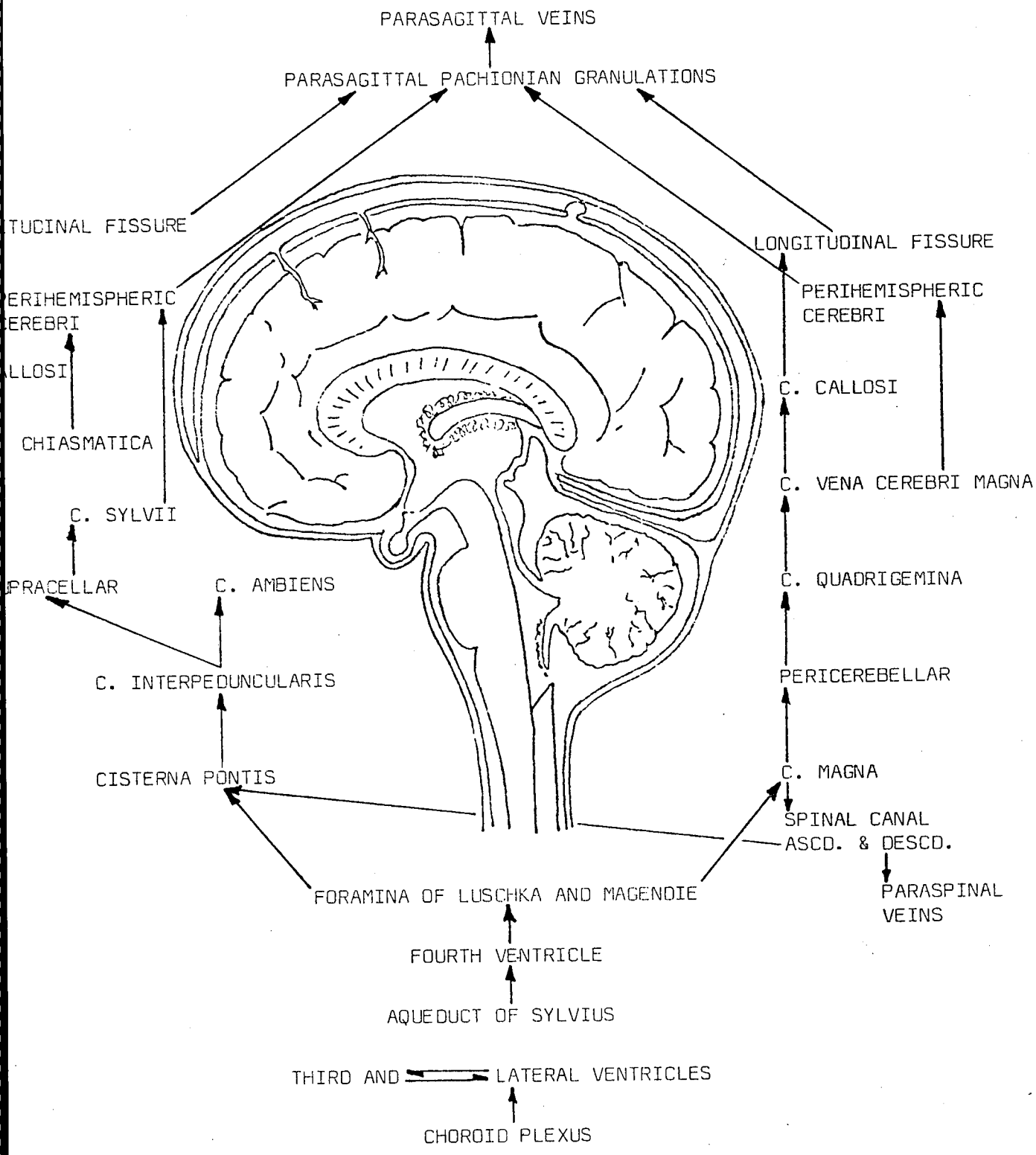

PARASAGITTAL VEINS
PARASAGITTAL PACHIONIAN GRANULATIONS
TUDINAL FISSURE
LONGITUDINAL FISSURE
ERIHEMISPHERIC
EREBRI
PERIHEMISPHERIC
CEREBRI
LLOSI
C. CALLOSI
CHIASMATICA
C. VENA CEREBRI MAGNA
C. SYLVII
PRACELLAR
C. AMBIENS
C. QUADRIGEMINA
C. INTERPEDUNCULARIS
PERICEREBELLAR
CISTERNA PONTIS
C. MAGNA
SPINAL CANAL
ASCD. & DESCD.
FORAMINA OF LUSCHKA AND MAGENDIE
PARASPINAL
VEINS
FOURTH VENTRICLE
AQUEDUCT OF SYLVIUS
THIRD AND
LATERAL VENTRICLES
CHOROID PLEXUS

FIGURE 6

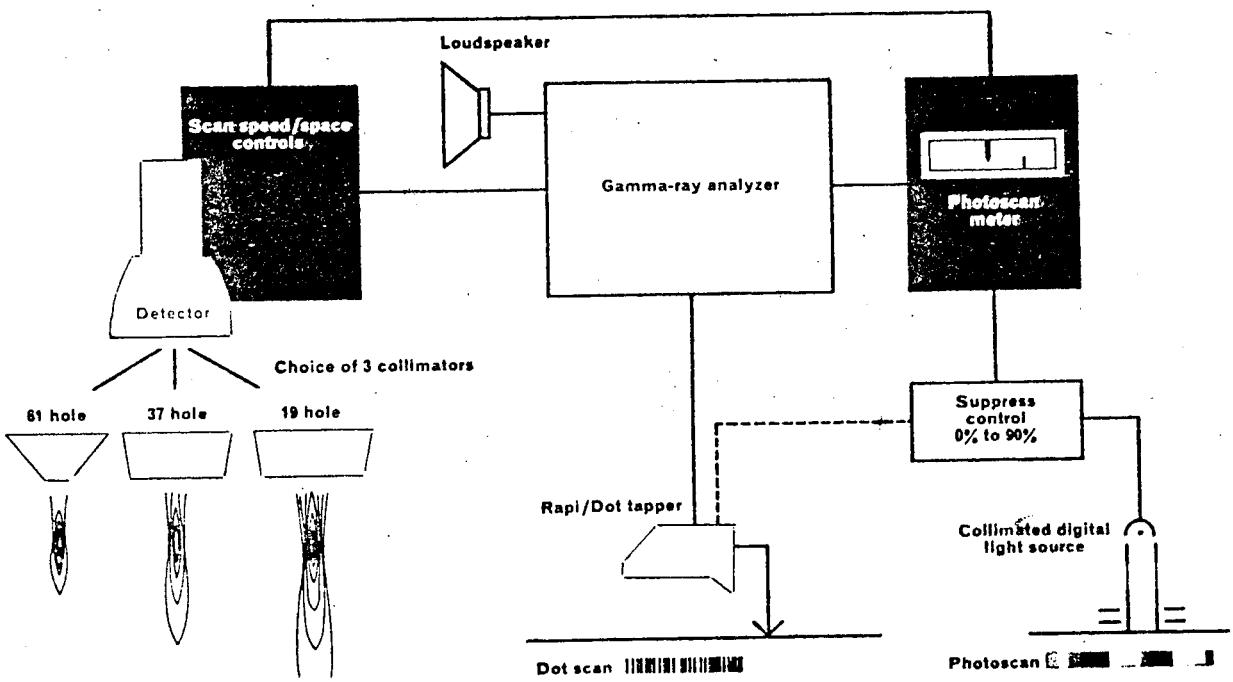

Loudspeaker
Scan speed/space controls
Gamma-ray analyzer
Photoscan meter
Detector
Choice of 3 collimators
61 hole
37 hole
19 hole
Suppress control 0% to 90%
Rapi/Dot tapper
Collimated digital light source
Dot scan
Photoscan

FIGURE 7

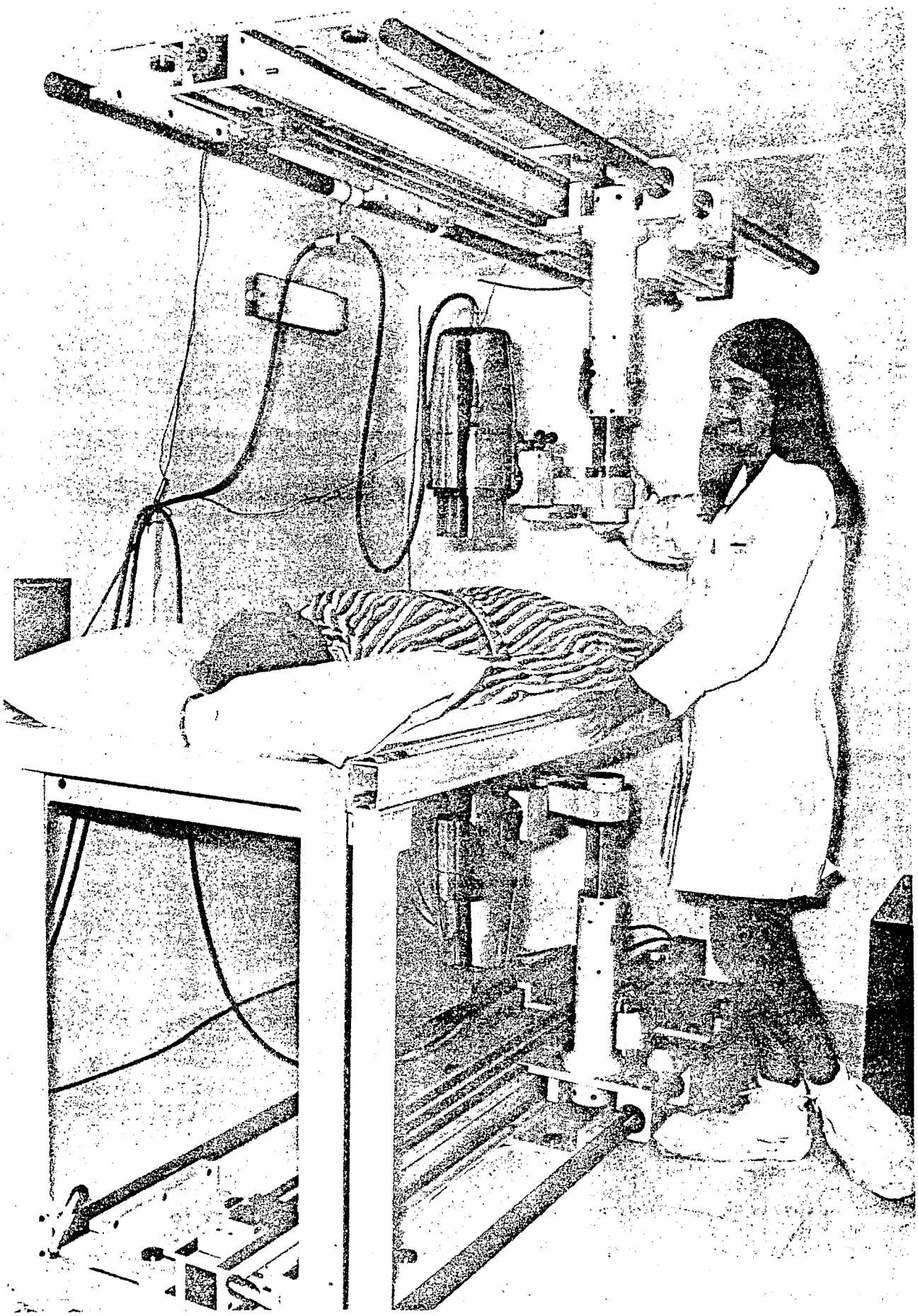


FIGURE 8

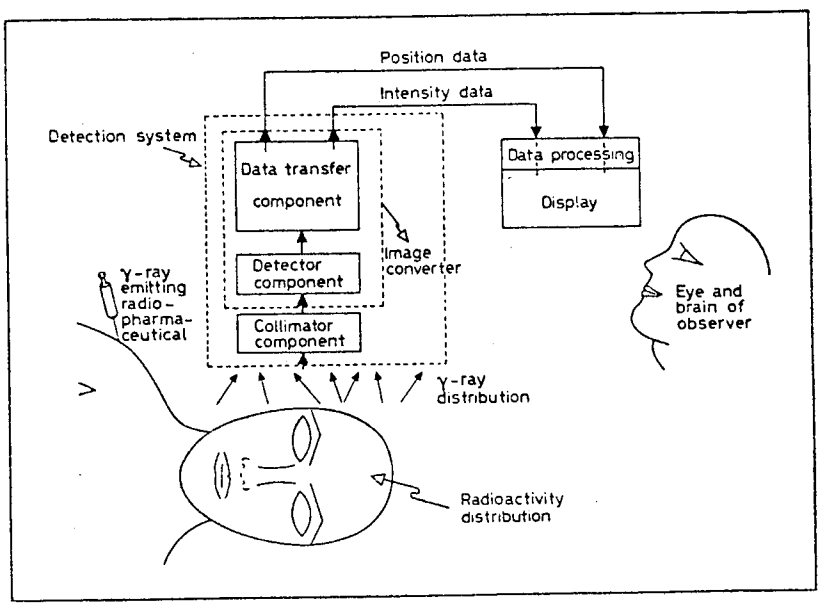

Position data
Intensity data
Detection system
Data transfer component
Data processing
Display
Image converter
Detector component
Collimator component
γ-ray emitting radio-pharma-ceutical
Eye and brain of observer
γ-ray distribution
Radioactivity distribution

FIGURE 9

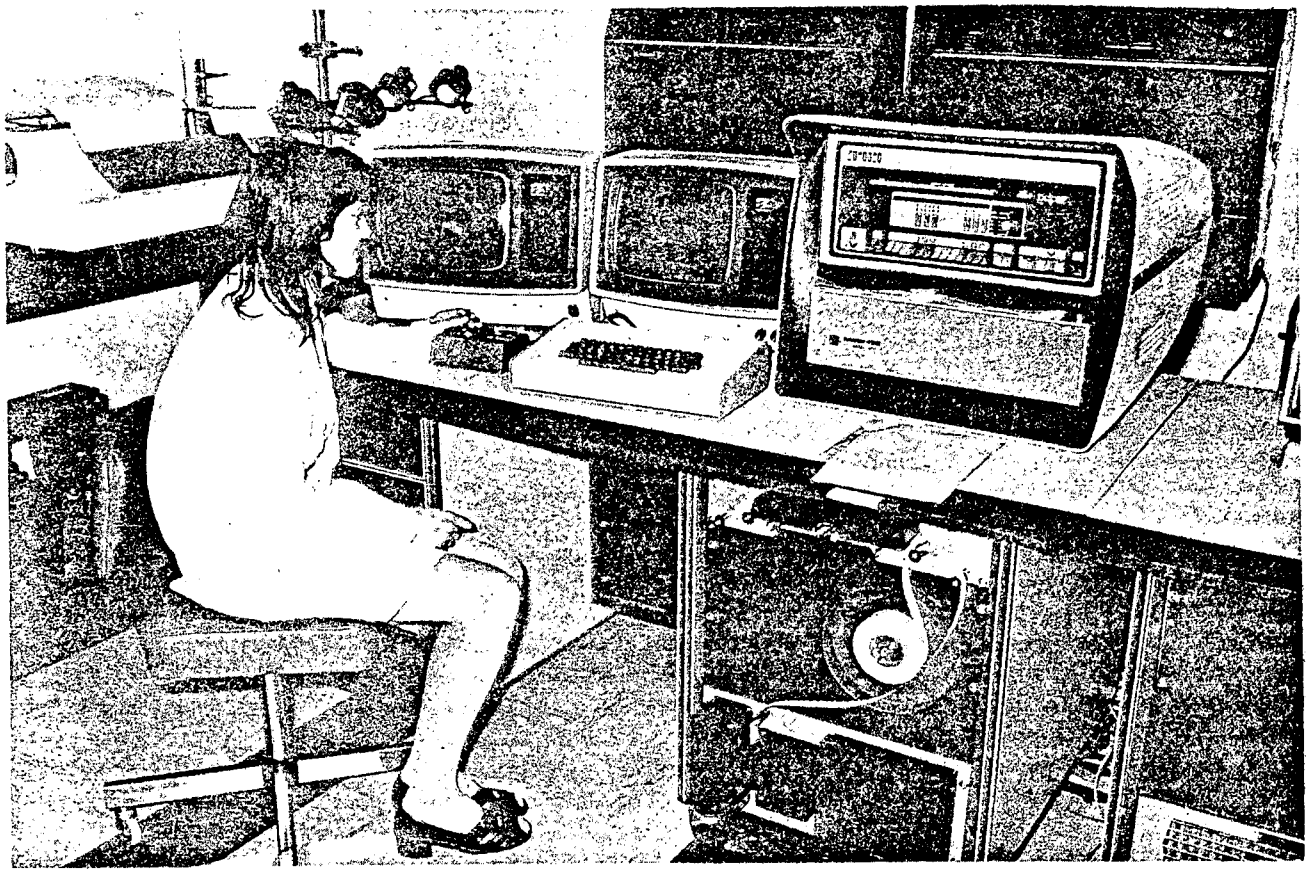
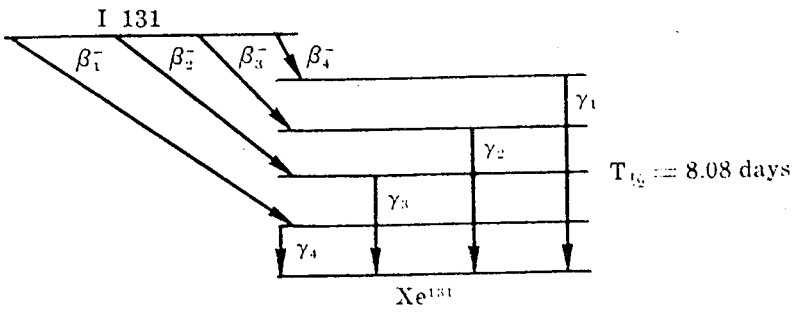


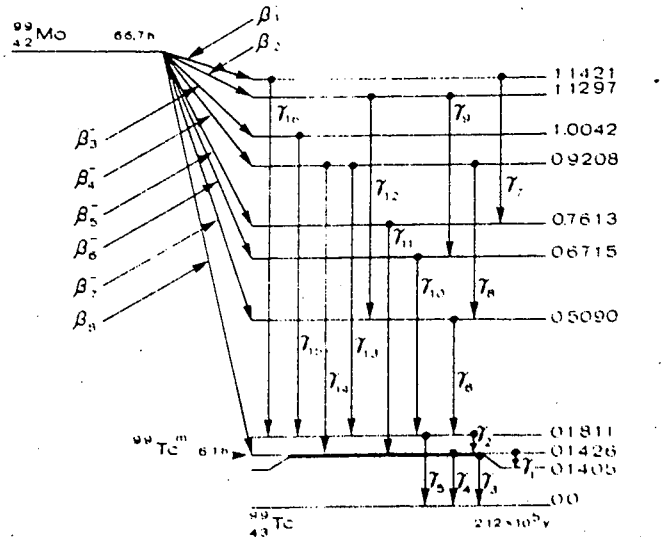
FIGURE 10



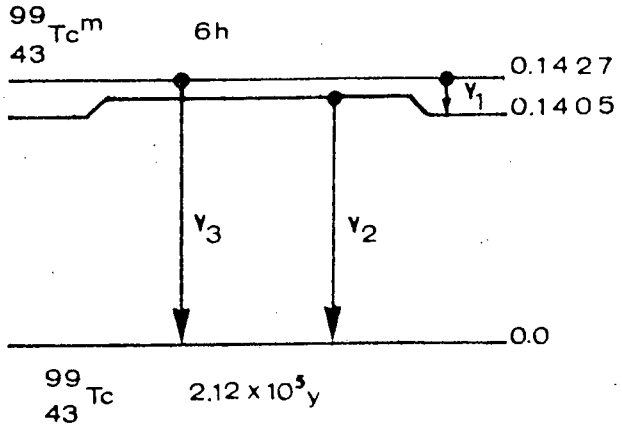
	ENERGY keV	ABUNDANCE
β^1	815	0,7%
β^2	608	87,2%
β^3	335	9,3%
β^4	250	2,8%
γ^1	722	2,8%
γ^2	637	9,3%
γ^3	364	87,2%
γ^4	164	0,7%

DECAY SCHEME IODINE-131

FIGURE 11



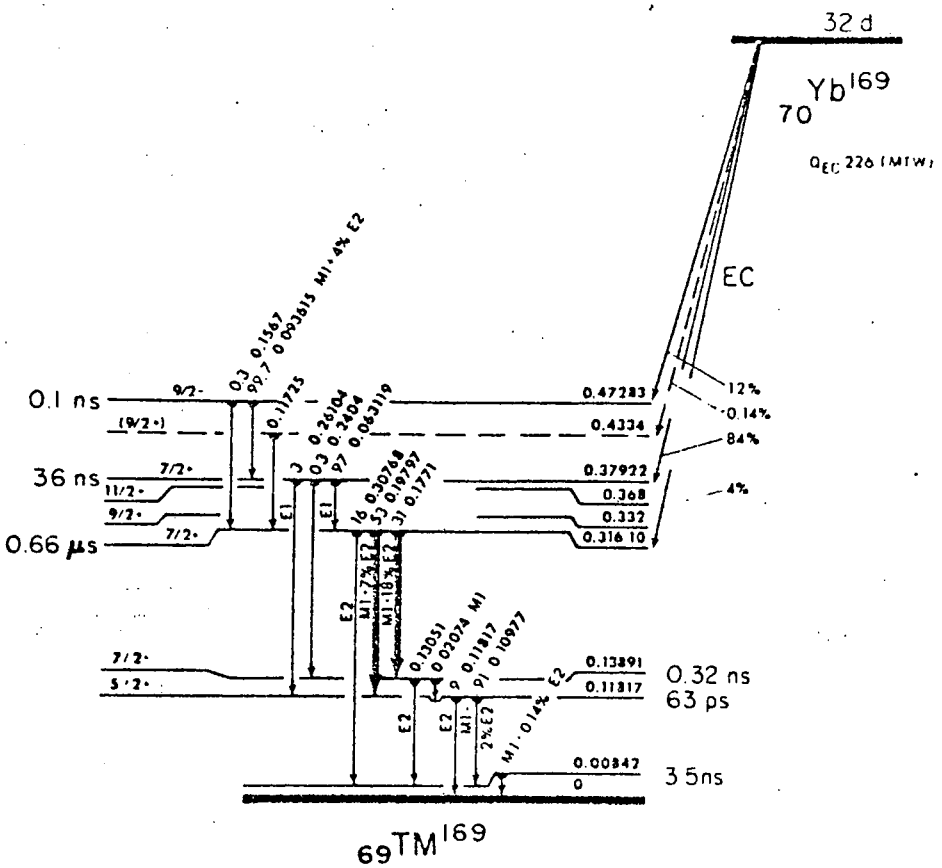
TECHNETIUM-99m ISOMERIC LEVEL DECAY



	ENERGY keV	ABUNDANCE
γ^1	2	99%
γ^2	140	99%
γ^3	142	1%

DECAY SCHEME TECHNETIUM-99m

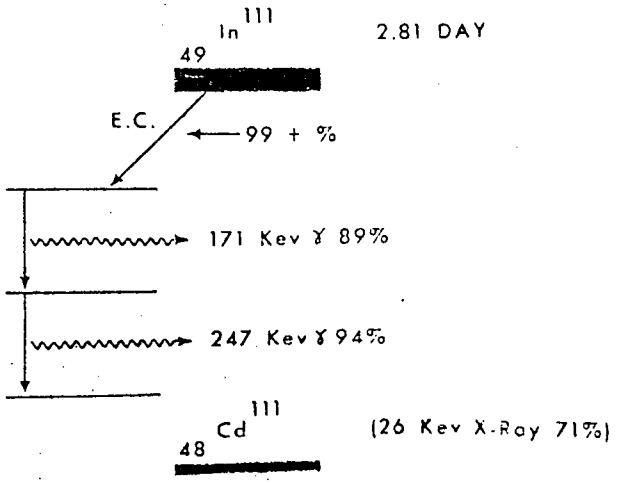
FIGURE 12



	ENERGY keV	ABUNDANCE
γ^1	63	45%
γ^2	110	18%
γ^3	131	11%
γ^4	177	21%
γ^5	198	33%
γ^6	308	10%
OTHERS		7%

DECAY SCHEME YTTERBIUM-169

FIGURE 13



	ENERGY keV	ABUNDANCE
E.C.		+99%
γ^1	171	88%
γ^2	247	94%

DECAY SCHEME INDIUM-111

FIGURE 14

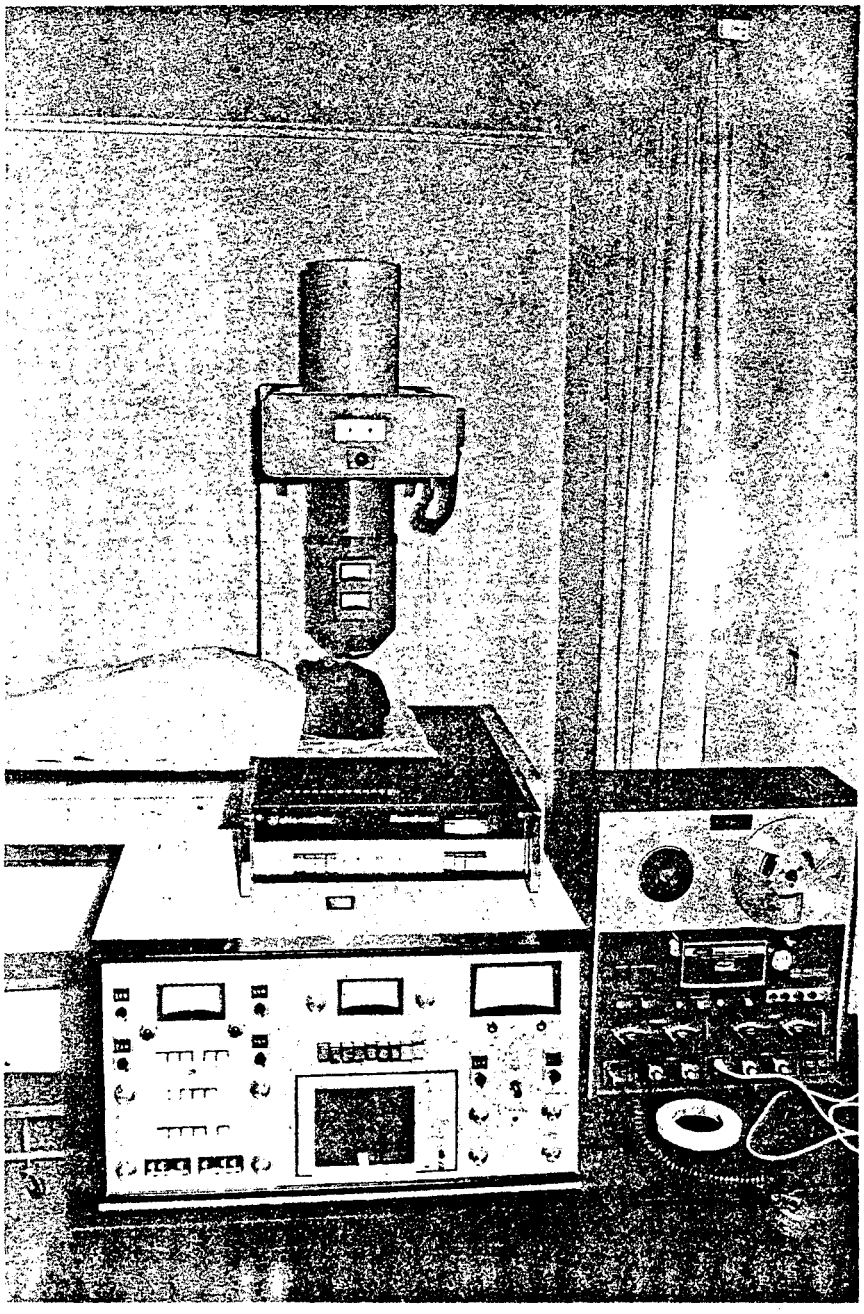
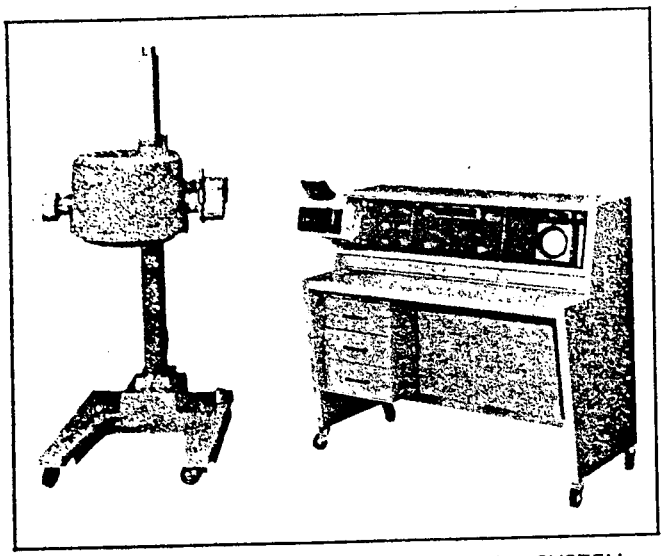
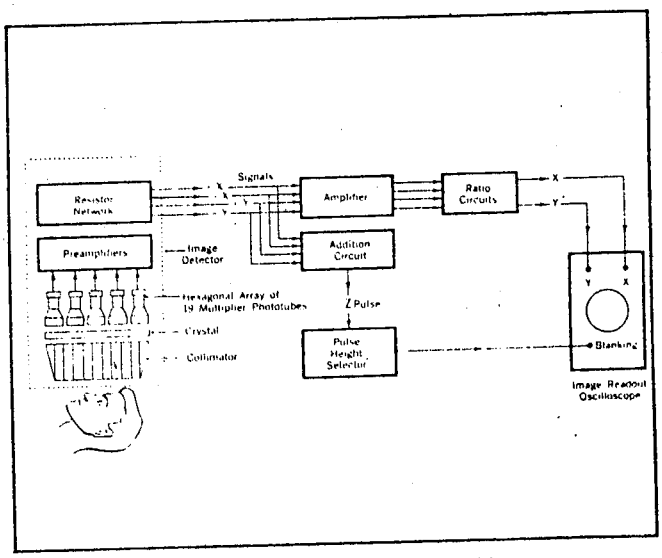


FIGURE 15



PHO/GAMMA III SCINTILLATION CAMERA SYSTEM



SIMPLIFIED BLOCK DIAGRAM

FIGURE 16

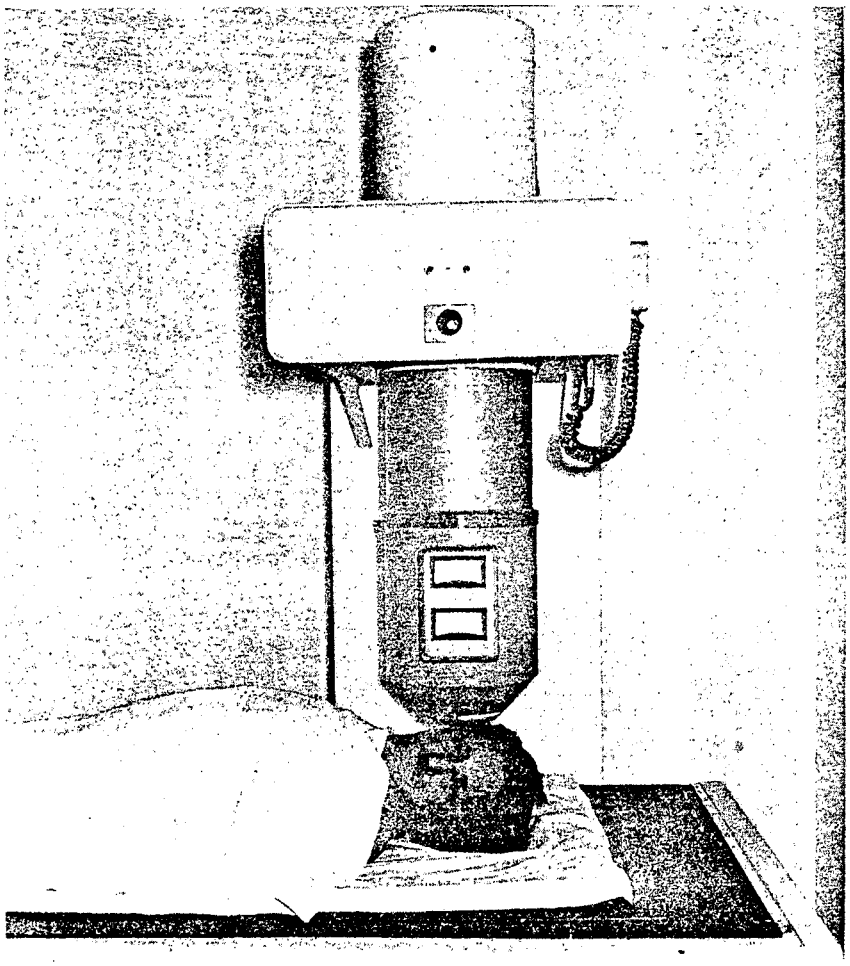


FIGURE 17

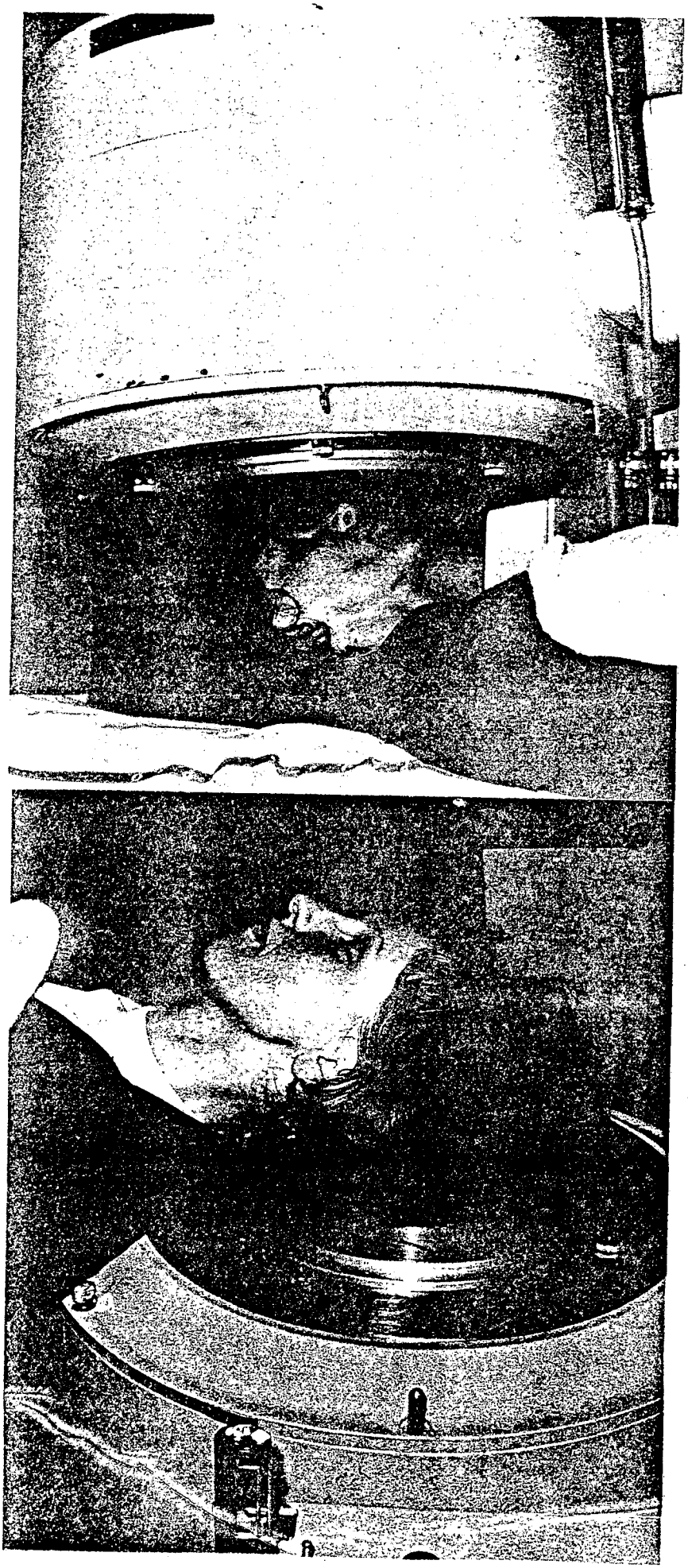


FIGURE 18

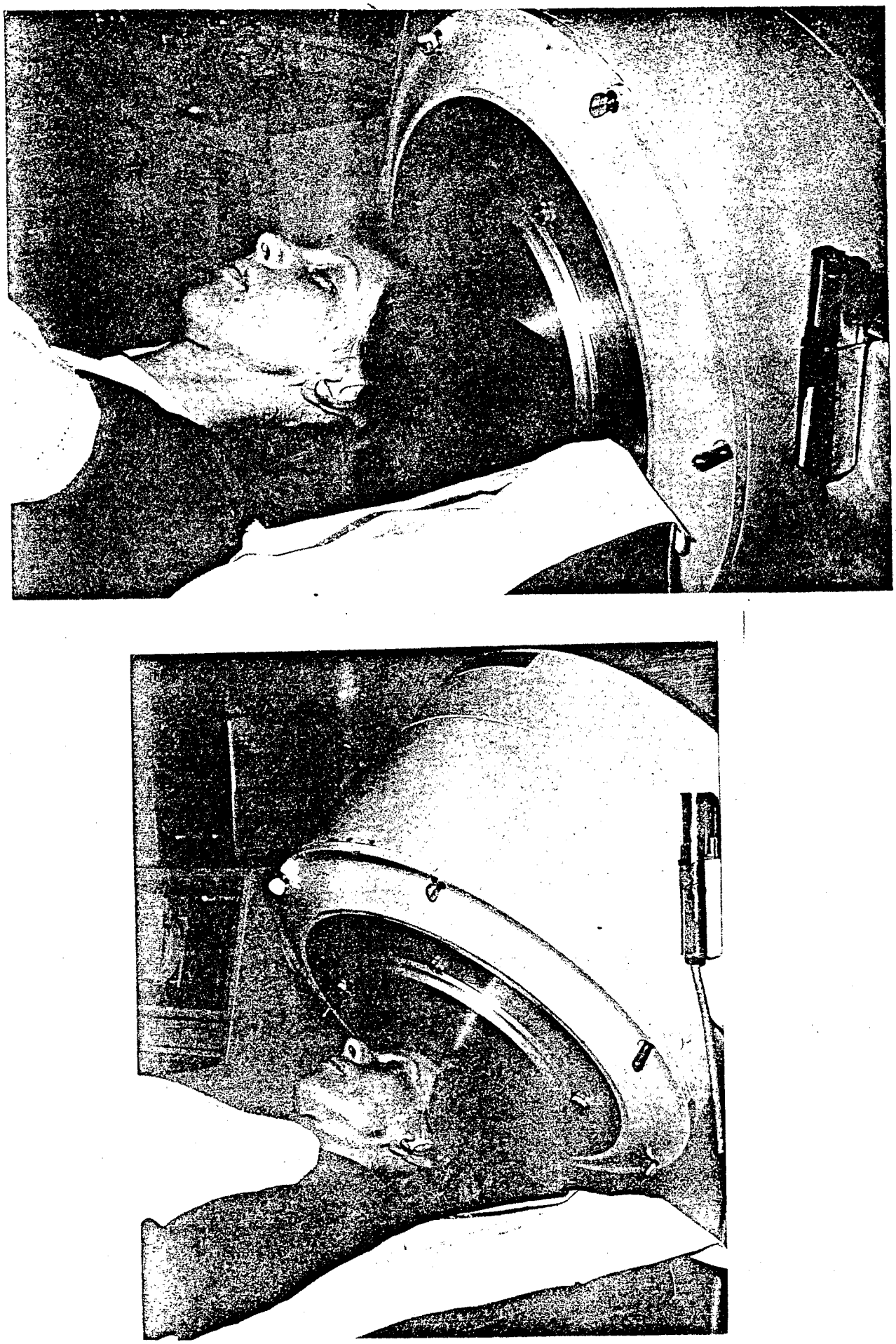


FIGURE 19

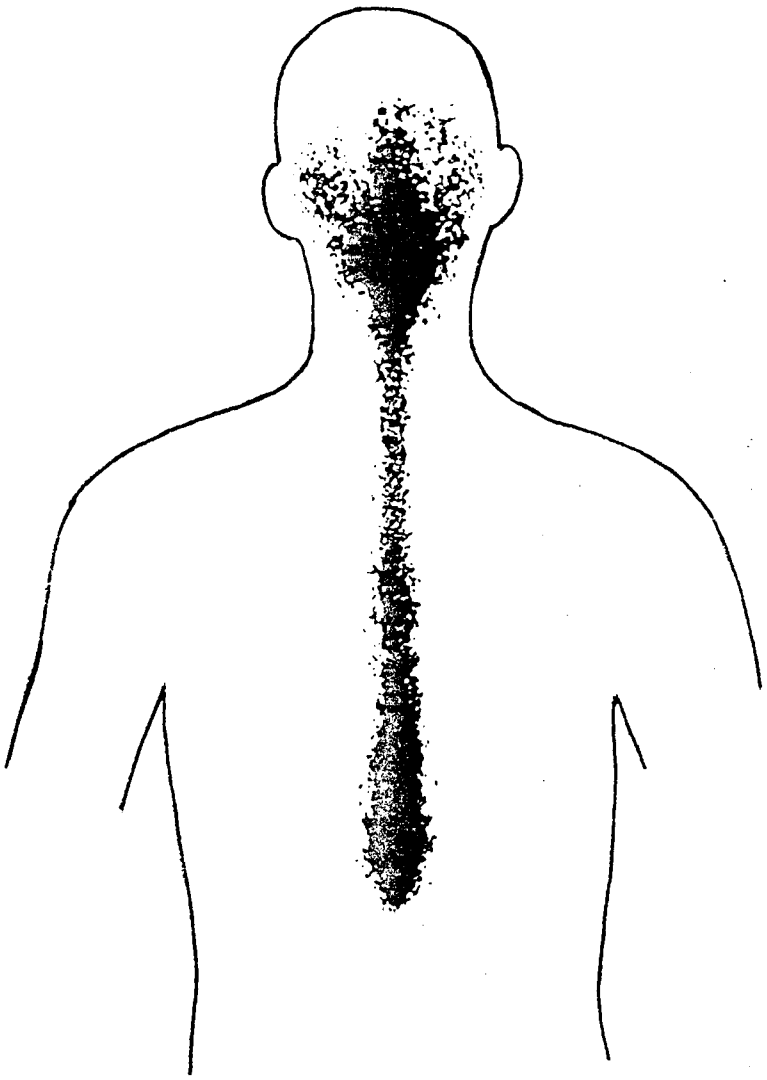
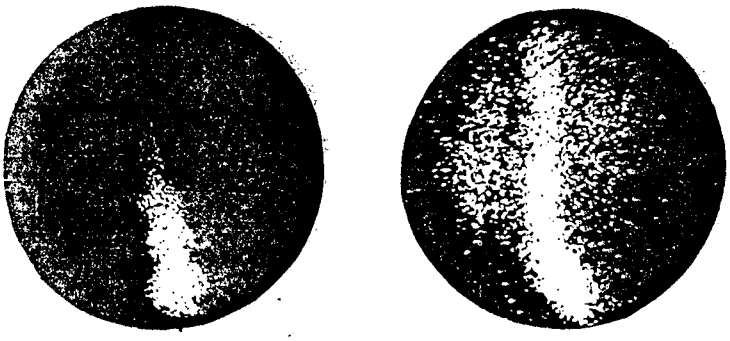


FIGURE 20



A B

FIGURE 21

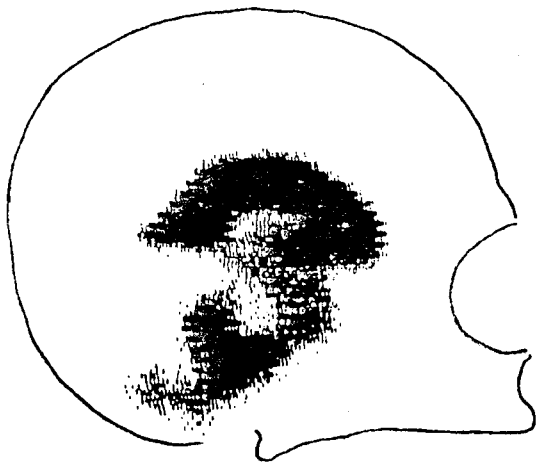


FIGURE 22

FIGURE 23

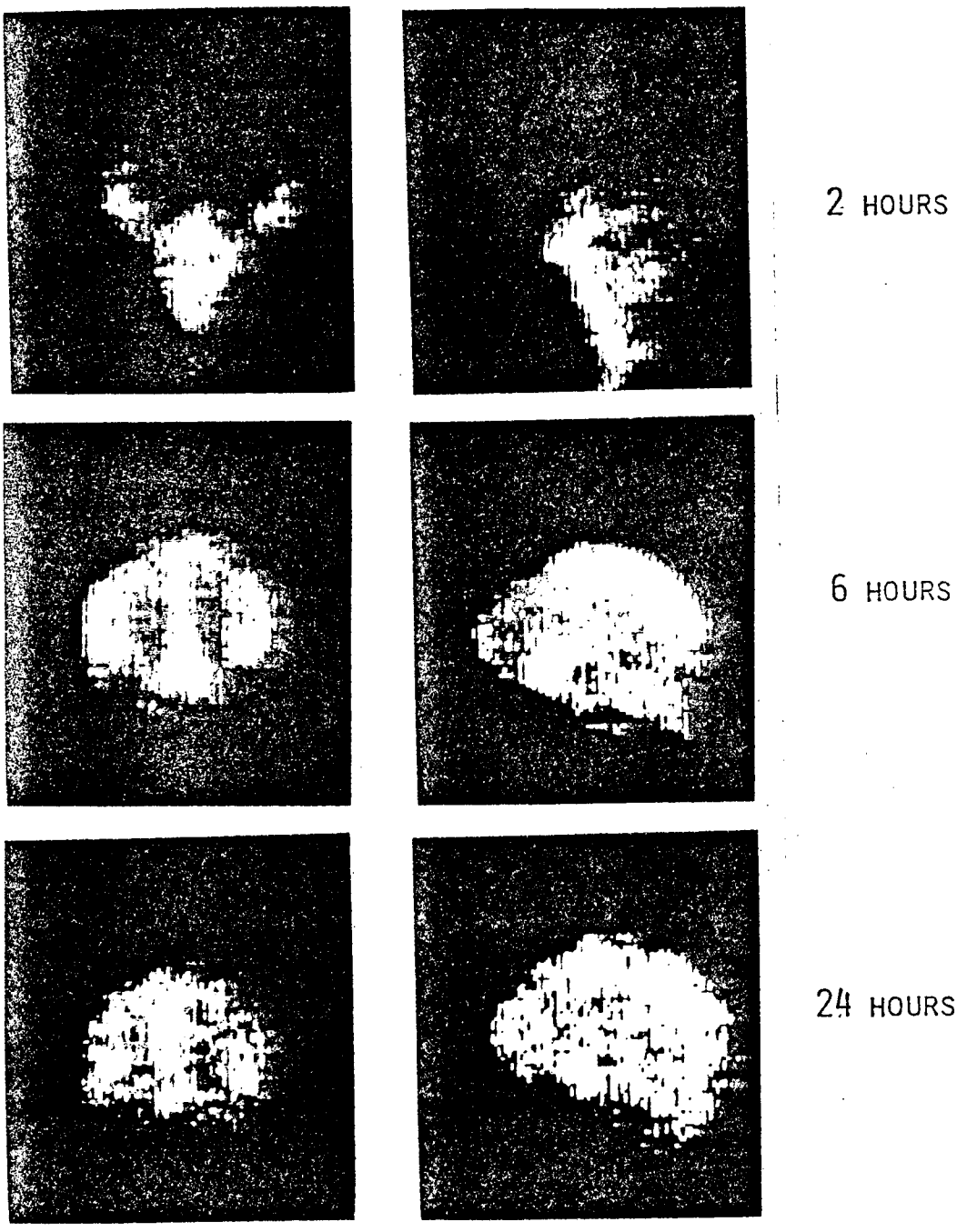


FIGURE 24

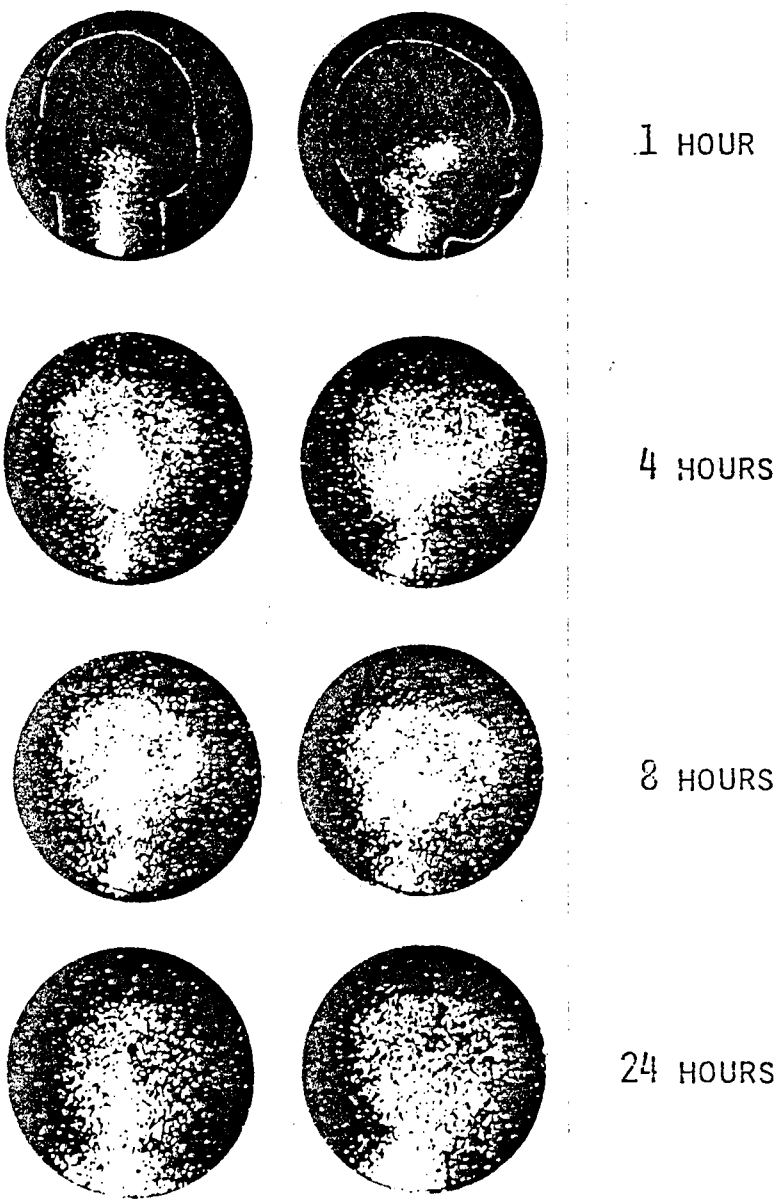
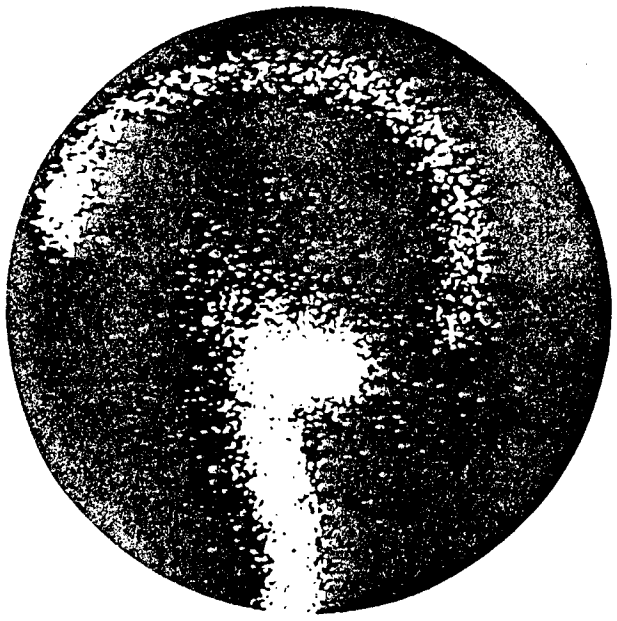
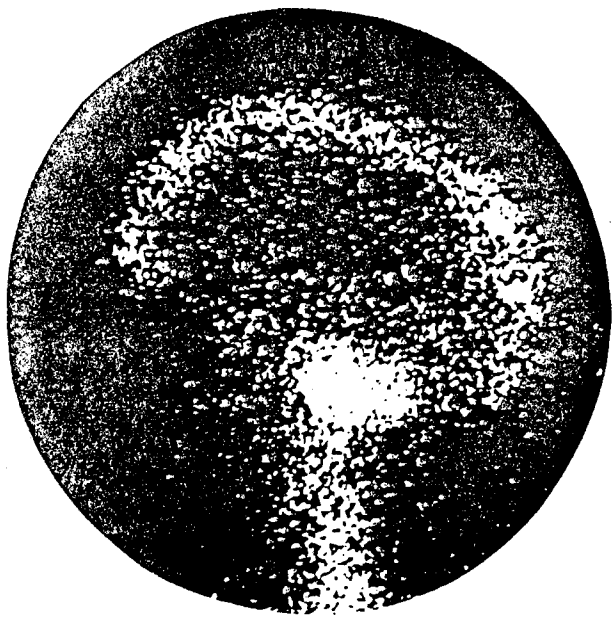


FIGURE 25



2 HOURS



6 HOURS

L LATERAL VIEW

FIGURE 26

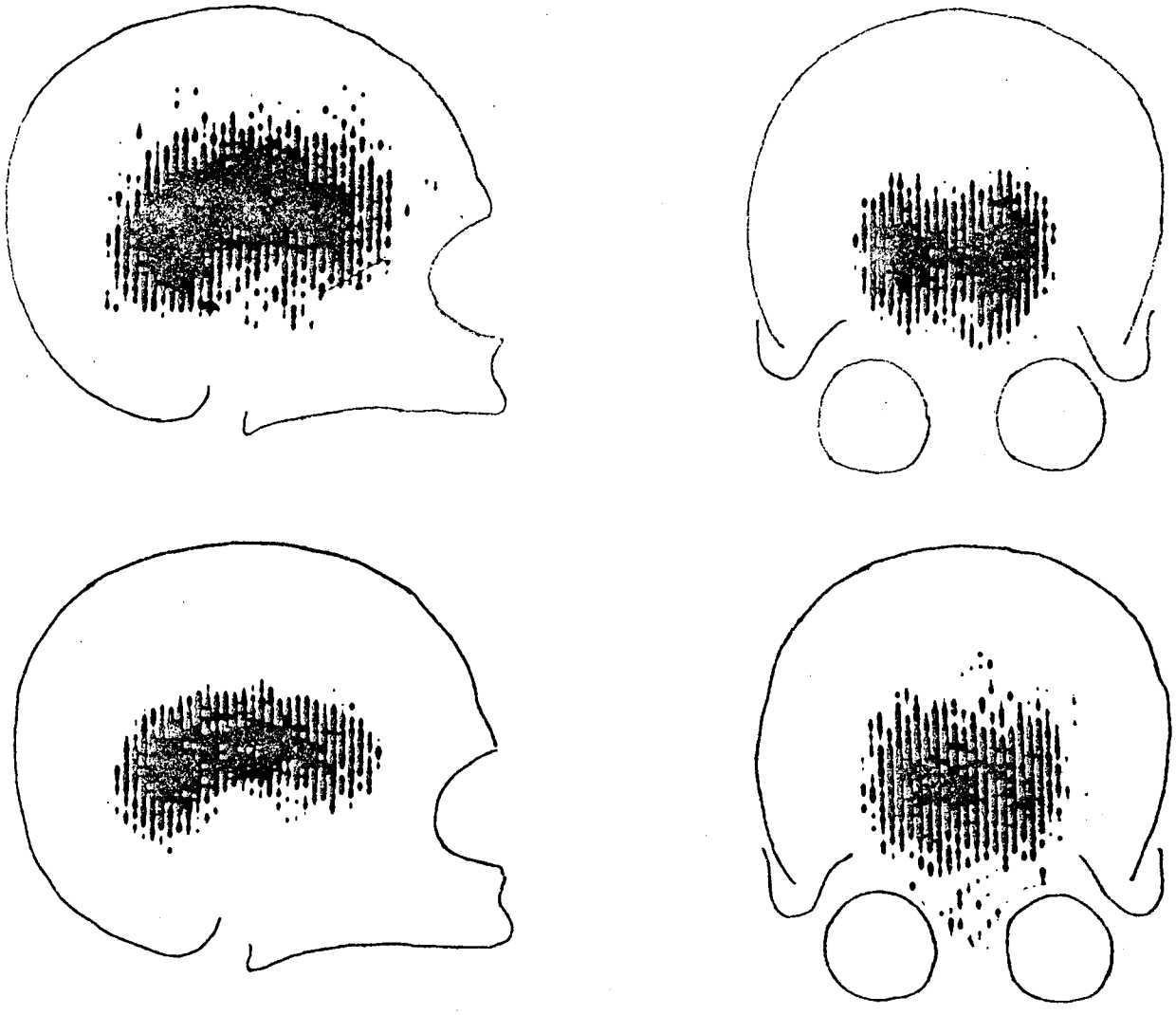


FIGURE 27

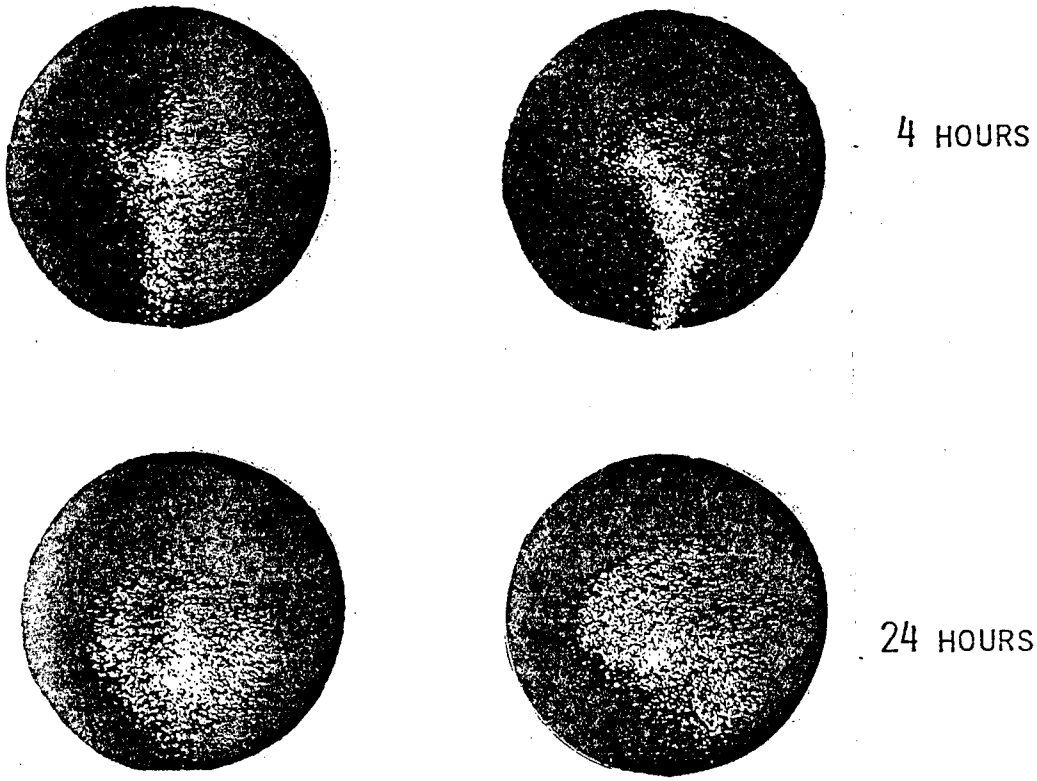


FIGURE 28-1

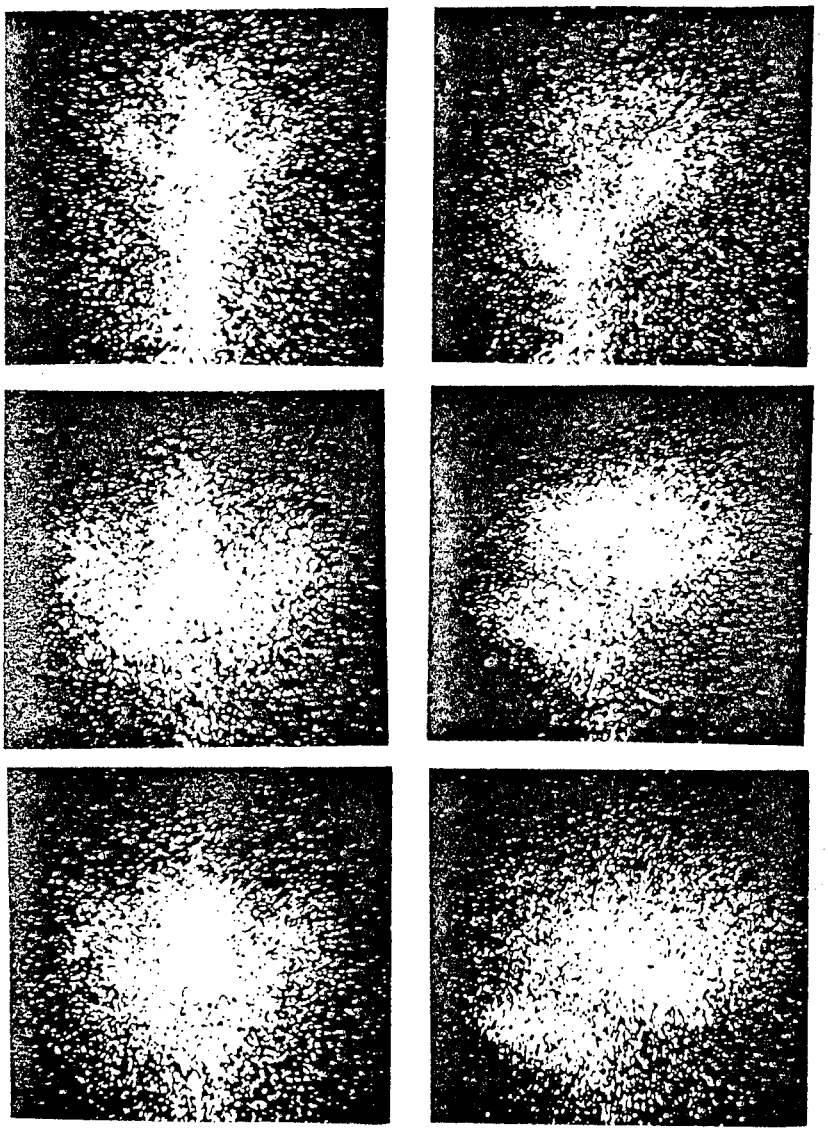
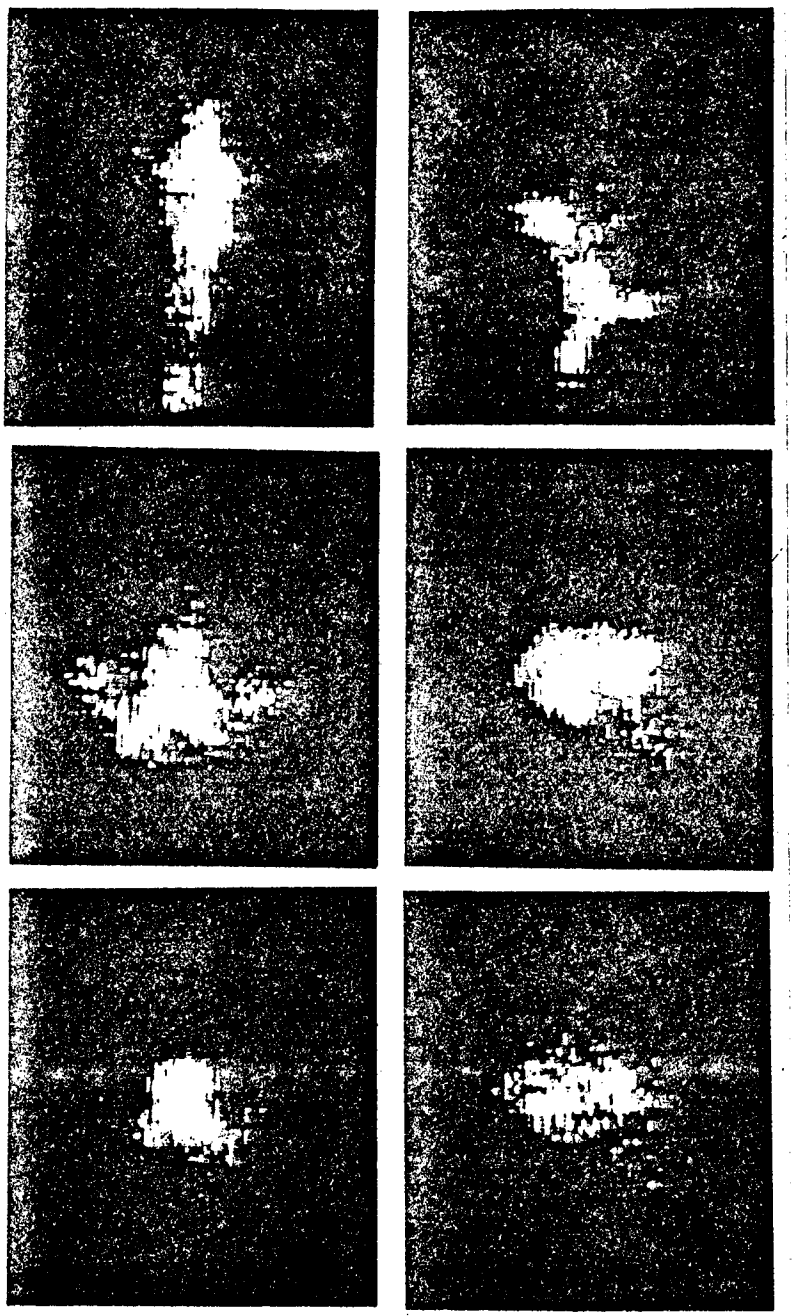


FIGURE 28-2



4 HOURS

24 HOURS

48 HOURS

POSTERIOR VIEW LATERAL VIEW

FIGURE 29

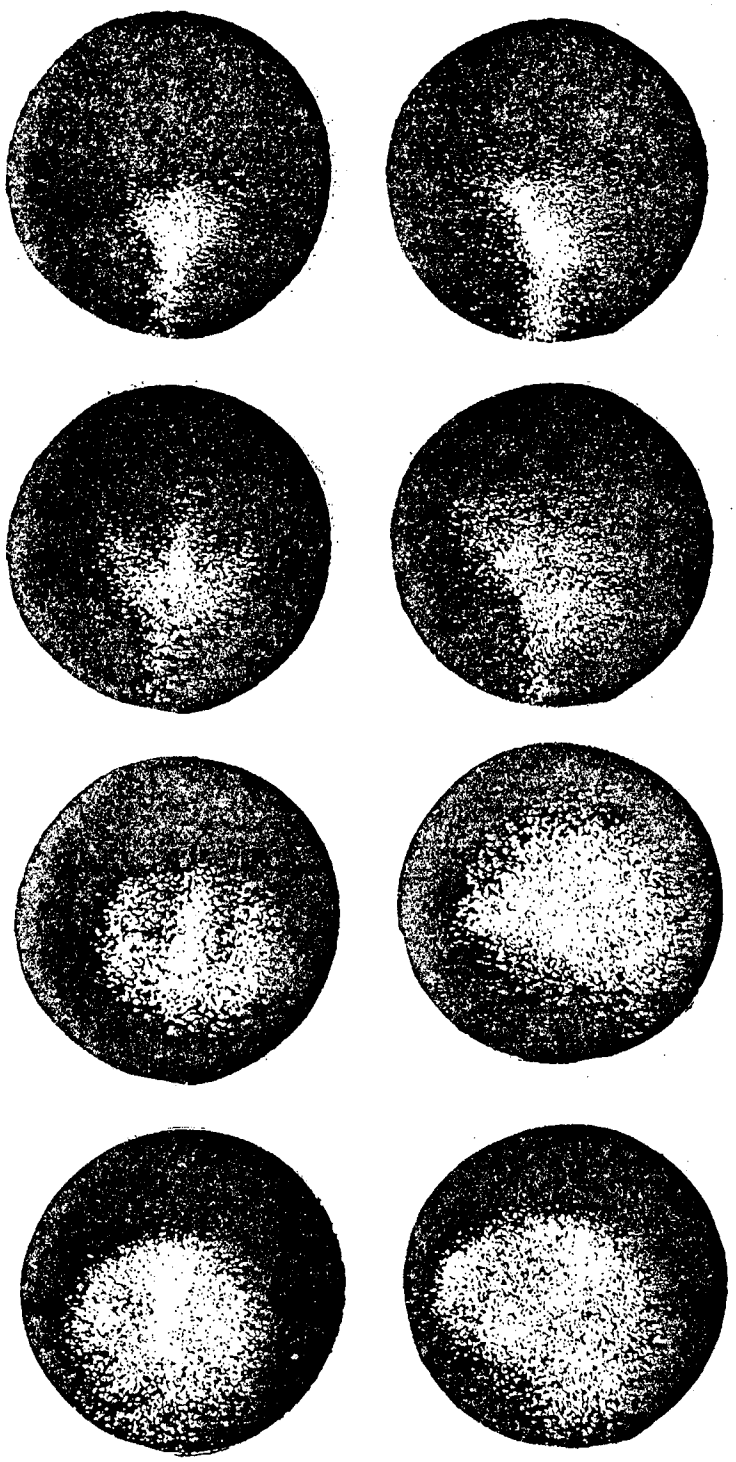
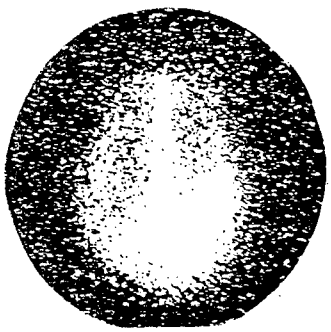
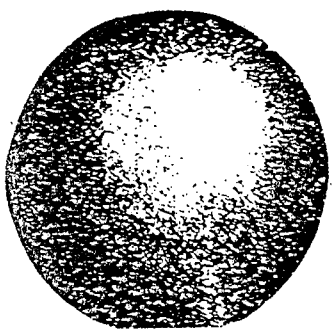


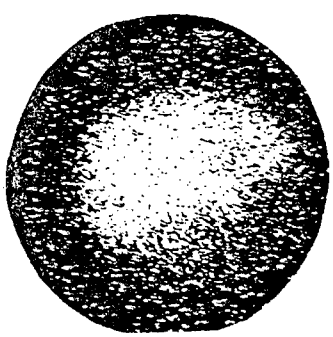
FIGURE 30



VERTEX VIEW



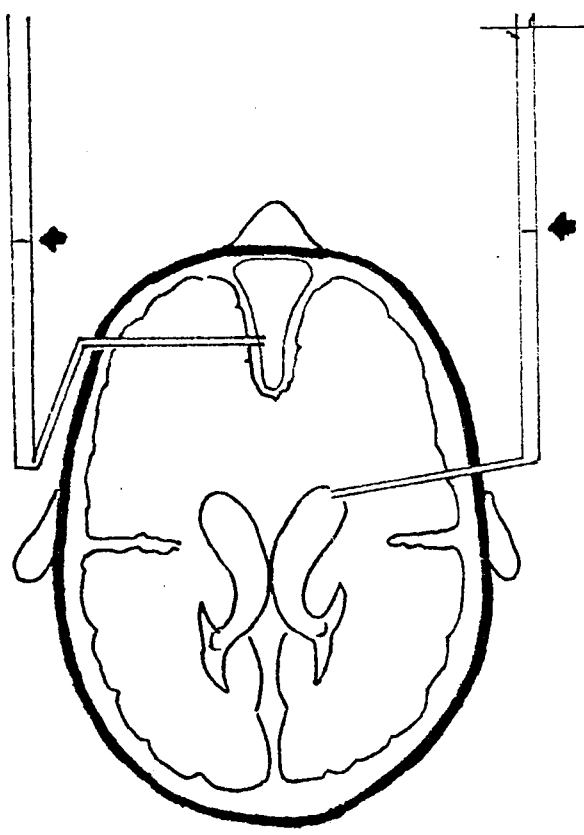
POSTERIOR VIEW



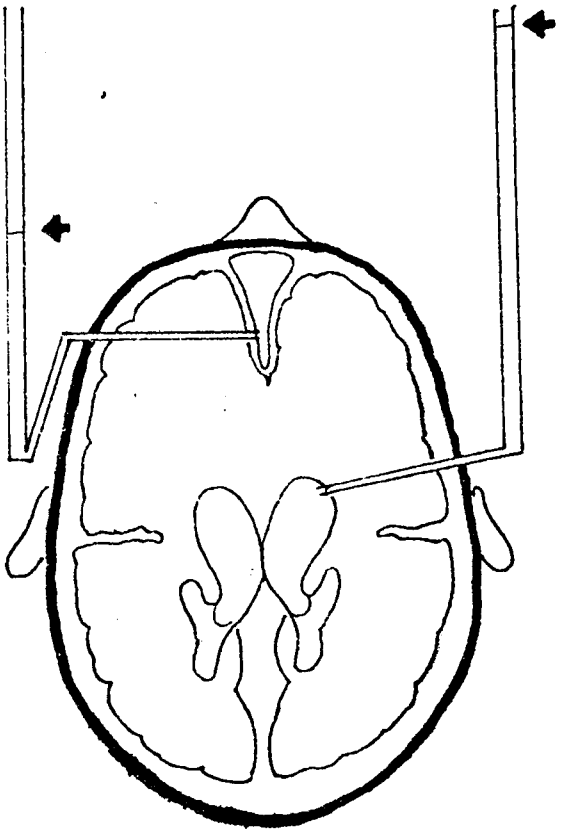
R LATERAL VIEW

24 HOURS

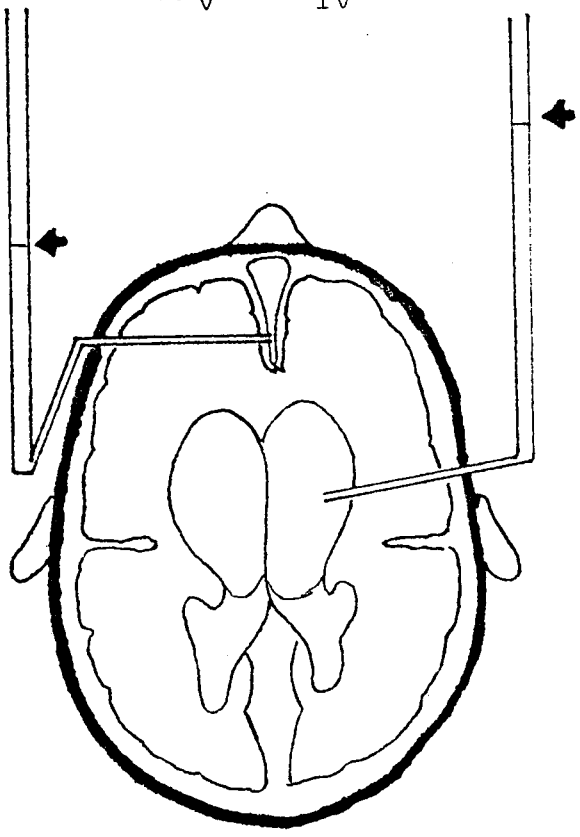
FIGURE 31



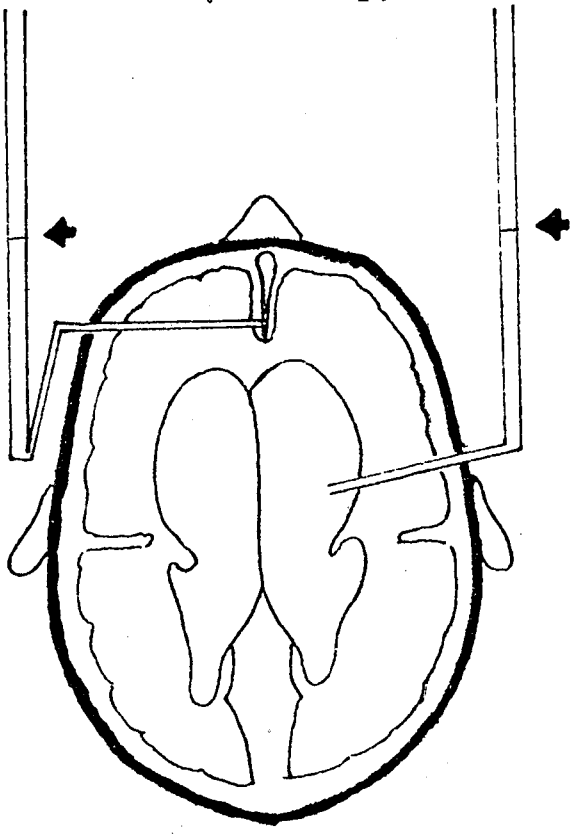
$PA_v = PA_{iv}$



$PA_v < PA_{iv}$



$PA_v < PA_{iv}$.



$PA_v < PA_{iv}$

FIGURE 32

$F_1 = P \times A_1$ $F_2 = P \times A_2$

$F_1 < F_2$

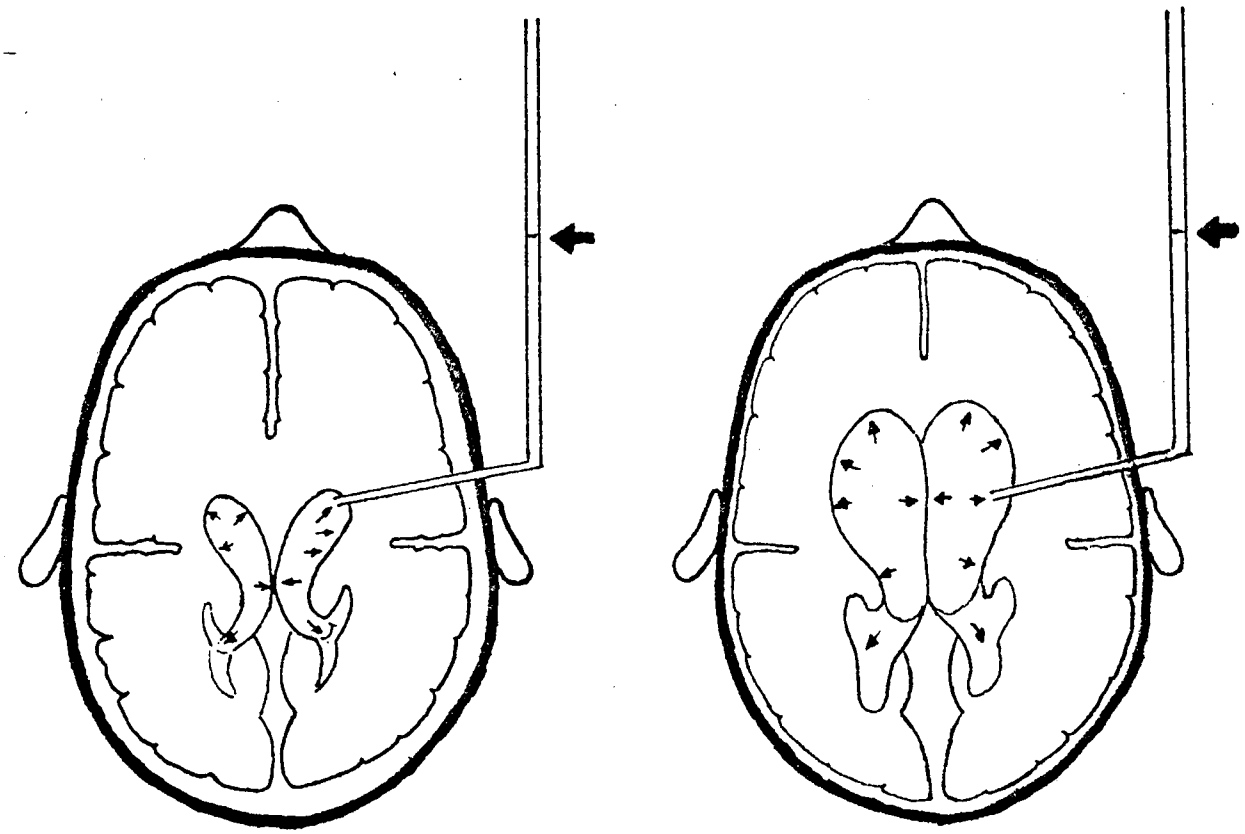
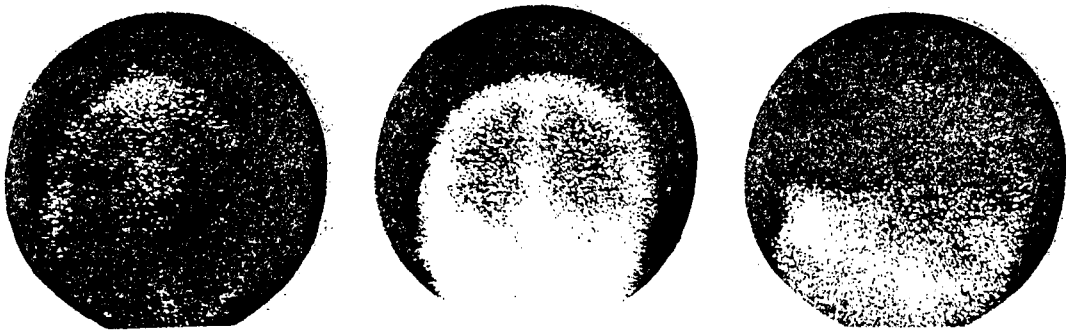


FIGURE 33

BRAIN SCANS

VERTEX POSTERIOR L LATERAL

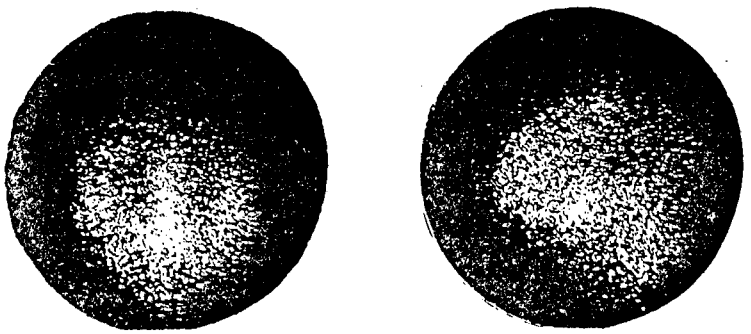


19.8.75

23.9.75

CISTERNOGRAPHY

POSTERIOR L LATERAL



19.9.75

FIGURE 34

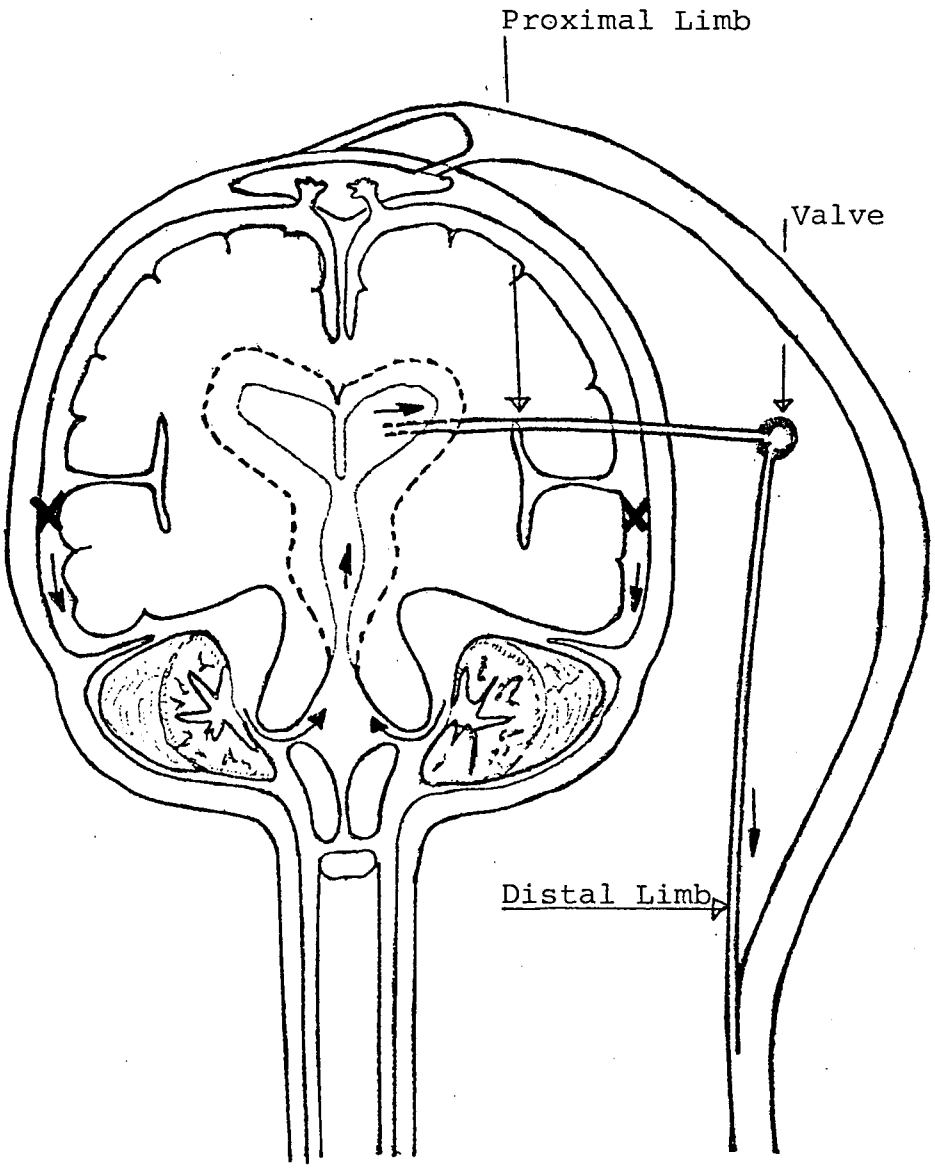
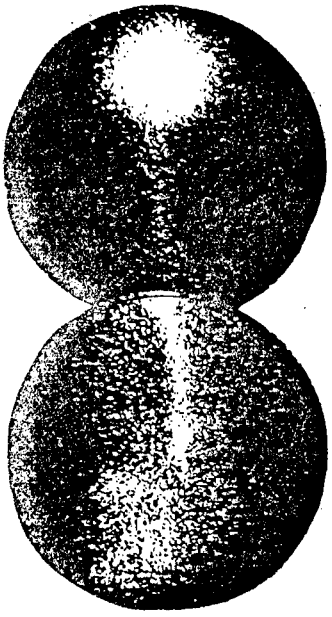


FIGURE 35

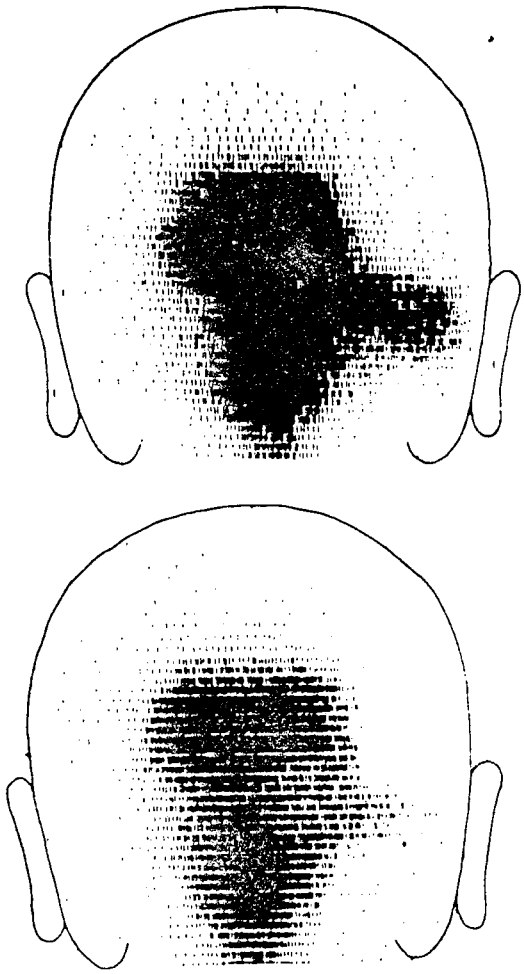
OBSTRUCTED VENTRICLES LATERAL AND POSTERIOR VIEWS. PRE-SHUNTING



COMPOSITE VIEW VENTRICULAR CSF DRAINING THROUGH VENTRICULOPERITONEAL SHUNT

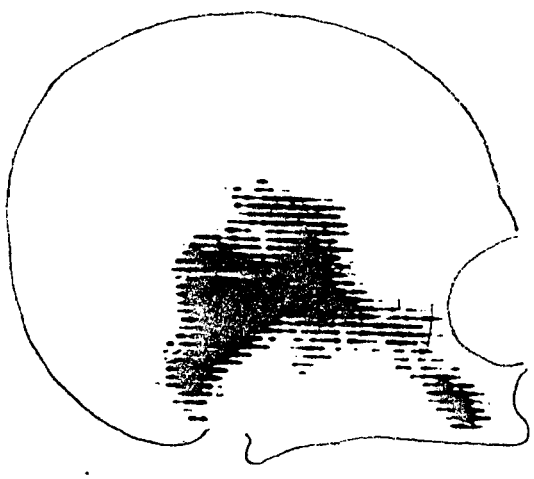
EMPTY VENTRICLES AFTER SHUNTING

FIGURE 36



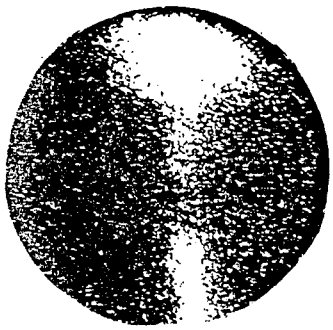
POSTERIOR VIEW

FIGURE 37



LATERAL VIEW

FIGURE 38

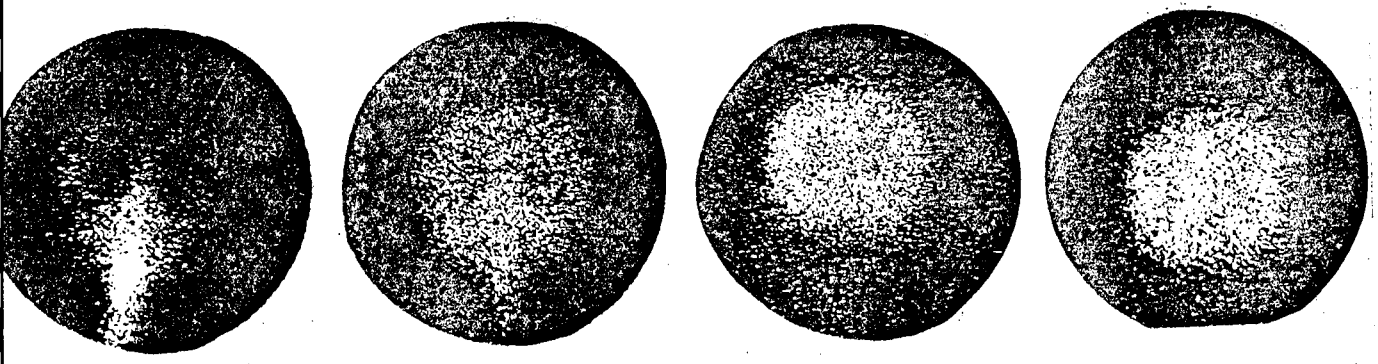


POSTERIOR VIEW
MIDCERVICAL REGION

FIGURE 39

4 HOURS 24 HOURS 14 DAYS 28 DAYS

POSTERIOR VIEW



LATERAL VIEW

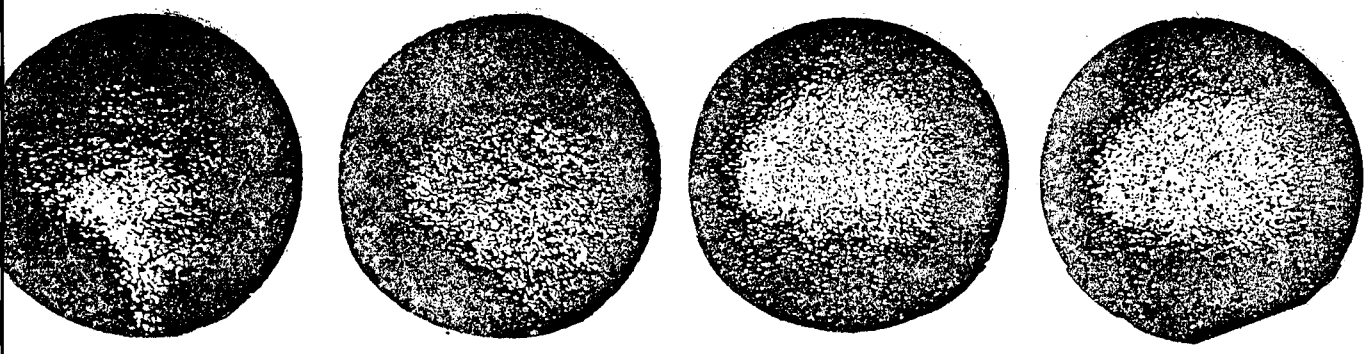


FIGURE 40

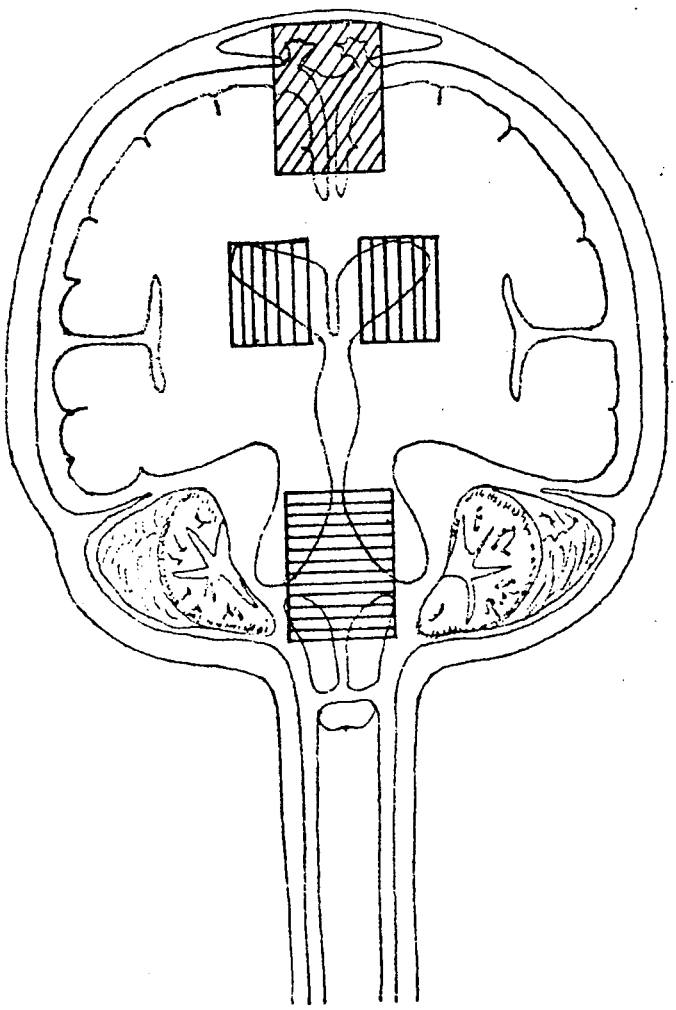


FIGURE 41

NAME : MRS. MA STEYN
NUMBER : R1/1299/75
DATE : 25/11/75

+ - BASAL CISTERNS
* - SUP. SAGITTAL SINUS
□ - VENTRICULAR SYSTEM

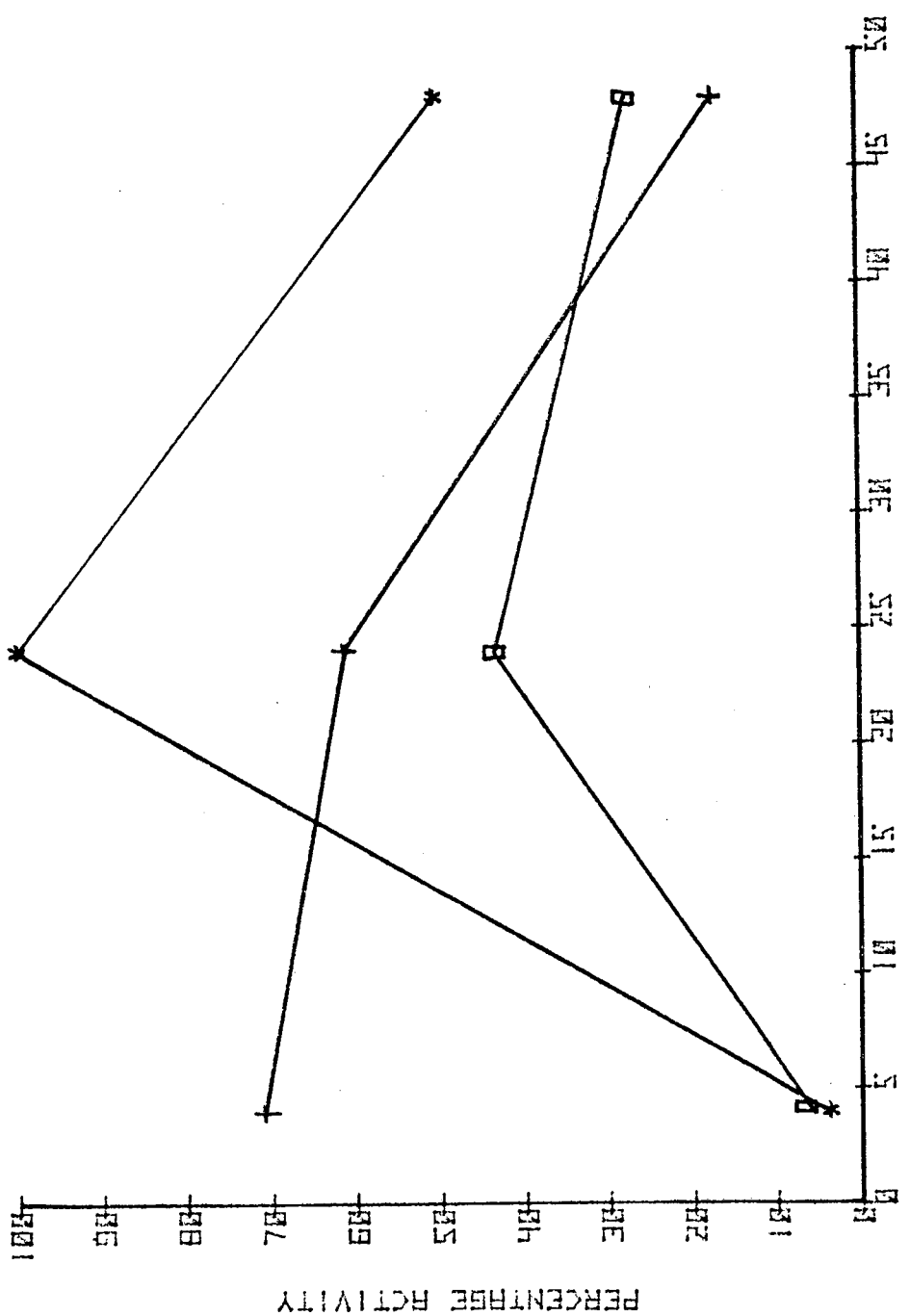


FIGURE 42

NAME : MRS. MC POTGIETER
NUMBER : R1/1273/75
DATE : 12/11/75

+ - BASAL CISTERNS
* - SUP. SAGITTAL SINUS
□ - VENTRICULAR SYSTEM

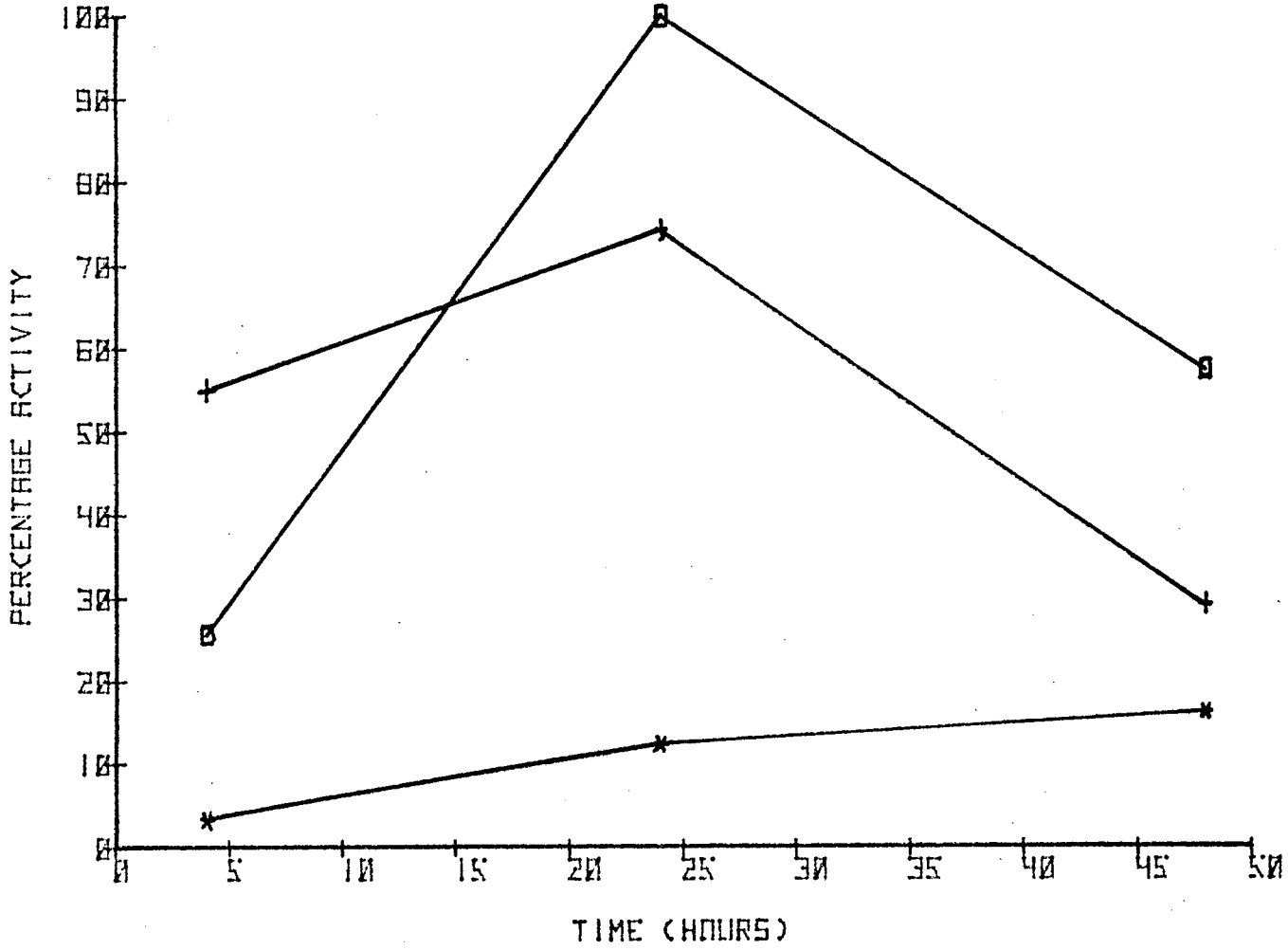


FIGURE 43

NAME : PETRUS MGOMEZULU
NUMBER : RI/NB/429/75
DATE : 15/9/75

+ - BASAL CISTERNS
* - SUP. SAGITTAL SINUS
□ - VENTRICULAR SYSTEM

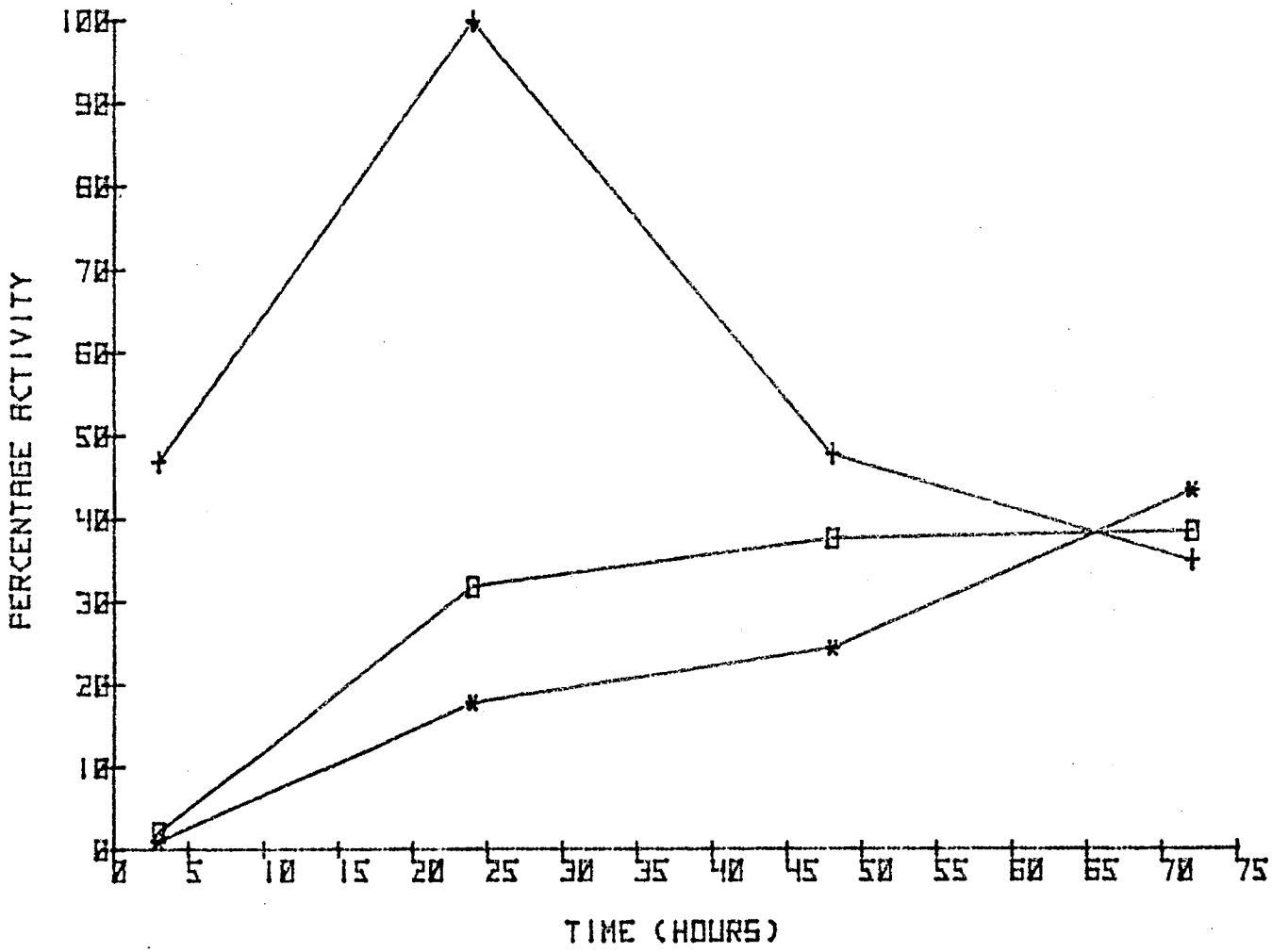


FIGURE 44 A

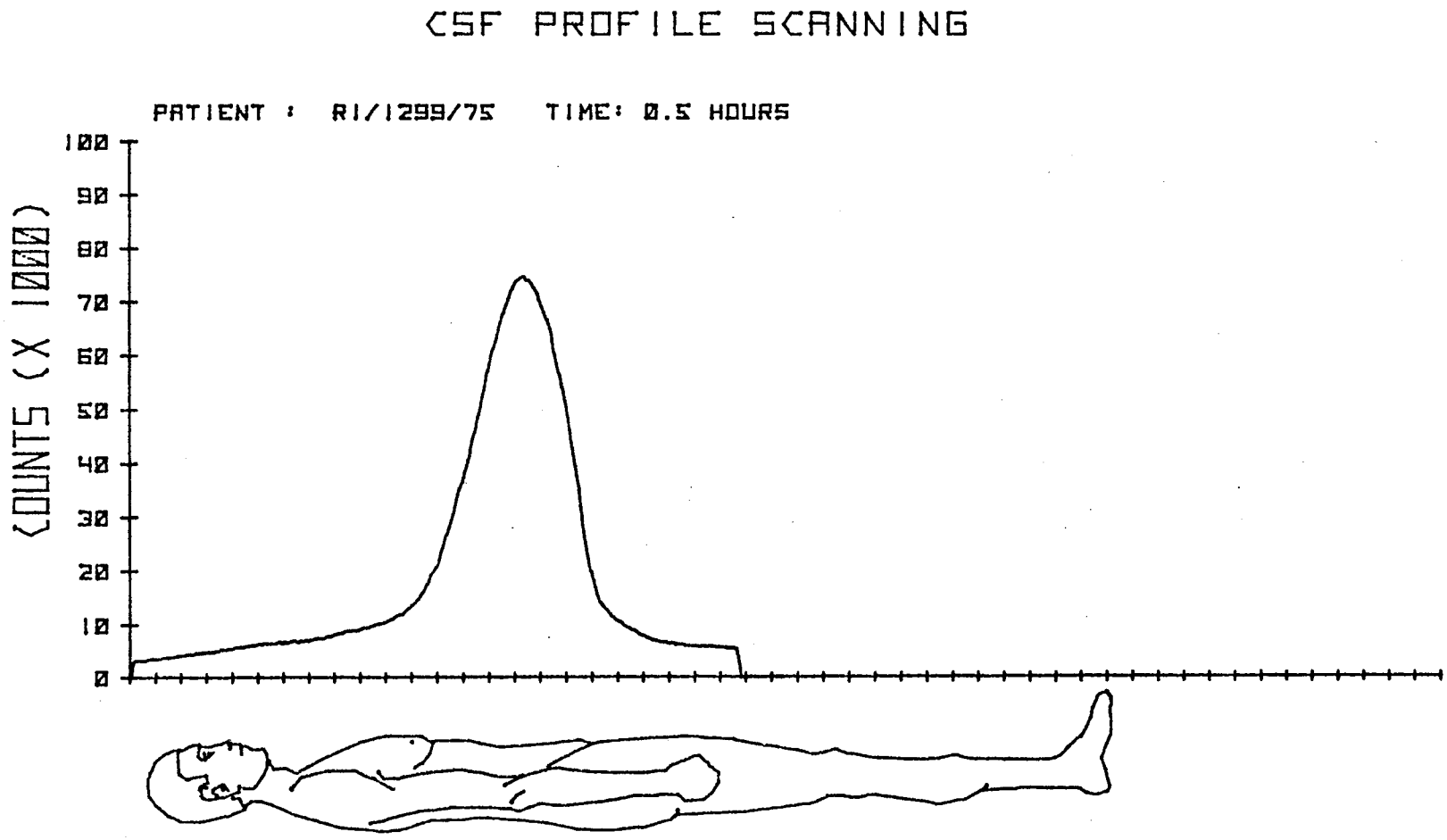

CSF PROFILE SCANNING
PATIENT : RI/1299/75 TIME: 0.5 HOURS
COUNTS (X 1000)
100
90
80
70
60
50
40
30
20
10
0

FIGURE 44 B

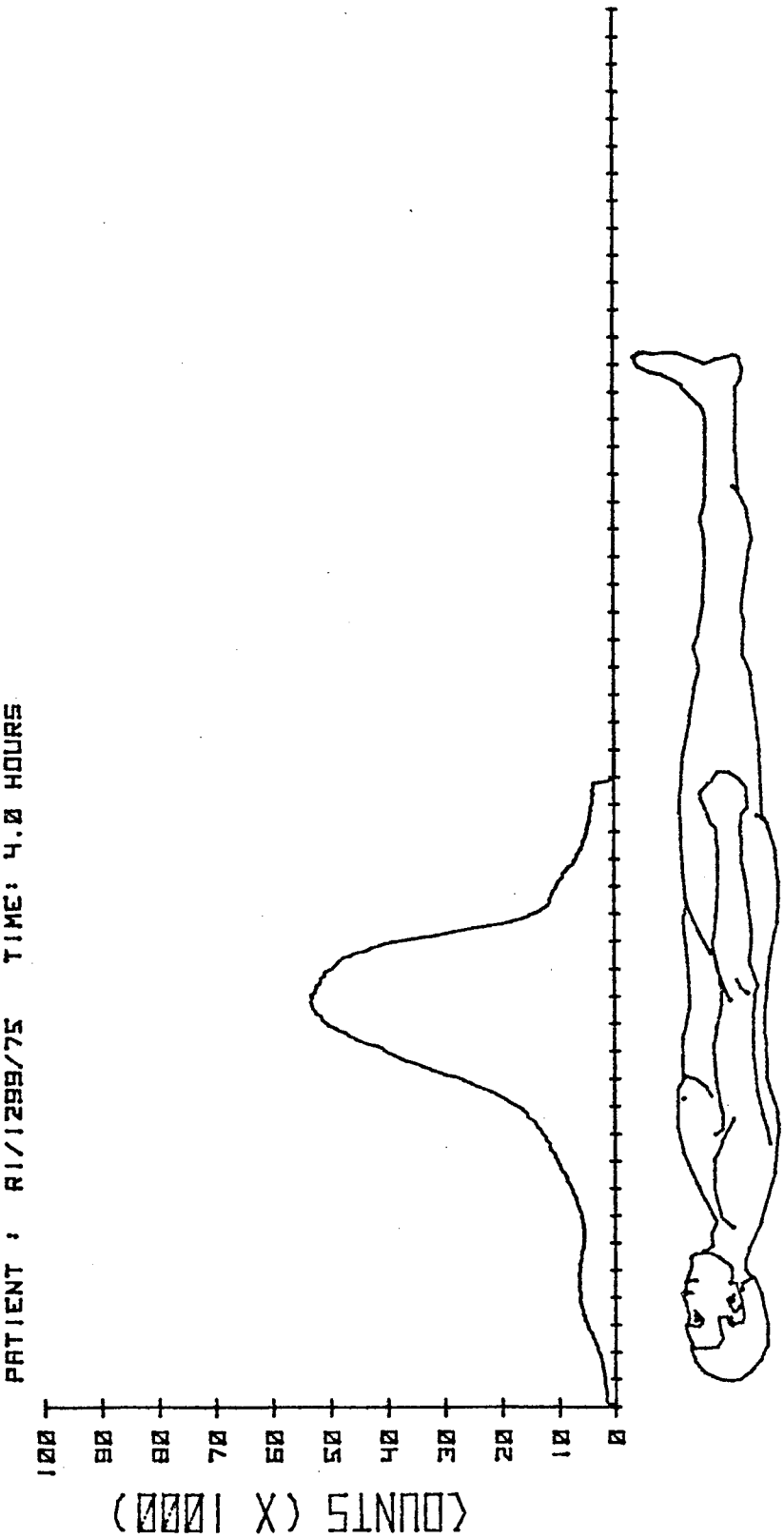

CSF PROFILE SCANNING
PATIENT : RI/1299/75 TIME: 4.0 HOURS
COUNTS (X 1000)
100
90
80
70
60
50
40
30
20
10
0

FIGURE 44 C

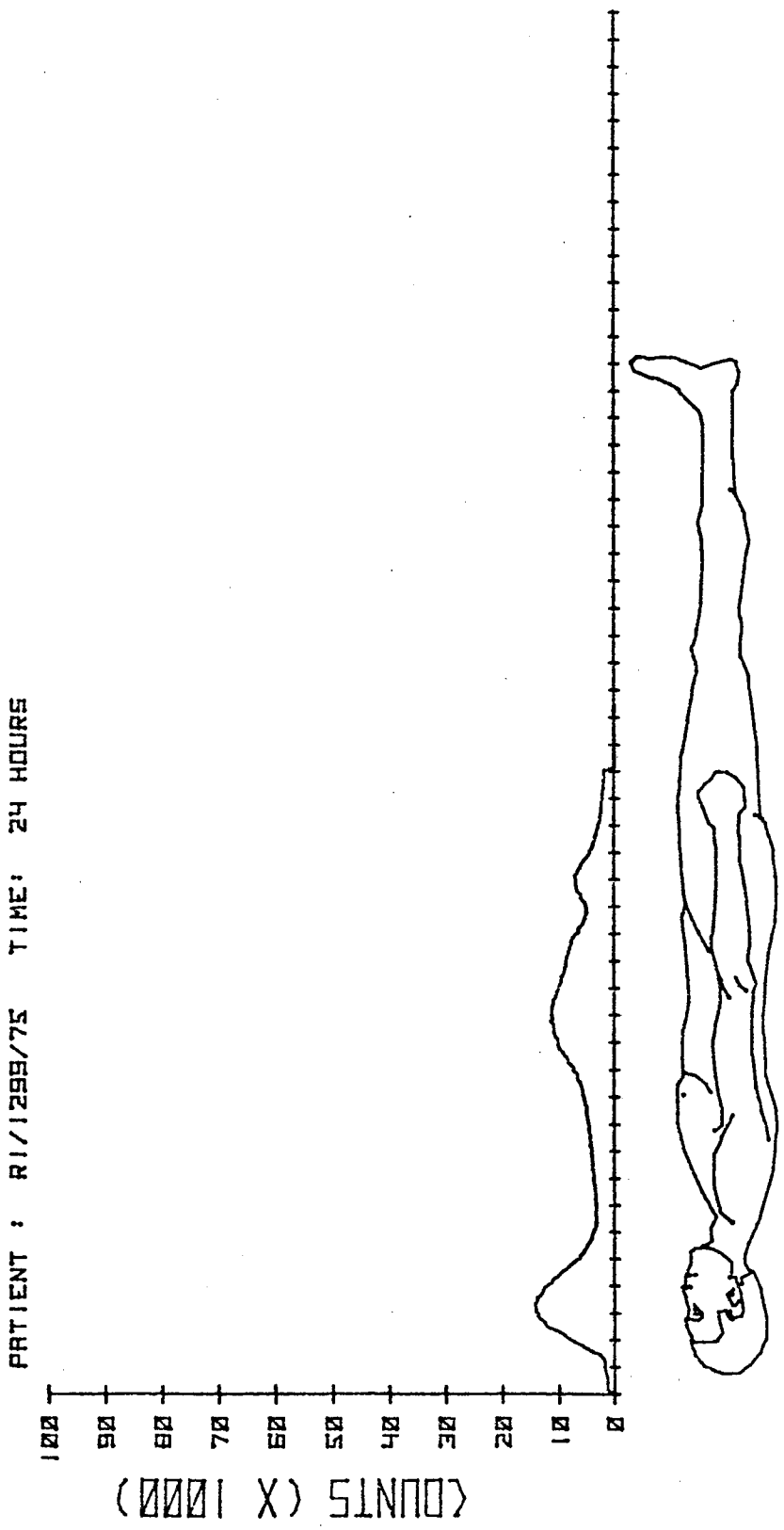

CSF PROFILE SCANNING
PATIENT : RI/1299/75 TIME: 24 HOURS
COUNTS (X 1000)
100
90
80
70
60
50
40
30
20
10
0

FIGURE 44 D

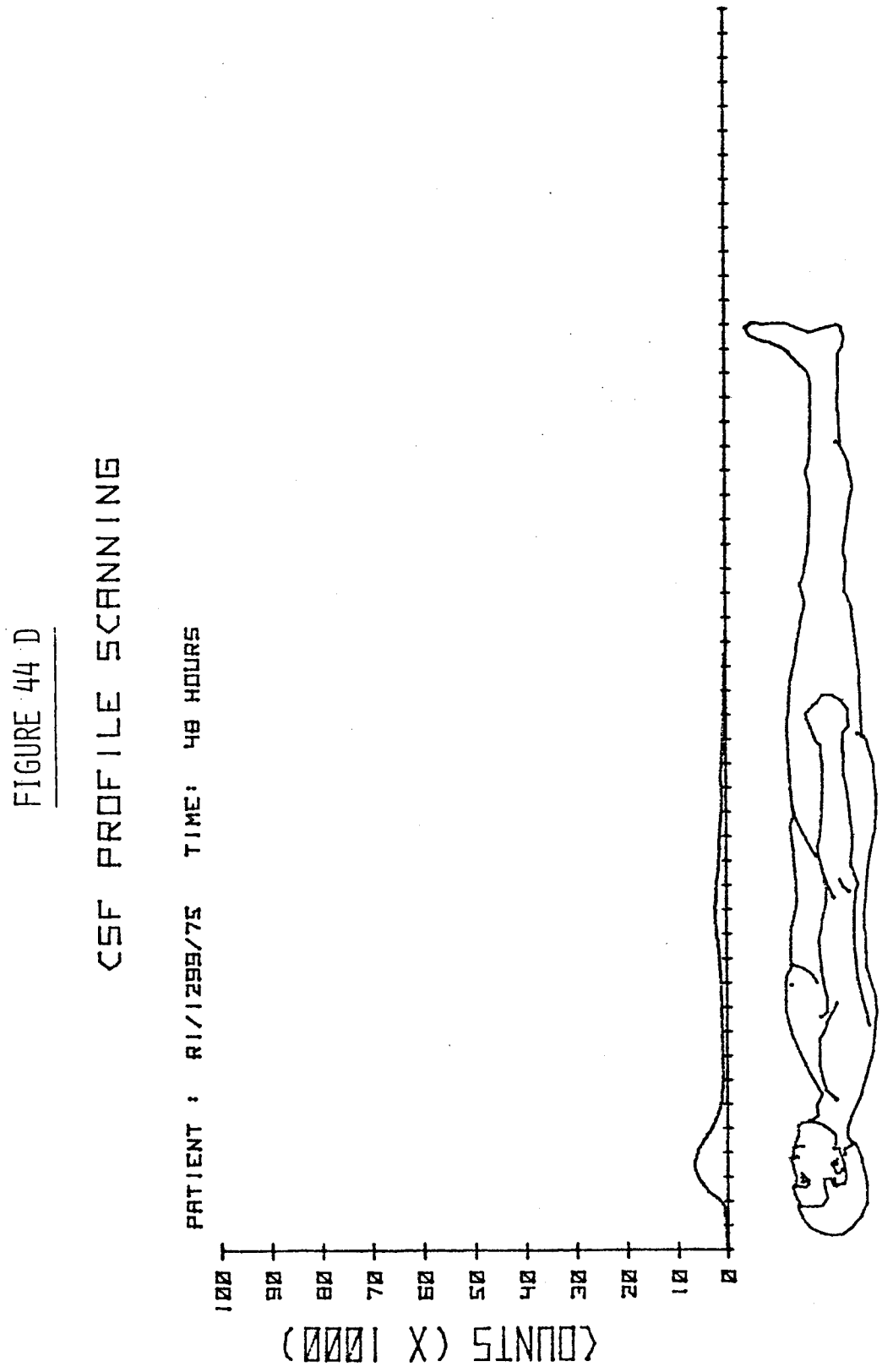

CSF PROFILE SCANNING
PATIENT : RI/1299/75 TIME: 48 HOURS
COUNTS (X 1000)
100
90
80
70
60
50
40
30
20
10
0

FIGURE 45 A

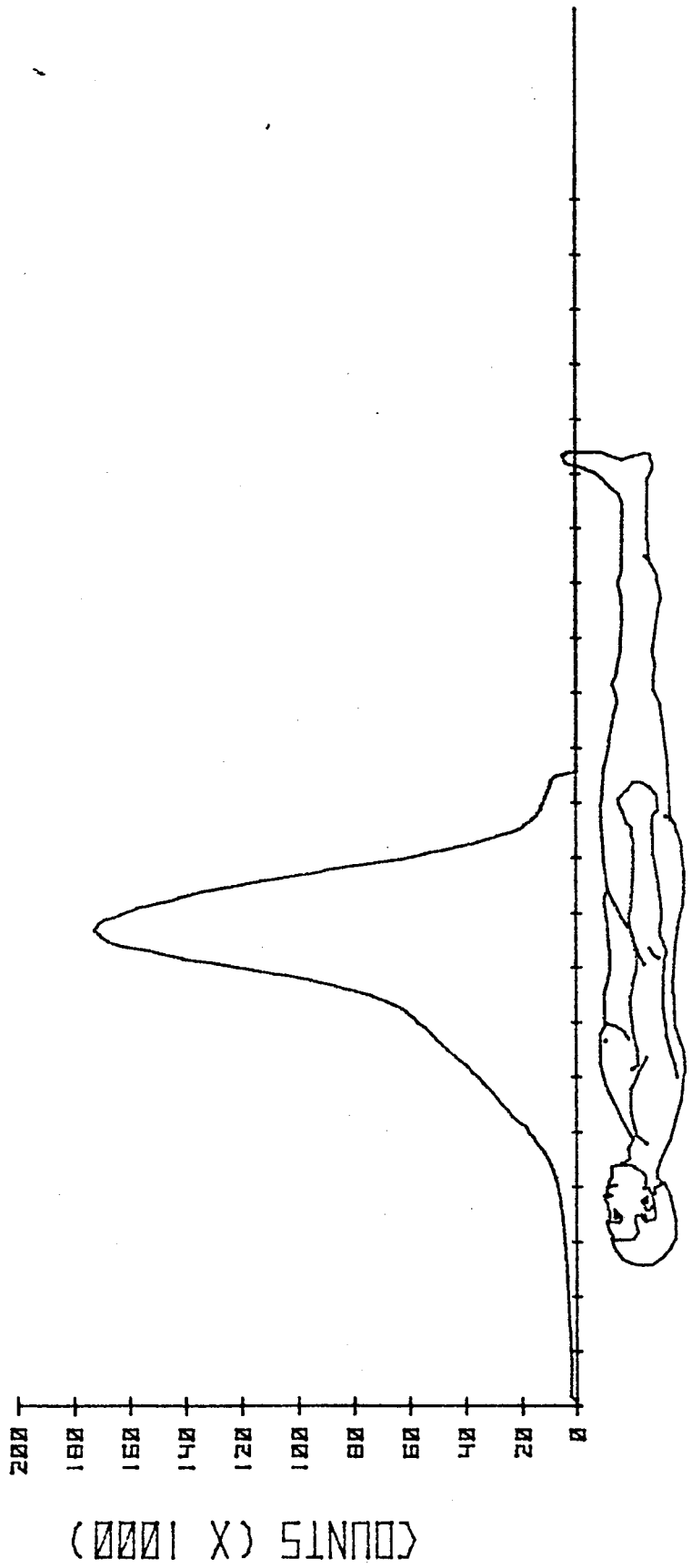

CSF PROFILE SCANNING
PATIENT : RI/NB/429/75 TIME: 0.5 HOURS
COUNTS (X 1000)
200
180
160
140
120
100
80
60
40
20
0

FIGURE 45 B

CSF PROFILE SCANNING

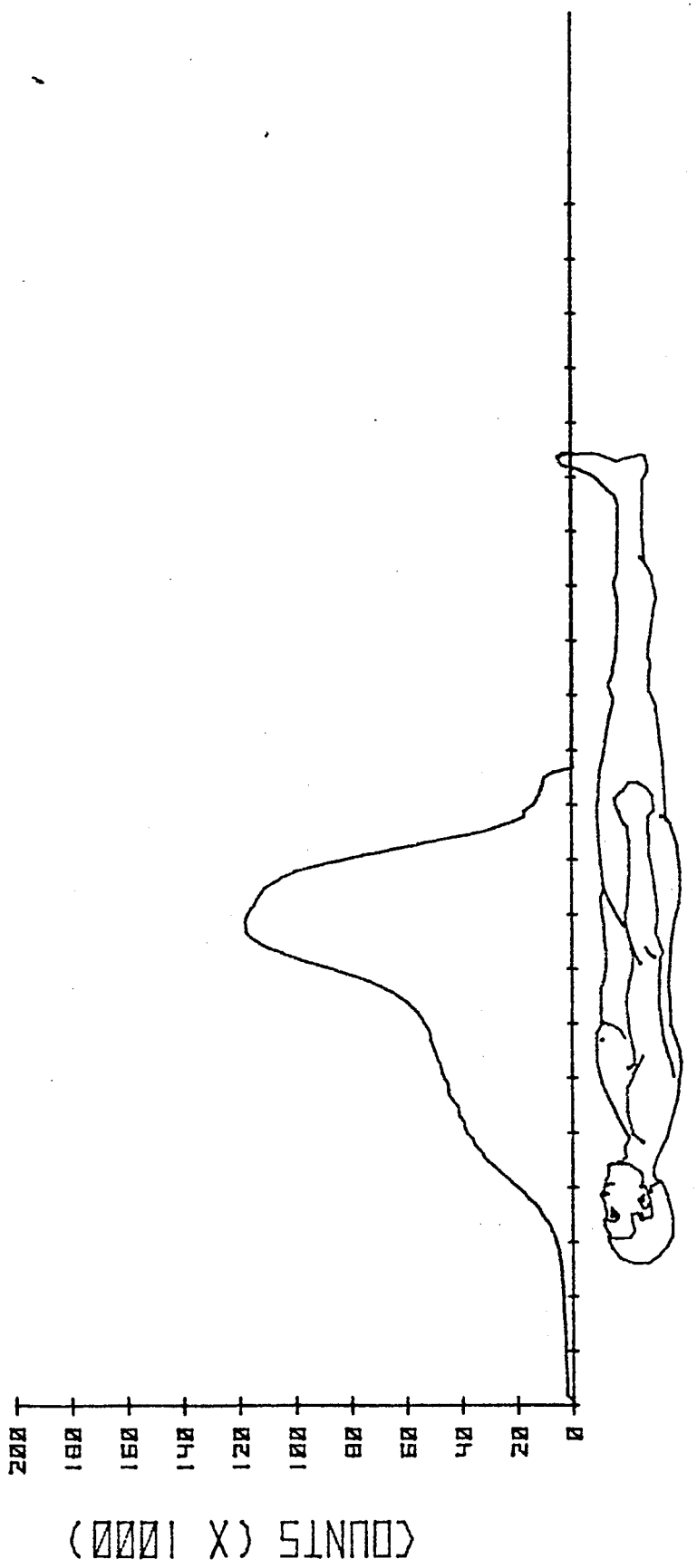


FIGURE 45 C

CSF PROFILE SCANNING

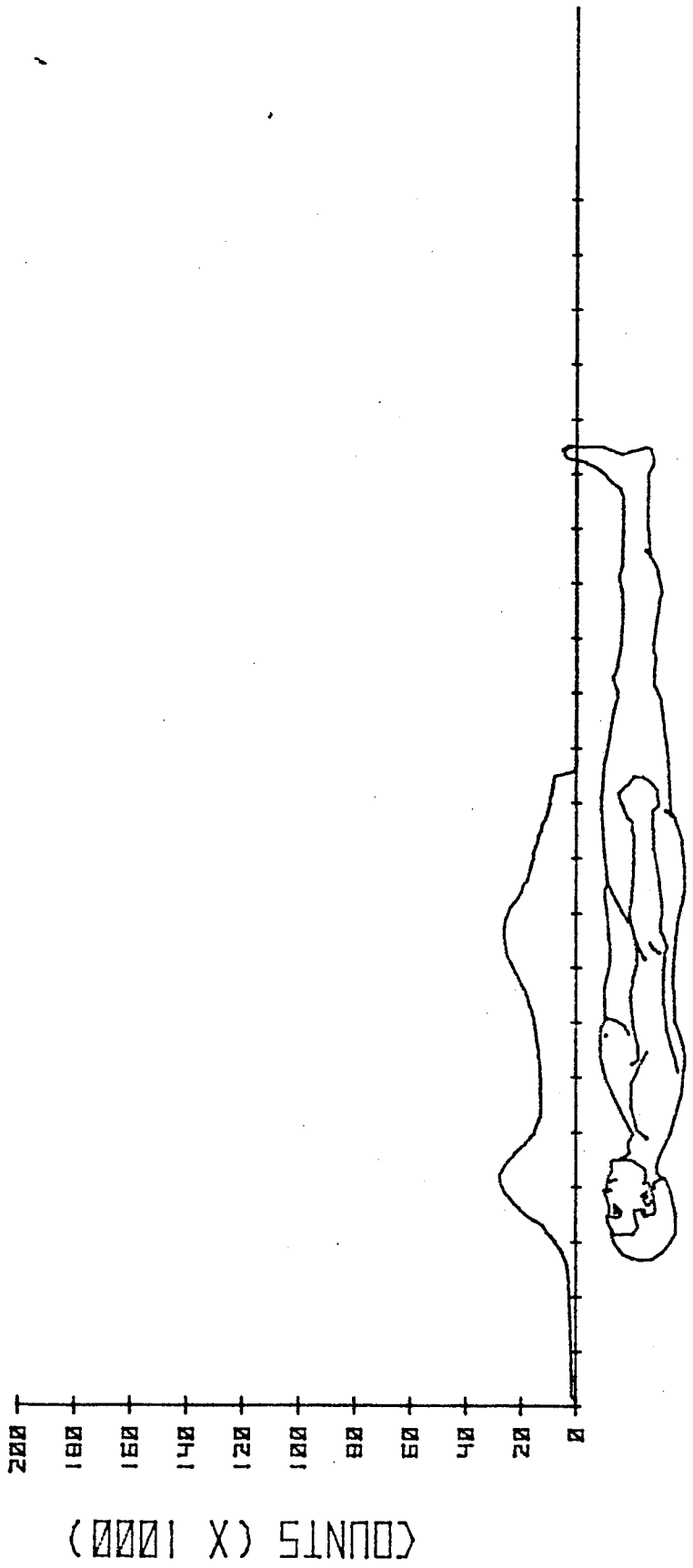


FIGURE 45 D

CSF PROFILE SCANNING

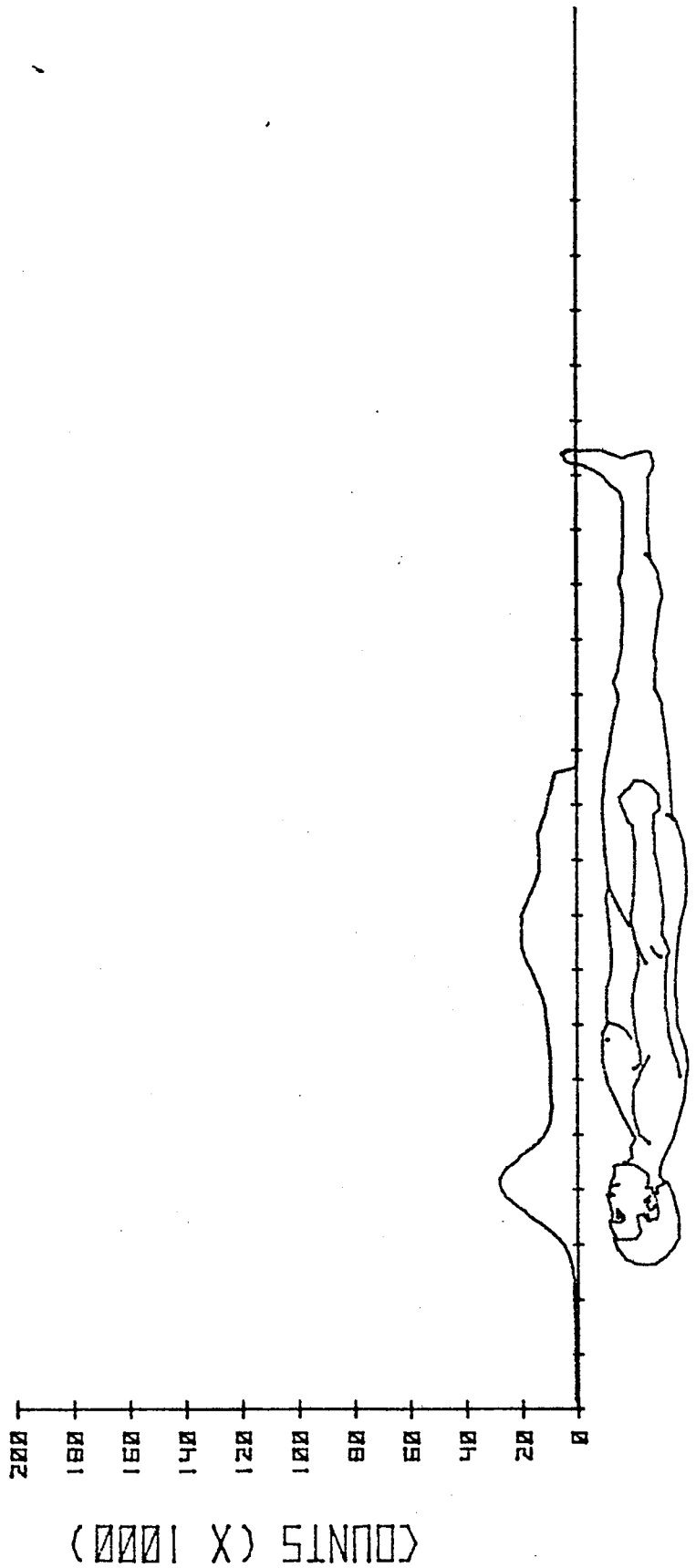


FIGURE 45 E

CSF PROFILE SCANNING