Review Article

The Rationale of Carrying out Specific Investigations prior to Hyperbaric Oxygen Therapy

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Abstract

Hyperbaric oxygen therapy (HBOT) is gaining wider acceptance in present day clinical management for its various indications. HBOT has its associated risks and hazards. Selection of patients for HBOT poses significant challenges for physicians operating the hyperbaric chambers. The paper discusses a couple of interesting cases at IAM Bangalore. A review of the existing investigation protocol prior to exposure of a patient to hyperbaric chamber has been discussed. Based on experience gained over the past 10 years at thisInstitute and a detailed literature review, a standardised and mandatory pre-run investigation protocol for HBOT is recommended.

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Introduction

The history of hyperbaric oxygen therapy (HBOT) can be traced back to the 17th century, when Henshaw, a British clergyman, constructed the first pressurised chamber and called it "*chamber domicilium*" [1]. Paul Bert of France described in detail the central nervous system (CNS) toxicity on exposure to HBOT (the "Paul Bert effect") and carried out number of experiments in the field [2]. Dawn of the 20th century saw HBOT as a mode of therapy, initially for decompression sickness (DCS), and thereafter, for clinical conditions.

Presently, HBOT is increasingly being instituted across the globe for its various indications. Benefits of HBOT cover an entire spectrum of indications well explained by the administration of O_2 at pressures higher than 1 ATA. However, administration of HBOT has its associated risks and hazards. These risks and hazards have been studied over several years and are amply documented. These risks can be classified broadly into equipment failure related and those occurring due to problems in the human body. This paper discusses the risks involving the human body in the backdrop of two very typical cases encountered at the Department of Hyperbaric Medicine. These cases bring to light, challenges of a different kind for the hyperbaric physician with respect to the selection of patients and their follow up throughout the HBOT sessions.

Case No 1 – Otitic Barotrauma: 45 yr old male with chronic non healing ulcer of size 4.5 x 3cm on the dorsum of right foot persisting for duration of one year was referred for HBOT. He was evaluated for fitness to withstand HBOT and was found to be fit. He was given the standard protocol and he tolerated the same without any complaints on the first two days. On the third day he complained of mild ear pain during decent. The chamber descent was stopped, nasal decongestants were administered and he was made to equalize his middle ear pressure. The rate of ascent was reduced and he was brought out. He gave no history of any cough / cold or any upper respiratory infection prior to the run. Examination of ear revealed congestion

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of tympanic membrane with mild haemorrhage within the middle ear cavity which was suggestive of otitic barotrauma (Fig 1).

Case No 2 – Pulmonary Pathology: 55 yr old lady, a case of right skull base osteomyelitis and diabetes mellitus type-2, presented with complaints of earache for the past seven months with ear discharge. She also had complaints of right sided facial weakness with difficulty in swallowing and deviation of the tongue to the right. In view of progression of disease while being on antibiotics, she was referred for HBOT. X-Ray of the chest showed Hyper-inflated lungs (Fig 2). A pulmonary medicine opinion was sought for fitness for HBOT. Despite her inability to perform a satisfactory spirometry owing to facial weakness, a provisional fitness was given by the pulmonologist based on lack of respiratory symptoms, PEF & FEV_1 values of 245L/min and 0.90.

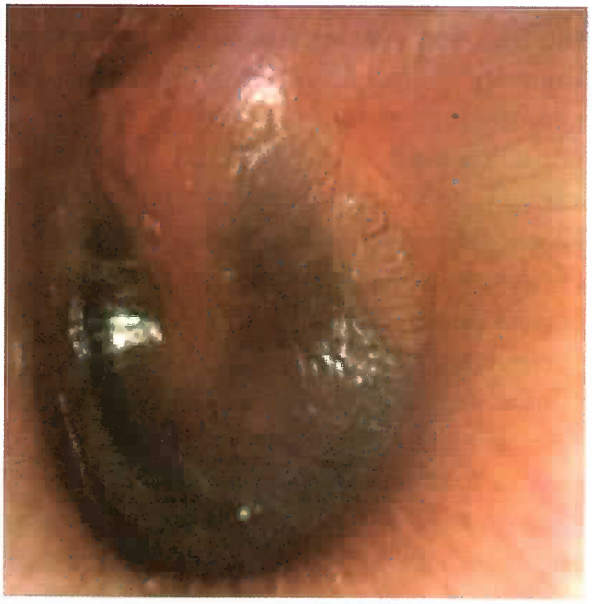

Fig 1: Grade II, injection plus slight haemorrhage within the substance of the tympanic membrane

However, with a high index of suspicion, a high-resolution computed tomography (HRCT) Scan of the chest for the patient was deemed necessary, to ensure her fitness for HBOT. HRCT revealed presence of centriacinar emphysema with mild tubular bronchiectatic changes and nodular

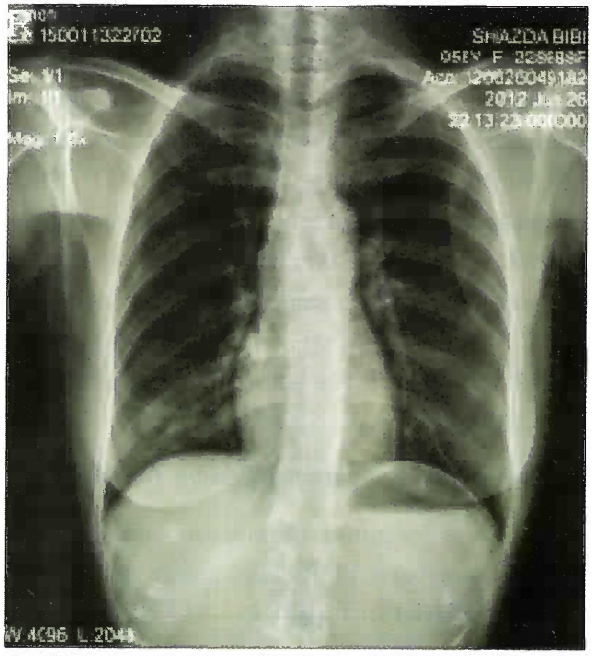

Fig 2: Plain Chest X Ray showing hyperinflation and no other abnormality.

acinar opacities in right lower lobe, suggestive of pneumonitis. Since exposure to hyperbaric chamber could have been detrimental, she was not accepted for HBOT in the chamber.

Such cases pose a dilemma to the hyperbaric physician about acceptance criteria for patients for HBOT in the hyperbaric chamber.

The risks that call for critical judgement by the hyperbaric physician are the ones that arise due to changes in ambient pressure i.e. **barotrauma**, in its various forms; and the ones due to increased oxygen concentration in the blood i.e. **oxygen toxicity**. To obviate these risks and hazards, it is imperative for all centres providing HBOT to evaluate every patient prior to exposing them to the chambers. The purpose of such evaluation is to identify any pre-existing condition that could aggravate and incapacitate the patient on exposure to changes in ambient pressure, or breathing 100% oxygen, as experienced inside a hyperbaric chamber.

Various institutions and hyperbaric societies differ on the guidelines for such evaluation. No clear

consensus is available on the investigations that need to be mandatorily carried out during the pre-exposure evaluations. Hence, there is a need to formulate such a guideline to streamline and justify screening procedures prior to HBOT. Such evaluation should include beside clinical assessment, specific laboratory tests and specialized procedures. Based on experience gained over the years at the HBOT chamber at this Institute, the recommendations for screening procedure are discussed.

Concerns for Accepting a Patient for HBOT

Two major groups of problems cause concern among hyperbaric physicians before accepting a patient for HBOT:

(a) Barotrauma related: Otitic, Pulmonary, Sinus, Gastrointestinal and dental.

(b) Oxygen Toxicity related: Fever (decreased seizure threshold), side effects of increased Oxygen Free radicals (OFC).

Clinical Examination of Patient Referred for HBOT runs

The clinical examination of the patient should lay special emphasis on the issues that could cause problems in the chambers as brought out. Hence the detailed systemic examination is warranted to look for relevant problems.

Investigations

As discussed earlier; two major groups of problems cause concern among hyperbaric physicians before accepting a patient for HBOT, thus, for sake of convenience the problem may be approached by:-

(a) Investigations to prevent the complications due to the barotraumas

(b) Investigations to prevent the complications due to oxygen toxicity

Investigations to Prevent the Complications Due to the Barotrauma

Otitic Barotrauma

The barotrauma due to HBOT may affect the ears, sinuses, lungs, teeth and rarely the intestines. Warning signs of **middle ear barotrauma,** with pain being the most conspicuous of these, usually develops within the first 2 to 3 m of descent [3]. Patients with Eustachian tube (ET) dysfunction due to a common cold or any other cause are most susceptible. Occasionally a blocked ET may be severe enough to create a pressure difference of 45 mm Hg or more with the ambient, leading to asymmetrical stimulation of the vestibular apparatus, thereby causing the Lundgren syndrome or the alternobaric vertigo of ascent [4]. Other extremely rare forms in the middle ear include alternobaric facial palsy and surgical emphysema. The **inner ear barotrauma** is extremely rare in HBOT, and present rarely as vertigo and hearing loss. Susceptible patients should be evaluated for evidence of nystagmus, sensory-neural hearing loss (SNHL) and sensory ataxia in the form of Romberg's sign, followed up by a complete neurological evaluation. HBOT should be discontinued till complete clinical and objective recovery. In case HBOT cannot be avoided, or the patient develops problems during the course of therapy, a myringotomy may be considered to prevent further damages [5]. It is important and interesting here to keep in mind the fact, that the clinical features of inner ear barotrauma and decompression sickness involving the inner ear are difficult to distinguish from each other. **External ear barotrauma** is common in diving but extremely rare during HBOT. Intervening wax in the external auditory meatus has been defined as the culprit. Hence, it is always advisable to ensure that the external ear canal is devoid of wax before HBOT is initiated.

Sinus Barotrauma

The predisposing factors responsible for **sinus barotrauma** include nasal polyps, allergic conditions, foreign bodies and structural deformities

of the nose and adnexa. Sinus barotrauma can occur during ascent as well as descent, with the frontal and maxillary sinuses being the most commonly involved. Former being twice more frequent than during descent [6].In the presence of a sinus blockade during descent there is hydrostatic pressure gradient into the gas space from the surrounding mucus membranesleading to vasodilatation, rupture and haemorrhage, and eventually haematoma formation in the sinus space [7]. Occasionally a branch of the sensory division of the fifth cranial nerve may get involved leading to paraesthesia of the face [8]. Meningitis and loss of vision are extremely rare, but have been reported [9]. Hence, a thorough assessment of the paranasal sinuses must be included in the pre-exposure evaluation of patients.

Pulmonary Barotrauma

The complications associated with pulmonary barotrauma are much more serious. During decompression, the gases in the alveoli expand; this extra volume usually escapes as a part of the routine dynamics of normal ventilation. However, if there is an underlying obstructive airway disorder, the intra-pulmonary pressure can rise up to the threshold where barotrauma occurs. The consequences can be a collection of gas within the lung parenchyma (interstitial emphysema), entry of gas into the pleural, pericardial, peritoneal or mediastinal space (pneumothorax, pneumopericardium, pneumoperitoneum and pneumomediastinum, respectively), or into the subcutaneous tissue of the chest and neck (surgical emphysema) [10]. As much as 10% of pulmonary barotrauma cases have been found to be accompanied with a pneumothorax [11]. The pulmonary conditions that can give rise to barotrauma are: a past history of spontaneous pneumothorax, chronic obstructive pulmonary disease i.e. COPD, comprising of chronic bronchitis and emphysema (especially bullous emphysema), pulmonary cysts, sub-pleural blebs, blunt trauma to the chest, acute lower respiratory tract infections, pulmonary fibrosis and atelectasis. COPDs notably have been documented as being notorious in causing alveolar over-expansion proximal to the obstruction, thereby leading to entry of gas into the pulmonary capillaries, eventually causing a gas embolism, which can be a serious affair [12].

An X-ray of the chest is mandatory to rule out many of these conditions. Spirometry must be done to exclude any underlying obstructive airway disease. In case spirometry is not possible due to any reason, or in case there is a high degree of suspicion due to history and clinical examination, a high-resolution computed tomography (HRCT) of the chest must be done as an alternative. X-ray chest and spirometry, however, must be performed in patients despite normal pulmonary status clinically.

Barodontalgia

This refers to pain in the teeth or teeth cavity during pressure changes. This can be extremely painful and HBOT runs may get interrupted midway. It is always advisable to rule out underlying dental pathologies which are known to cause the condition, like a dental cyst or a peri-apical infection. Recent dental fillings within past 48 hours also may cause barodontalgia due to expansion of trapped gases. All such conditions need to be evaluated and treated before subjecting the patient into the chambers. Hence, an opinion of a dental surgeon must be sought under such circumstances.

Gastrointestinal Barotrauma

Occurrence of GI Barotrauma is rare. However, it would be prudent to exercise caution while recommending cases of GI surgery for HBOT, because cases of rupture of the stomach followed by acute peritonitis and pneumoperitoneum have been reported in literature [13, 14].

Ocular Barotrauma

There are reported incidents of ocular barotrauma because of entry of gas into the anterior chamber or vitreous body of the eye manifesting

as retinal, uveal or vitreous haemorrhage, and possibly with a partial collapse of the globe [15]. An opinion of the ophthalmologist must be obtained before subjecting such post-operative patients to HBOT.

Recommended Investigations to prevent the complications Due to the Barotrauma

The following routine and mandatory investigations are hence necessary to prevent barotrauma to patients subjected to HBOT:

(a) Chest X-ray

(b) Spirometry

(c) High-resolution computed tomography of the chest (if required)

(d) A complete otorhinolaryngological examination

Spirometry findings suggestive of an obstructive airway disease must be handled with extreme caution. An out of proportion reduction in the forced expiratory volume at the end of the first second (FEV_1) as compared to the forced vital capacity (FVC) is indicative of obstructive airway disease. The percentage of the ratio of FEV_1/FVC (FEV_1%) indicates the severity of the condition. An $FEV_1\% > 70$ indicates mild obstruction. Values ranging from 60-69 signify moderate, 50-59 moderately severe, 35-49 severe and < 35 is very severe disease [16]. However, patients with mild obstruction (e.g. borderline chronic obstructive pulmonary disease) may be accepted provided there are no other predisposing factors for pulmonary barotrauma. A positive reversibility test with inhaled bronchodilators (performed after the initial spirometry had shown obstruction) may be accepted for HBOT. In such a case, the patient should be administered the bronchodilator prior to entering the chamber [17]. Cases with severity grades higher than mild obstruction must be treated before accepting them for HBOT. Patients with no history, symptoms, clinical or radiographic evidence of pulmonary disorders may still be detected to have an obstructive disorder of the airways on spirometry [18], and hence spirometry must be performed routinely for all patients prior to HBOT.

In patients who are unable to perform spirometryor if X-ray of the chest is inconclusive, or if the history and clinical examination is suggestive of an underlying pre-disposing factor for barotrauma, then an HRCT needs to be undertaken. X-ray and HRCT evidences of pulmonary pathology that may predispose to barotrauma are contraindications for HBOT.

Patients detected to have ear or paranasal sinus disorders likely to progress into barotrauma on exposure to HBOT, need to be treated for their conditions, and HBOT should be administered only when the diseases have been corrected.

Special cases like a recent surgery of the gastro-intestinal tract or the eye, needs to be opined by the concerned specialist on a case-to-case basis, before being accepted for HBOT. Patients with dental problems need to be evaluated by a dental surgeon prior to the therapy. Despite these measures barotrauma during HBOT may still occur, and we recommend that the unit involved in administering HBOT must be trained and made to be prepared adequately to suspect, diagnose and manage such an eventuality on time, as and when it occurs.

Investigations to Prevent the Complications Due to Oxygen Toxicity

Although the toxic effects of oxygen have been long described primarily as the Paul Bert, Lorraine Smith and several other effects also need to be considered. All tissues in the body are vulnerable to oxygen toxicity, and care must be exercised to prevent them.

Molecular oxygen, by itself, is a benign gas. However, when it undergoes a reduction reaction by sequential addition of electrons, it forms the highly reactive oxygen free radicals (OFRs), with

the electron transport mechanisms of the mitochondria, and, to a lesser extent, the electron transport system of the endoplasmic reticulum being the chief sources for their production. The body responds to this assault by enzymatic (catalase, superoxide dismutase, glutathione peroxidase etc) and non-enzymatic (vitamins C and E) methods [19, 20, 21]. The role of nitric oxide as a potent modulator to the OFR insult is convincingly getting established [22].

Pulmonary Oxygen Toxicity – Role of Spirometry

The earliest change occurring in the lungs due to oxygen toxicity is an acute and progressive reduction in the vital capacity. The subsequent effects include absorption atelectasis, pulmonary oedema and inflammation. All of these combine to produce an increase in alveolar surface tension, causing further reduction in the vital capacity, reductions in lung compliance, tidal volume and inspiratory capacity and increase in residual volume and functional residual capacity [22, 23, 24, 25]. Prolonged exposures to oxygen in toxic levels have also shown to cause significant airway obstruction, the primary cause of which may be attributed to pulmonary oedema [22, 25].

The spirometry performed prior to exposing the patient to HBOT must therefore rule out the possibility of an existing obstructive pathology, as it can worsen further due to oxygen toxicity. In addition spirometry must be performed as follow up at 10 day intervals in patients showing clinical features suggestive of pulmonary toxicity.

Haemoglobin and Erythrocytes

Haemoglobin (Hb) needs to be estimated prior to exposure to HBOT. Oxygen toxicity can cause haemolysis. An important response of red blood cells (RBCs) to oxygen radicals is rapid degradation of damaged cell proteins. Increased proteolysis seems to occur independently of membrane damage and to be a more sensitive indicator of cell exposure to oxygen radicals than is lipid peroxidation [26]. Research shows thatNeutrophils promote OFR mediated haemolysis [27]. Thus, patients with existing haemolytic conditions may be at a higher risk from the effects of oxygen toxicity. As a routine screening method, it is not reasonable to perform investigations to detect or rule out haemolysis. Hence, along with the clinical sign of pallor, Hb estimation can be performed instead, the value of which will, in case there is an underlying haemolytic condition, be lower than its normal.

Blood Glucose and Glycosylated Hb Estimation

Effect of HBOT on diabetics is multipronged. Insulin sensitivity of cells increases in presence of hyperbaric oxygen. This would mandate a reduction in the insulin dosage of patients prior to the exposure [28]. In addition, uncontrolled diabetes and its long term complications are associated with oxidative reactions, particularly those which are catalysed by decompartmentalised transition metals [29]. Cytokines mediated destruction of human pancreatic islet beta cell by inducing oxygen free radicals, lipid peroxidation and aldehyde production has been documented [30]. Hence, blood glucose, fasting and post prandial and Glycosylated Hb (HbA_1C) should be measured while exposing a patient to HBOT.

Total and Differential Leucocyte Counts

Total leucocyte count (TLC) and differential leucocyte count (DLC) are routinely done at almost all HBOT centres prior to exposure. Fever has been considered as a contraindication to HBOT, as it is a risk factor for precipitation of seizures and other manifestations of oxygen toxicity of the central nervous system. In the absence of a raised body temperature during clinical examination, fever, especially the intermittent type, may go undetected. Hence it is always advisable to perform basic laboratory tests like DLC and TLC, which will provide some indication towards an underlying infective state.

Urine examination – Routine and Microscopic

Urine examination is yet again resorted to by almost all HBOT centres as a screening tool. It not only provides information about an underlying infection of the urinary tract, but also about the blood glucose and glomerular filtration. Many diabetic patients deemed to benefit from HBOT may have some degree of existing nephropathy. Where diabetic ulcers may heal on exposure to HBOT, OFRs can further augment nephropathy. Hence, patients detected to have sugar and albumin on urinalysis, must be treated for the same before HBOT.

Electrocardiogram (ECG)

An ECG is to be recorded prior to exposure to HBOT. OFRs are an important cause for reperfusion induced arrhythmias [31]. OFRs also appear to be important in the genesis of relatively mild and sub-lethal forms of myocellular damage [32]. The bradycardia caused immediately after diving (the "diving reflex") is not a matter of concern in an HBOT set up. Cases of arrhythmias must therefore be considered with due caution, and an opinion of a Cardiologist may be solicited.

Lipid Profile

Cholesterol is a known factor that accelerates the process of atherosclerosis. OFRs have been implicated in the genesis and maintenance of cholesterol-induced atherosclerosis [33, 34]. The low density lipoprotein (LDL) is known to undergo oxidative modifications on exposure to OFRs. This causes its uncontrolled uptake by macrophages. It may also contribute to the formation of foam cells in the developing atherosclerotic lesions in the body. There is report that the superoxide radical is responsible for such modifications [35]. Hence it is important to take a note of the LDL levels too, apart from cholesterol, while asking for a lipid profile for patients scheduled for HBOT.

Certain Areas that Need to be Considered Individually

(a) HBOT and Transcutaneous Oxymetry ($TcPO_2$): $TcPO_2$ has been suggested to predict the outcome of diabetic patients undergoing HBOT. Baseline sea-level air $TcPO_2$ has been shown to identify the degree of tissue hypoxia but has little statistical relationship with outcome prediction because some patients healed after HBOT despite very low pre-hyperbaric $TcPO_2$ values. Breathing oxygen at sea level has proved to be unreliable for predicting failure, but 68% reliable for predicting success after hyperbaric oxygen therapy. $TcPO_2$ measured in-chamber has been proven to be the best single discriminator between success and failure of HBOT using a cut-off score of 200 mm Hg. The reliability of in-chamber $TcPO_2$ as an isolated measure was 74% with a positive predictive value of 58%. A sea-level air $TcPO_2$ less than 15 mm Hg combined with an in-chamber $TcPO_2$ below 400 mm Hg has been found to predict failure of HBOT with a reliability of 75.8% and a positive predictive value of 73.3% [36]. One study has claimed to predictably identify patients who are likely to benefit from HBOT using $TcPO_2$ at the time of initial evaluation. An increase of tissue O_2 tension of e"10 torr when breathing pure oxygen suggests that the patients may benefit from HBOT. Those patients with an increase of <10 torr are unlikely to receive benefit from this treatment modality [37]. Another finding describes that when the initial distal $TcPO_2$ was below 100 mm Hg, all patients showed either no improvement or aggravation, and when the value was higher than 100 mm Hg, wound healing was achieved in all patients [38].Therefore, measurement of $TcPO_2$ does seem to have a role to play in HBOT for patients with diabetic ulcers in particular, but it is not, per se, one of the investigations that may be used for screening routine patients or to identify the ones that are prone to develop complications due to hyperbaria or oxygen toxicity.

(b) HBOT in patients with certain implants: It is a frequent feature to provide HBOT to patients who have undergone oral and

maxillofacial surgeries and have subsequently been rehabilitated with implants. Often such patients also undergo concomitant radiotherapy. Radiotherapy interferes with bone healing whereas HBOT increases the potential for bone regeneration [39]. Also, HBOT, either before or after implantation, increases the bone-to-implant contact in diabetic rats as compared to normal rats [40]. HBOT has also been found to improve survival rate in implants after radiotherapy [41].

However, a Cochrane review of randomised clinical trials was unable to find out any strong evidence to either support or refute the use of HBOT for improving implant outcome in patients who have received radiotherapy [42].

(c) HBOT in patients on certain medications: Cisplatin is a common drug used in various Oncological conditions. Nephrotoxicity induced by cisplatin has been shown to be preventable with once-daily HBOT and aggravated with twice-daily HBOT [43]. HBOT is protective against the ototoxic effects of cisplatin [44].

Studies in rats have shown that the drug disulfiram potentiates oxygen toxicity by getting reduced to diethyldithiocarbamate, which in turn acts by inhibiting superoxide dismutase [45].

Conclusion

The complications due to either barotrauma or oxygen toxicity may complicate the existing clinical picture of a patient. However, by observing the above guidelines, many of them may be prevented, thereby allowing for a better outcome during and at the end of the course of HBOT. Despite the extensive list of investigations, a proper and meticulous history and clinical examination, with special attention to those that have been discussed above, are the mainstay of a successful and uneventful HBOT run for any disorder for which the therapy is indicated.

Recommendations

The authors hence recommend the following screening method as mandatory for patients undergoing HBOT:

(a) **Complete Clinical Examination.**

(b) **Investigations:** Complete Blood Count, Urinalysis, Blood Biochemistry to include RFT, lipids profile, Sugar F & PP, GlycosalatedHb, ECG, Chest roentgenogram, Spirometry.

(c) **Additional Investigations if Required:** HRCT chest (if individual unable to perform spirometry), Reticulocyte count & Peripheral blood smear (to rule out haemolyticanaemia).

(d) **Follow up Investigations During HBOT runs:** Hb estimation and Spirometry at 10 day interval in suspected cases.

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