

Brain death (also known as brain stem death) is when a person on an artificial life support machine no longer has any brain functions. This means they will not regain consciousness or be able to breathe without support.

Cardiorespiratory death can be diagnosed after 5 min of observed asystole, long enough for irreversible damage to the brainstem to have occurred.

. **Brain death** is defined as the irreversible loss of all **functions** of the **brain**, including the **brainstem**. The three **essential** findings in **brain death** are coma, absence of **brainstem** reflexes, and apnoea

If someone's brain dead, the damage is irreversible and, according to UK law, the person has died.

It can be confusing to be told someone has brain death, **because their life support machine will keep their heart beating and their chest will still rise and fall with every breath from the ventilator.**

But they will not ever regain consciousness or start breathing on their own again. They have already died.

Historical Glimpse

- **Before 1960**, death was defined as the complete and irreversible cessation of spontaneous cardiac and respiratory functions.
- **1968**-“the definition of irreversible coma.” –
As apneic coma and absence of elicitable brainstem reflexes for a period of 24 h as confirmed by an electroencephalogram. [A definition of irreversible coma. Report of the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death.]

- **1971**, Mohandas and Chou emphasized the importance of irreversible loss of brainstem function in brain death (Minnesota criteria.) [Mohandas A, Chou SN. Brain death. A clinical and pathological study. J Neurosurg. 1971;35:211–8.[PubMed: 5570782]]

- ▶ □ **1976**–“irreversible loss of the capacity for consciousness combined with the irreversible loss of the capacity to breathe.” [Diagnosis of brain death. Statement issued by the honorary secretary of the conference of

- ▶ □ medical royal colleges and their Faculties in the united Kingdom on 11 October 1976. Br Med J. 1976;2:1187-8. [PMCID: PMC1689565] [PubMed: 990836]

It equated brainstem death with death of the whole person.



- **The brainstem death concept is based on arguments that asystole inevitably follows the diagnosis .**

- **“An individual who has sustained either**

- 1) irreversible cessation of circulatory and respiratory functions, or**
- 2) irreversible cessation of all functions of the entire brain, including the brain stem, is dead. (**

- **In 1995, American Academy of Neurology (AAN) published practice parameters for diagnosis of braindeath.** [Practice parameters for determining brain death in adults (summary statement). The Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 1995;45:1012–4. [PubMed: 7746374]]

- **The parameter emphasizes on irreversible coma (with a known cause), absence of brainstem reflexes and irreversible apnea.**
- **The diagnosis of brain death is clinical in nature and supplementary tests to be used in the presence of confounding factors.**

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- **Different countries have their own legal definition of death.**
 - **In India, there is no legal definition of death.**
 - **Section 46 of Indian Penal Code states, “the word death denotes death of a human being unless the contrary appears from the context**(Reddy KS. Ch. 6. 27th ed. 2008. The Essentials of Forensic Medicine and Toxicology; p. 119.)

Brainstem versus Whole Brain Death

- When the brain is dead, sustaining the other organs by artificial means is simply preserving a dead body and not keeping the individual alive.
 - Many countries (including US)- “whole” brain concept of brain death,
 - UK -brainstem formulation.
 - **In contrast to whole brain death,**
 - **the diagnosis of brainstem death does not require confirmation that all brain functions have ceased, rather that none of those functions that might persist should indicate any form of consciousness.**
- (A Code of Practice for the Diagnosis and Confirmation of Death. London: Academy of the Medical Royal Colleges; 2008)

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- Despite the apparent differences between practice in the UK and other parts of the world, **the clinical determination of whole brain and brainstem death is identical.**
 - The role of confirmatory investigations is different.
 - **Patients with preserved cortical electrical activity or intracranial blood flow can be considered to be dead in jurisdictions that utilize a brainstem approach, but not in those that apply a whole brain concept.**

- ▶ ☐ **The biological death of the whole human organism cannot (and is not required to) be proven during the diagnosis of brain death.** (Zamperetti

N, Bellomo R, Defanti CA, Latronico N. Irreversible apnoeic coma 35 years later. Towards a more rigorous definition of brain death? *Intensive Care Med* 2004;30(9):1715-1722)

- ☐ **When a threshold of irreversibility has been reached, and brainstem death is such a point, it is not necessary to wait for the death of the whole organism for the inevitable consequence of its biological death to be certain.** (Smith M. Brain death: time for

an international consensus. *Br J Anaesth* 2012;108(Suppl 1):i6-i9)

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- ▶ ☐ **Parts of the body may continue to show signs of biological activity after a diagnosis of irreversible cessation of brainstem function -withdrawal of all forms of supportive therapy.**

- ☐ It is for this reason that patients with such residual activity can no longer benefit from supportive treatment, and legal certification of their death is appropriate. (A Code of Practice for the Diagnosis and Confirmation of Death London: Academy of the Medical Royal Colleges; 2008)

Anatomical and Physiological Basis of Brainstem Death

- **The brainstem -midbrain, pons and medulla.**
- **Contains the nuclei of last ten cranial nerves and ascending and descending tracts.**
- The reticular formation (RF) is a complex network of nuclei and interconnecting fibers.
- The RAS, provides the anatomical and physiological basis for wakeful consciousness.

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- The medullary RF
 - heartbeat, breathing and circulation.
 - The pontine RF - coordination of acoustic, vestibular, respiratory and cardiovascular processes.
 - The midbrain RF - visuospatial orientation and eating behavior

Causes and pathophysiology of brain(stem) death

- **Brainstem is structurally and functionally very compact.**
- **Even small lesions can destroy vital cardiac and respiratory centers, disconnect cerebral cortex from brainstem, damage sensory fibers from higher centers of consciousness, perception and cognition.**

(Brainstem death: A comprehensive review in Indian perspective <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4166875/?report=printable> 5/13)

- **Damage to RF may lead to loss of cognition, persistent unconsciousness and coma.**

[Posner JB, Saper CB, Schiff ND, Plum F. Plum and Posner's Diagnosis of Stupor and Coma. 4th ed. New York: Oxford University press; 2007]

Region of brainstem	Function	Effect of lesion
Core of brainstem (reticular formation-reticular activating system)	Consciousness	Coma
Respiratory centers in pons and medulla	Respiratory drive	Apnea, loss of spontaneous breathing
Cardiac and vasomotor centers in medulla	Maintains BP, heart rate	Fluctuating BP, heart rate
All motor and sensory pathways (except vision and smell)	Mediates motor and sensory impulses	Bilateral paralysis, complete anesthesia
Cranial nerve nuclei	Mediates cranial nerve functions and reflexes	Bilateral loss of cranial nerve functions and reflexes

PRACTICAL (NON-EVIDENCE-BASED) GUIDANCE FOR DETERMINATION OF BRAIN DEATH(US)

- ☐ **I. The clinical evaluation (prerequisites)**
- ☐ **II. The clinical evaluation (neurologic assessment)**
- ☐ **III. Ancillary tests**
- ☐ **IV. Documentation**

The clinical evaluation (prerequisites)

□ A-Establish irreversible and proximate cause of coma.

Exclude the presence of

- CNS-depressant drug effect
- Neuromuscular blocking agents
- Severe electrolyte, acid-base, or endocrine disturbance

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- **B- Achieve normal core temperature.**
-warming blanket to maintain
temperature(>36°C)
 - **C. Achieve normal systolic blood pressure.**
 - **D. Perform neurologic examination**
(sufficient to pronounce brain death in most
US states).

The clinical evaluation (neurologic assessment)

A- Coma- Patients must lack all evidence of responsiveness.

-Eye opening/eye movement or motor response to noxious stimuli is absent.

B. Absence of brainstem reflexes-

- ☐ **Absence of pupillary response to a bright light is documented in both eyes.**
- ☐ **Usually the pupils are fixed in a midsize or dilated position (4–9 mm)**

- ❑ **Absence of ocular movements using oculoccephalic testing and oculovestibular reflex testing.**
- ❑ **Doll's eye mov.**
- ❑ **Caloric testing- The head is elevated to 30 degrees.**
- ❑ **Each external auditory canal is irrigated (1 ear at a time) with approximately 50 mL of ice water.**
- ❑ **Movement of the eyes should be absent during 1 minute of observation**

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- ☐ **Absence of corneal reflex.**
 - ☐ **Absence of facial muscle movement to a noxious stimulus.**
 - ☐ **Absence of the pharyngeal and tracheal reflexes.**

C. Apnea-

- ☐ **Absence of a breathing drive is tested with a CO₂ challenge.**
- ☐ **Documentation of an increase in PaCO₂ above normal levels is typical practice.**
- ☐ **Prerequisites:**
 - 1) Normotension,**
 - 2) Normothermia,**
 - 3) Euvolemia,**
 - 4) Eucapnia(paco₂ = 35–45 mm hg),**
 - 5) Absence of hypoxia, and**
 - 6) No prior evidence of CO₂ retention (I.E., Chronic obstructive pulmonary disease)**

Procedure-

- Adjust vasopressors to a systolic blood pressure ≥ 100 mm Hg.
- Preoxygenate for at least 10 minutes with 100% oxygen to a $\text{PaO}_2 \geq 200$ mm Hg.
- Reduce ventilation frequency to 10 BPM to eucapnia.
- Reduce PEEP to 5 cm H₂O.
- If pulse oximetry oxygen saturation remains 95%, obtain a baseline blood gas (PaO_2 , PaCO_2 , pH,

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- ❑ Disconnect the patient from the ventilator.
 - ❑ Preserve oxygenation (e.g., place an insufflation catheter through the endotracheal tube and close to the level of the carina and deliver 100% O₂ at 6 L/min).
 - ❑ Look closely for respiratory movements for 8–10 minutes.
 - ❑ Respiration is defined as abdominal or chest excursions and may include a brief gasp.

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- Abort if -SBP <90 mm Hg.
 - Oxygen saturation measured by pulse oximetry is < 85% for >30 seconds.
 - Retry procedure with T-piece, CPAP 10 cm H₂O, and 100% O₂ at 12 L/min.
 - If no respiratory drive is observed, repeat blood gas (PaO₂, PaCO₂, pH, bicarbonate, base excess) after approximately 8 minutes.

□ **The apnea test result is positive If –**

- respiratory movements are absent
- arterial PCO₂ is 60 mm Hg (or 20 mm Hg increase in arterial PCO₂ over a baseline normal arterial PCO₂).

- If the test is inconclusive it may be repeated for a longer period of time (10–15 minutes) after preoxygenation.

Ancillary tests

- ☐ **EEG**
- ☐ **Cerebralangiography**
- ☐ **Nuclear scan**
- ☐ **TCD**
- ☐ **CTA, and MRI/MRA**

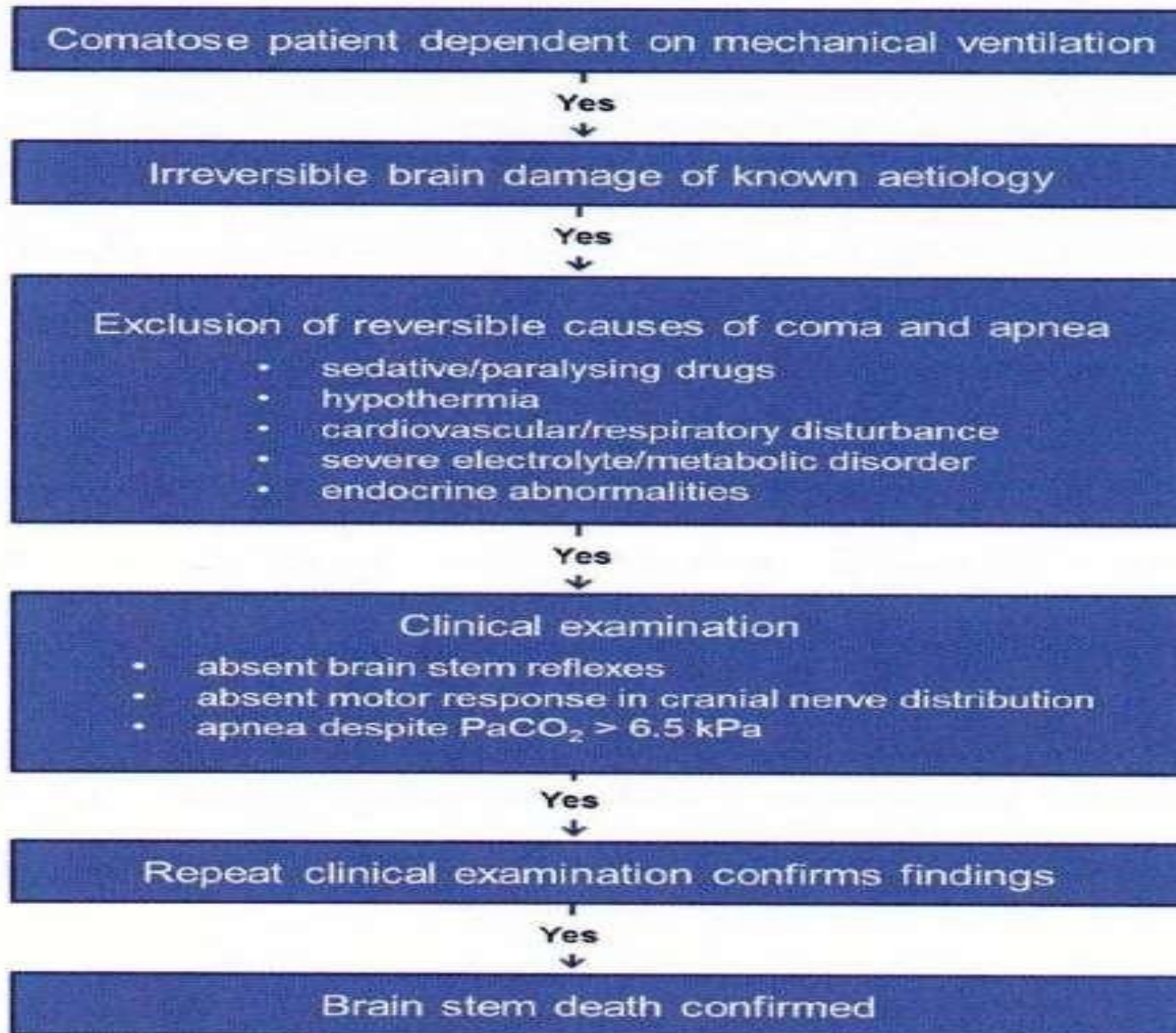
Documentation

- The time of brain death is documented in the medical records.
- Time of death is the time the arterial PCO₂ reached the target value.
- In patients with an aborted apnea test, the time of death is when the ancillary test has been officially interpreted.
- Federal and state law requires the physician to contact an organ procurement organization following determination of brain death.

UK

- The United Kingdom (UK) has incorporated a brainstem formulation into its brain death criteria since the first guidelines were published in 1976
- **Reason for confirming brain death**
 - **To allow the withdrawal of life-sustaining therapies, including mechanical ventilation irrespective of any subsequent potential for organ donation.**

Steps for diagnostic criteria of brainstem death in the UK



UK

- **The 2008 code of practice notes states that-“clinical tests must always be performed on two occasions.”**
- **“to remove the risk of observer error,”**
- **There is no specified time interval between the tests.**
- **The interval “need not be lengthy,” but determined for each patient individually.**

BRAIN DEATH IN CHILDREN

- **Most commonly occurs as a result of trauma and anoxic encephalopathy, Infections and cerebral neoplasms.**
- **United States guidelines for criteria for brain death in children were updated in 2011** [Nakagawa TA, Ashwal S, Mathur M, et al.

Clinical report—Guidelines for the determination of brain death in infants and children: an update of the 1987 task force recommendations. *Pediatrics* 2011; 128:e720.].

- **These are:**
- **The diagnosis of brain death cannot be made in preterm infants less**

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- Hypotension, hypothermia, and metabolic disturbances should be treated and corrected
 - Two examinations including apnea testing with each examination separated by an observation period are required.
 - Examinations should be performed by different attending physicians.

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- Apnea testing may be performed by the same physician.
 - An observation period
 - 24 hours for term newborns to 30 days
 - 12 hours for 30 days to 18 years.
 - Assessments in neonates and infants should be performed by pediatric specialists with critical care training.

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- Apnea testing is positive if arterial PaCO₂ ≥20mm Hg above the baseline and ≥60mm Hg with no respiratory effort during the testing period.
 - If the apnea test cannot be safely completed, an ancillary study should be performed.
 - Ancillary studies (EEG and radionuclide cerebral blood flow) are not required to establish brain death .



□ Ancillary studies may be used to assist in making the diagnosis of brain death:

- When components of the examination or apnea testing cannot be completed safely due to the underlying medical condition of the patient;
- If there is uncertainty about the results of the neurologic examination;
- If a medication effect may be present; or to reduce the inter examination observation period.

Indian Context and legal aspects

- Awareness about braindeath is extremely low in India.

[Wig N, Gupta P, Kailash S. Awareness of brain death and organ transplantation among select Indian population. J Assoc Physicians India. 2003;51:455–8. [PubMed: 12974425]

- Various aspects of braindeath, its importance for organ donation and its legality needs to be elaborated.
- India follows the UK concept of brainstem death.

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- Transplantation of Human Organs (THO) Act was passed by Indian parliament in 1994 which legalized the Brainstem death.
 - In 1995, THO rules were laid down which describe braindeath certification procedure.

[Government of India. Ministry of Law, Justice and Company Affairs (Legislative Department) New Delhi. The Transplantation of Human Organs Act, 1994. Central Act 42 of 1994./2011 [Last accessed on 2014 Jul 11].



□ Highlights of this act are:

1. Statutory sanction to the brain death concept.
2. Regulation of removal, storage and transplantation of human organs for therapeutic purposes.
3. Commercial dealings in human organs prevented

- The Act was initiated at the request of Maharashtra, Himachal Pradesh and Goa (who therefore adopted it by default) and was subsequently adopted by all states except Andhra Pradesh and Jammu & Kashmir. ([Laws of Organ Donation in India | Laws Made Easy](#) www.organindia.org/laws-made-easy)
- The state of Maharashtra has recently passed a resolution making it mandatory to declare and certify “braindeath” (Government of Maharashtra, Public Health Department, Government Resolution No. MAP2012/C.R.289/AROGYA6. Mumbai: Mantralaya; 2012. Sep 13)

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- The Government Resolution underlines the responsibilities of hospitals registered under THO Act 1994 & NTORCs.
 - It is mandatory now for these hospitals to certify and notify the brainstem death cases to Zonal Transplantation Coordination committee.

Diagnosis of Brain Stem Death In India

- **Brainstem death is medically and legally defined as the total and irreversible cessation of all brainstem functions.**

Why?

- **To discontinue artificial ventilation**
- **To ask legal consent for organ donation from relatives.**

Who should diagnose

Team of four medical experts including

- ☐ **Medical Administrator In charge of the hospital.**
- ☐ **Authorized Specialist**
- ☐ **Authorized Neurologist/NeuroSurgeon**
- ☐ **Medical Officer treating the patient.**

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- Amendments in the THO Act (2011) -a surgeon/physician and an anesthetist/intensivist, when approved neurosurgeon/ neurologist are not available.
 - **None of the doctor's who participate in diagnosis of brain death should have any interest in transplantation or organ removal from cadaver.**

Damage to cerebral cortex,
brainstem intact

Patient awake with cycles of eye
opening and closing (simulate sleep
and wakefulness) but unaware

Spontaneous respiration continues

Circulation stable

Not in need of life-sustaining
treatment, requires nutrition and
hydration only

Cranial nerve reflexes preserved

Recovery may occur though very
rare

Brainstem lesion

Damage to ascending reticular
activating system: Deep coma

Damage to respiratory centers:
Loss of spontaneous breathing
Fluctuating blood pressure
Patient need life-sustaining
treatment (ventillator, pressor
drugs)

Loss of cranial nerve functions
and reflexes

Irreversible and incompatible
with life

Organ donation

- In case the family wishes to donate the organs/ tissue, medications are usually continued until the time the patient is declared brain dead.
- These medications help to keep the blood pressure and heart rate under control and some reduces swelling in brain.
- Legality of brainstem death in India needs to be highlighted

Removal of life supporting system

- There is a line of demarcation when the artificial aids should be stopped so that the doctor may not get involved in the offence of culpable homicide and negligence.
- Thus he should first consult with other doctors.
- Clinician should make it clear to the relatives that ventilation is not being withdrawn to let the patient die but because continued ventilation is immaterial for a patient who is already dead except in case of organ transplant

Reluctance to accept brain death

- ☐ Lack of understanding the concept.
- ☐ Special emotional attachment to the dead person
- ☐ Loss of confidence in medical practice
- ☐ Ethical questions related to earlier organ transplant procedure
- ☐ Perceived insufficient participation of government and medical associations.

Criteria for Diagnosis of Brainstem Death in India

- ☐ **Patient should be deeply comatose (due to irreversible brain damage of known etiology); exclude reversible causes of coma**
- ☐ **Patient should be on a ventilator because of the cessation of spontaneous respiration. Exclude neuromuscular blocking agents as a cause of respiratory failure**

All brainstem reflexes should be absent:

- Pupillary light reflex Pupils are dilated, fixed and do not react to light
- Doll's head eye movements (oculocephalic reflex) (absence of conjugate deviation of eyes when head is fully rotated to one side)
- Corneal reflex is absent

- No motor response to stimulation within any cranial nerve distribution (e.g. no response to the supraorbital pressure)
- No Gag (Pharyngeal) reflex (to stimulation of pharynx)
- No Cough reflex (to suction catheter in the trachea)
- Vestibuloocular reflex (oculovestibular reflex/caloric testing) is absent (No eye movements after installation of 50 ml of ice cold water into each external acoustic meatus for 1 min)
- Apnea test -absence of respiratory movements and pCO₂ rise above threshold (>60 mmHg) .

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- All the prescribed tests are required to be repeated,
after minimum interval of 6 h, “to eliminate observer error” and persistence of the clinical state
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Role of investigations

- The diagnosis is based only on the clinical examination.
- A neurophysiological or imaging study neither form part of the diagnostic requirements nor are legally required.
- Confirmatory tests may however be carried out if the panel of doctors is in doubt or disagreement of the diagnosis.