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Editorial

Tropical (pulmonary) eosinophilia, or **TPE**, is characterized by coughing, asthmatic attacks, and an enlarged spleen, and is caused by *Wuchereria bancrofti*, a filarial infection. It occurs most frequently in India and Southeast Asia. Tropical eosinophilia is considered a manifestation of a species of microfilaria. The filariasis is transmitted by a vector, specifically the bite of a *Culex*, *Anopheles*, or *Aedes* mosquito, and the microfilariae (larvae) take up residence in the lung tissue, hindering respiration and causing chest pain as the disease progresses. This disease can be confused with tuberculosis, asthma, or coughs related to roundworms.

Tropical pulmonary eosinophilia is a rare, but well recognised, syndrome characterised by pulmonary interstitial infiltrates and marked peripheral eosinophilia. This condition is more widely recognised and promptly diagnosed in filariasis-endemic regions, such as the Indian subcontinent, Africa, Asia and South America. In nonendemic countries, patients are commonly thought to have bronchial asthma. Chronic symptoms may delay the diagnosis by up to five years. Early recognition and treatment with the antifilarial drug, diethylcarbamazine, is important, as delay before treatment may lead to progressive interstitial fibrosis and irreversible impairment.

The condition of marked eosinophilia with pulmonary involvement was first termed tropical pulmonary eosinophilia in 1950. The syndrome is caused by a distinct hypersensitive immunological reaction to microfilariae of *W. bancrofti* and *Brugia malayi*. However, only a small percentage (< 0.5%) of the 130 million people globally who are infected with filariasis apparently develop this reaction. The clearance of rapidly opsonised microfilariae from the bloodstream results in a hypersensitive immunological process and abnormal recruitment of eosinophils, as reflected by extremely high IgE levels of over 1000 kU/L. The typical patient is a young adult man from the Indian subcontinent. The **DISEASE DIAGNOSIS** section talks about **Pulmonary Eosinophilia** in general, not just Tropical one (though it is more often seen in the sub-continent).

INTERPRETATION segment outlines Turbidimetry and compares it with Nephelometry while **TROUBLESHOOTING** portion troubleshoots problems while performing Turbidimetric analyses.

BOUQUET, as always, makes its presence felt this time too!



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DISEASE DIAGNOSIS

Pulmonary Eosinophilia

Background

Pulmonary diseases associated with tissue and/or blood eosinophilia are a heterogeneous group of disorders. Various nosologies have been offered, but this article classifies these syndromes as extrinsic or intrinsic in origin. Some syndromes overlap, but this approach is convenient from the diagnostic standpoint. **Inhaled or ingested extrinsic factors, including medications and infectious agents** (eg, parasites, fungi, mycobacteria), may trigger an eosinophilic immune response. This may be mild and self-limited, as in Loeffler syndrome. **Intrinsic pulmonary eosinophilic syndromes are generally idiopathic in nature.** They include a diverse group of autoimmune and idiopathic syndromes ranging from blood dyscrasias to vasculitis. This group includes chronic eosinophilic pneumonia (CEP), **hypereosinophilic syndrome (HES)**, **eosinophilic granulomatosis with polyangiitis (EGPA)**, formerly called Churg-Strauss syndrome), and **eosinophilic granuloma (EG)**; pulmonary histiocytosis X or Langerhans cell granulomatosis). **Eosinophilia and pulmonary infiltrates have been reported in patients with AIDS**, lymphoma, a variety of inflammatory lung diseases, and collagen vascular diseases (see **Etiology**). **Asthma may manifest with marked eosinophilia**, with or without infiltrates. **The airway inflammation of chronic obstructive pulmonary disease (COPD) is largely neutrophilic**, but 20-40% of induced sputum samples from individuals with stable COPD have eosinophilic airway inflammation, associated with elevated levels of sputum interleukin (IL)-5. **Nonasthmatic eosinophilic bronchitis (NAEB) is characterized by cough for at least 2 months**, a sputum eosinophil count greater than 3%, and no evidence of airway obstruction. Affected patients are usually middle-aged, are nonatopic, and have no history of smoking. Activation and eosinophilic infiltration of the superficial airway occurs, rather than of airway smooth muscle. **Eosinophilia may often be seen in the bronchoalveolar lavage fluid** in patients with desquamative interstitial pneumonitis, ciliastasis, and influence mucus production. Tissue injury may also be caused by the release of reactive oxygen species. The release of platelet-activating factor and leukotrienes contributes to bronchospasm. In some syndromes, such as tropical pulmonary eosinophilia (TPE) and chronic eosinophilic pneumonia (CEP), interstitial fibrosis may result from chronic inflammation. Commonly, lung parenchyma is affected, but in certain extrinsic and intrinsic syndromes, other organs may be affected.

Extrinsic eosinophilic syndromes

Loeffler syndrome

The pathogenesis of Loeffler syndrome is unknown but presumably reflects a hypersensitivity response to an ingested or inhaled antigen from food, medication, or an infectious agent. Many of the original cases of Loeffler syndrome were thought to be related to *Ascaris* infection.

DRESS syndrome

The Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a severe drug hypersensitivity reaction, notable for skin rash, fever, lymphadenopathy, and involvement of various tissues, such as hepatitis, pneumonitis, or myositis. Numerous drugs, such as sulfonamides, phenobarbital, sulfasalazine, carbamazepine, and phenytoin, have been reported to cause the DRESS syndrome. Among antimicrobials, DRESS syndrome can be caused by vancomycin,

sulfonamides, tetracyclines, β -lactams, and flouroquinolones.

Parasitic infections

Migrating parasites traversing the lungs may cause bronchospasm, dyspnea, and pulmonary infiltrates. Embolization of microfilariae or eggs, which degenerate and expose antigens to the local immune system, leads to granuloma formation. Local elaboration of chemokines and cytokines plays a role in T-cell recruitment and granuloma formation. Persistent inflammation may lead to parenchymal necrosis and fibrosis.

Schistosomiasis

The most common pulmonary complication is pulmonary hypertension from chronic embolization of ova.

Tropical pulmonay eosinophilia (TPE)

These patients have marked immune responses to filariae, while other individuals infected with *Wuchereria bancrofti* or *Brugia malayi* have suppressed parasite-specific immune responses. Patients with TPE rarely have signs of lymphatic filariasis. Elevated immunoglobulin E (IgE) and immunoglobulin G (IgG) levels in patients with TPE reflect polyclonal B-cell activation. The *Brugia malayi* larval gamma-glutamyl transpeptidase has similarities with that found on human pulmonary epithelium, suggesting a pathogenetic role for this transpeptidase.

Strongyloidiasis

Patients who are immunocompromised, including those recently prescribed systemic corticosteroids, may develop hyperinfection syndrome, in which large numbers of recently released larvae burrow through the intestine and migrate to the lungs. Sepsis and respiratory failure may result from accompanying enteric bacteremia.

Fungal causes

Allergic bronchopulmonary aspergillosis (ABPA) is an immunologic response to *Aspergillus* antigens in the airways of individuals with obstructive lung disease. Both IgE-mediated and immune complex-mediated hypersensitivity responses are active. Chemokines recruit CD4 T helper 2 antigen-specific cells to the lung. The inflammatory responses lead to airway reactivity, mucus hypersecretion, epithelial damage, bronchiectasis, eosinophilic pneumonia, and parenchymal injury and fibrosis. *Aspergillus* proteases likely also contribute to airway damage. Other fungi have also been found to cause a similar disorder, prompting some to suggest renaming this disorder allergic bronchopulmonary mycosis.

Bronchocentric granulomatosis

This idiopathic condition, in which the mucosal epithelium is supplanted by epithelioid histiocytes and then by granuloma formation, is often associated with ABPA.

Acute eosinophilic pneumonia (AEP)

Increasing evidence suggests an association with inhaled exposures and, in some cases, infections. An association between AEP and new-onset cigarette smoking has been reported. Many patients have engaged in dusty outdoor activities, suggesting a hypersensitivity response to inhaled antigens. AEP has also been reported following allogeneic hematopoietic stem cell transplantation, coexisting with graft versus host disease. Eosinophilic alveolitis may be extensive, and profound hypoxemia with respiratory failure may result.

Intrinsic eosinophilic syndromes

Chronic eosinophilic pneumonia (CEP)

The pathogenesis is unknown. CEP may occur in isolation and/or in

association with polyarteritis nodosa, rheumatoid arthritis, scleroderma, ulcerative colitis, breast carcinoma, and histiocytic lymphoma. Most patients have evidence of asthma and atopy. Although not a prominent feature, microgranulomata are occasionally seen on biopsy specimens, suggesting that an antigen-driven, T-cell-mediated process is active.

Hyper eosinophilic syndrome (HES)

HES is a myeloproliferative disorder (MPD). Some patients display overproduction of chemokines, proeosinophilic factors, including interleukin (IL)-4 and IL-5 by clonally expanded differentiation clusters 3 and 4 (CD3⁺ and CD4⁺) and Th2-like lymphocytes. These patients also have evidence of polyclonal hypergammaglobulinemia. Other patients have increased numbers of stem cells committed to the eosinophil lineage. Pulmonary involvement is manifested as wheezing, coughing, pulmonary edema, and pleural effusions. Pulmonary emboli result from a hypercoagulable state. Multiple organ systems may be affected, resulting in gastrointestinal tract dysfunction, skeletal muscle weakness (which may lead to respiratory failure), endomyocardial fibrosis, myocarditis, congestive heart failure, and/or valvular disease.

Eosinophilic granulomatosis with polyangiitis (EGPA)

The pathogenesis is unknown. Inhaled or ingested antigens have been proposed as causative agents in susceptible individuals. The frequency of T regulatory cells that produce IL-10 and transforming growth factor (TGF)-beta (Treg1) has been reported to be decreased in active EGPA, in comparison with asthma, EP, and inactive EGPA. Reports linking the syndrome with the leukotriene inhibitors zafirlukast and montelukast in the setting of steroid withdrawal suggest these agents unmask preexisting EGPA rather than suggesting that EGPA is a direct causal effect of these agents. Similarly, omalizumab treatment allowing weaning of corticosteroids or their initiation has been reported to unmask EGPA. Vasculitis may affect the sinuses, central and peripheral nervous systems, gastrointestinal tract, kidneys, and heart.

Eosinophilic granuloma (EG)

The cause is unknown, but the reactive histiocytic proliferation suggests a reactive process, perhaps to an unknown antigen. Patients develop reticulonodular interstitial and cystic disease. EG is strongly associated with cigarette smoking. This may affect the lungs, bones (including the skull, resulting in diabetes insipidus), and other organs. Tissue and peripheral eosinophilia are generally not prominent features of this condition.

Etiology

Extrinsic syndromes and the eosinophilic immune response can be triggered by inhaled or ingested substances, including medications, drugs (eg, cocaine), food (eg, contaminated cooking oil), dietary supplements (eg, L-tryptophan), and infections (eg, parasites, fungi, mycobacteria).

Medications that have been implicated include the following:

- Antibiotics (among the most common offending agents)
- Nonsteroidal anti-inflammatory drugs (among the most common offending agents)
- Antidepressants
- Contraceptives
- Antihypertensives
- Leukotriene inhibitors
- Anticonvulsants

- L-tryptophan
- Cocaine

Parasitic infections due to nematodes, filariae, and helminths may cause pulmonary infiltrates and eosinophilia. Such infections include strongyloidiasis, ascariasis, paragonimiasis, schistosomiasis, dirofilariasis, ancylostomiasis, trichomoniasis, clonorchiasis, and visceral larva migrans. **Fungal processes, such as ABPA and coccidioidomycosis,** may also cause pulmonary eosinophilia. Bronchocentric granulomatosis is most commonly related to *Aspergillus* infection. Other infections may include tuberculosis and *Pneumocystis carinii* pneumonia. **Although AEP was initially described as an idiopathic acute respiratory illness,** multiple identifiable causes have been identified, including smoking, environmental/occupational inhalational exposures, use of recreational inhalant drugs, and connective tissue diseases. **Intrinsic syndromes (ie, CEP, HES, EGPA, EG) are idiopathic.** Asthma can cause pulmonary eosinophilia. Occasionally, eosinophilia and pulmonary infiltrates have been associated with AIDS, bronchiolitis obliterans organizing pneumonia (BOOP), hypersensitivity pneumonitis, idiopathic pulmonary fibrosis, sarcoidosis, Hodgkin disease, rheumatoid lung disease, and other collagen vascular diseases.

Epidemiology

International data

Worldwide, the most common cause of eosinophilia is parasitosis. Intrinsic syndromes are uncommon. Regarding extrinsic syndromes, in much of the world, parasitic infections are endemic. Note the following:

- *Ascaris* is likely the most prevalent nematode infecting humans worldwide but tends to occur in tropical or subtropical areas.
- *Ancylostoma duodenale* is commonly found in the Eastern Hemisphere.
- Visceral larva migrans is found throughout the world.
- Strongyloidiasis, which usually occurs in warmer climates, has a worldwide prevalence of approximately 50-100 million individuals.
- Schistosomiasis is common in Africa, Asia, Latin America, and South America. Paragonimiasis and clonorchiasis are common in Asia.
- TPE is often observed in southern Asia, Southeast Asia, and South America. Most reported cases have occurred in ethnic Indians, while it is uncommon in Chinese persons. TPE is actually observed in a minority of patients infected with the causative filariae.

Race-, sex-, and age-related demographics

No clearly defined racial predispositions have been identified in these syndromes. Parasitic infections are endemic in many geographic areas, but they reflect public health conditions rather than racial predispositions. **TPE has been reported to have a male predominance,** at a male-to-female ratio of 4:1. Acute eosinophilic pneumonia (AEP) is more common in men than in women. Among the intrinsic syndromes, chronic eosinophilic pneumonia (CEP) is twice as common in women as in men, but this sexual disparity declines with increasing age. For HES, approximately 90% of cases are found in men and 10% are found in women. For EGPA and EG, no sexual predisposition has been reported. **Extrinsic syndromes tend to affect adults,** but exceptions exist. Toxocariasis tends to occur in children and is often associated with geophagia. Ascariasis tends to occur in children. ABPA usually occurs in adults but may occur in children, including some patients with cystic fibrosis. AEP usually occurs in persons in their third decade of life.

Intrinsic syndromes generally affect adults. CEP peak incidence is in the fourth decade of life. HES usually occurs in people aged 20-50 years; however, it has also been infrequently reported in children. Most cases of EGPA have been reported in adults. EG may affect individuals ranging in age from infancy to old age, but it most frequently affects patients in their second to third decade of life.

Prognosis

With the exception of Loeffler syndrome and drug-induced disease, these syndromes may be associated with significant morbidity. While most are responsive to corticosteroids, recognition of infection and institution of an appropriate therapy are important in preventing chronicity of symptoms and, in some cases, respiratory failure.

Extrinsic diseases

Acute eosinophilic pneumonia (AEP)

Patients with AEP often develop respiratory failure, but, with treatment and supportive measures, they generally survive.

Medication-induced and Loeffler syndrome

Removal of the offending agent usually results in a resolution of symptoms.

Schistosomiasis

Schistosomiasis results in eosinophilia and pulmonary nodules in early infection because the schistosomes migrate through the lung. Later, granuloma formation and pulmonary arterial occlusion with chronic pulmonary hypertension are caused by embolization of ova.

Parasitic diseases

Parasitic diseases are usually successfully treated but may require a repeated course of therapy.

Strongyloidiasis

Patients with strongyloidiasis may be critically ill with sepsis and respiratory failure. Severe disseminated infection (hyperinfection) may occur in individuals who are immunocompromised because this nematode can replicate within humans.

Tropical pulmonary eosinophilia (TPE)

If left untreated for more than 6 months, TPE commonly leads to interstitial pulmonary fibrosis and restrictive defects.

Allergic bronchopulmonary aspergillosis (ABPA)

Patients with ABPA usually have lifelong symptoms with intermittent exacerbations. Complications may include respiratory failure, bronchiectasis, hemoptysis, aspergilloma, and/or complications of steroids.

Coccidioidomycosis

Coccidioidomycosis usually resolves spontaneously. Respiratory failure may occur in patients with progressive or disseminated disease. Patients who are immunocompromised may present with disseminated disease or persistent primary coccidioidomycosis; both are associated with significant morbidity and mortality. Patients who are older may develop a chronic illness resembling reactivation tuberculosis.

Intrinsic diseases

Chronic eosinophilic pneumonia (CEP)

Patients with CEP have a rapid response to therapy but may develop relapse within 6 months. Some patients who initially present with only pulmonary involvement actually have HES. Fibrosis may develop if

patients are left untreated or if the disease is extensive. If CEP is left unrecognized and untreated, it can progress, resulting in significant gas exchange abnormalities.

Hyper eosinophilic syndrome (HES)

Half of the patients with HES respond to steroids, while patients who do not respond go on to have significant disease requiring increasingly complex regimens. Now, 80% of patients survive 5 years, and 40% survive 10-15 years. The most serious complication of hyper eosinophilic syndrome is cardiac involvement, which can result in myocardial fibrosis, chronic heart failure (CHF), and death.

Eosinophilic granulomatosis with polyangiitis (EGPA)

Patients with EGPA generally respond well to steroids, but they require lifelong therapy. Renal failure, pulmonary fibrosis, and neuropathy may develop. Development of eosinophilic myocarditis is a poor prognostic indicator. The mortality rate in cases of EGPA has been decreasing, with approximately 75% of patients surviving 5 years. Novel treatments, including immunomodulatory drugs and targeted biotherapies show promise for improving the prognosis for patients with refractory/relapsing disease.

Eosinophilic granuloma (EG)

The course of EG is highly variable. Patients at age extremes, those with multiorgan or skin involvement, and those with pneumothoraces tend to have a poor prognosis. Diabetes insipidus may develop from pituitary involvement, and pneumothorax may develop from cystic lung disease.

Clinical Presentation

History

Methodical history taking, to exclude infections, foods, medications, or other precipitants, is important before labeling a pulmonary eosinophilic syndrome as intrinsic or idiopathic. The duration of symptoms and the presence of concomitant medical illnesses, such as collagen vascular disease, may be relevant. **Loeffler syndrome is precipitated by food, medications, or infections.** It is self-limited (usually < 1 mo duration). Symptoms are mild, and the syndrome is characterized by blood eosinophilia and fleeting pulmonary infiltrates, with or without dyspnea. Query patients about the usage of all medications, including dietary supplements, and illicit drugs. **An acute onset of rapidly progressing dyspnea**, often accompanied by abdominal complaints and myalgias, usually occurs within 1 week of presentation of acute eosinophilic pneumonia (AEP). Commonly, recent antecedent outdoor activity with considerable dust exposure has occurred. Marked acute hypoxemia, often progressing to respiratory distress, is typical. AEP is distinguished from chronic eosinophilic pneumonia (CEP) by its rapid progression, the presence of fever and severe hypoxemia, and no associated history of hypersensitivity to drugs. **Obtaining a careful travel history is important for assessing the risk of fungal or parasitic infection.** Travel to or from areas endemic for parasites (eg, Asia, Africa, Latin America, South America, southeast region of the United States) is of particular relevance to parasitic infection. Parasitic infections tend to cause fever, weight loss, fatigue, dyspnea, dry cough, wheezing, chest discomfort, and, occasionally, hemoptysis. Relevant historical elements for parasitic infections include the following:

- Strongyloidiasis: Patients may report skin contact with sand or soil, abdominal pain or distension, and/or diarrhea, with or without immunocompromise. Marked wheezing and/or respiratory distress may occur.

- **Ascariasis:** Mild pulmonary symptoms are accompanied by pruritic dermatitis.
- **Schistosomiasis:** Patients may report contact with contaminated water and the presence of skin lesions. Symptoms of early infection are mild, but the manifestations of chronic infection include chronic dyspnea. Other symptoms are bladder and gastrointestinal dysfunction, cirrhosis, and, commonly, pulmonary hypertension.
- ***Clonorchis sinensis* infection:** Patients may relate a history of ingestion of inadequately cooked or pickled fish, abdominal pain, nausea, vomiting, and/or diarrhea.
- **Paragonimiasis:** Ingestion of inadequately cooked or pickled crustaceans, abdominal pain, nausea, vomiting, diarrhea, testicular pain, and/or CNS manifestations are reported findings. Patients may develop significant hemoptysis or extensive infiltration.
- **Toxocariasis:** Findings include skin or oral contact with soil contaminated by canine feces, contact with puppies, and/or seizures. This condition can lead to significant wheezing and, occasionally, respiratory distress. Patients with toxocariasis may also be asymptomatic.

Fungal infections associated with pulmonary infiltrates and eosinophilia include *Aspergillus* infections, *Coccidioides immitis* infections, and other less common infections. Note the following:

- ***Aspergillus* infections:** Although *Aspergillus* species are ubiquitous, ask about contact with soil or contaminated water sources.
- **Allergic bronchopulmonary aspergillosis (ABPA):** Although technically not an infection because it is the host response to colonization by *Aspergillus* that is etiologic, it is considered here. Wheezing may be severe, and patients eventually develop prominent central bronchiectasis. The mildest form of ABPA is serologically positive (ABPA-S), the moderate form has central bronchiectasis (ABPA-CB), and the severe form includes both central bronchiectasis and other radiologic features (ABPA-CB-ORF). Early treatment has been suggested to prevent progression to more severe parenchymal disease.
- ***C immitis* infection:** Inquire about recent travel to the southwestern United States.
- The clinical course of coccidioidomycosis is highly variable, with more than 60% of patients being asymptomatic, while most of the remainder have mild symptoms.

For intrinsic syndromes, seek the following historical elements:

- **Chronic eosinophilic pneumonia (CEP):** Gradual onset of cough, fever, dyspnea, constitutional symptoms, and weight loss occurs. Wheezing, night sweats, chest pain, and, occasionally, hemoptysis may be reported. Respiratory failure is occasionally reported. Half the patients with CEP have a history of asthma.
- **Hypereosinophilic syndrome (HES):** Patients may complain of constitutional symptoms, dyspnea, cough, wheezing or angioedema (occasionally), and symptoms related to multiple affected organs, particularly those in the cardiovascular, gastrointestinal, and musculoskeletal systems. Symptoms related to arterial and venous thromboembolic disease may be present (eg, pulmonary emboli, vascular insufficiency, cerebrovascular accident).
- **Eosinophilic granulomatosis with polyangiitis (EGPA):** Patients often have antecedent rhinitis, sinusitis, and nasal polyps, followed by the development of asthma symptoms. Symptoms related to vasculitis

occur years later and include mononeuritis multiplex, abdominal pain, gastrointestinal bleeding, symptoms of heart failure, arthralgias, myalgias, urticaria, purpura, and nodular skin lesions.

- **Eosinophilic granuloma (EG):** Approximately one fourth of patients are asymptomatic. Most have a cough, dyspnea, fever, and chest discomfort. Wheezing may be reported. Patients may develop symptoms related to the pneumothorax, bony lesions, and diabetes insipidus. Cigarette smoking is nearly universal in these patients and is considered etiologic. The course of EG is highly variable. Patients at age extremes, those with multiorgan or skin involvement, and those with pneumothoraces tend to have a poor prognosis.

CLINICAL PRESENTATION

Physical Examination

A complete physical examination of these patients is necessary. For this heterogeneous group of diseases, clues to establishing a diagnosis are found in virtually every portion of the examination. All of the syndromes discussed can cause rales and wheezing.

Skin examination may include the following:

- A pruritic rash, which may be raised or seriginous
- Medication-related syndromes may result in skin manifestations.
- Parasitic infection, commonly with *Strongyloides*, *Ascaris*, *Toxocara*, *Ancylostoma*, *Necator*, and *Trichinella* species, may cause skin symptoms.
- Disseminated coccidioidomycosis is related to patients' skin symptoms.
- A rash associated with HES may be due to skin infiltration by eosinophils. Splinter hemorrhages and evidence of vascular occlusion may be seen.

Head, eyes, ears, nose, and throat examination: Evidence of rhinitis/sinusitis may be observed in persons with EGPA and CEP. Vascular occlusion may be observed during the eye examinations of patients with HES. Proptosis may be seen in patients with EGPA.

Chest examination: Physical signs of cardiac decompensation (eg, valvular insufficiency, S₃, rales, jugular venous distension [JVD], peripheral edema) may be present in patients with HES and EGPA. Patients with chronic schistosomiasis may present with signs of pulmonary hypertension (eg, loud P₂, JVD, peripheral edema, right-sided S₃).

Abdominal examination: Patients with chronic schistosomiasis may present with signs of cirrhosis (eg, distended abdomen, shifting dullness, peripheral edema, telangiectasias, icterus). Nonspecific abdominal tenderness is common in patients with parasitic diseases and intrinsic diseases.

Neurologic examination: Neuropathy may be observed in patients with HES and EGPA. Evidence of CNS deficits due to cerebrovascular accident may be observed in patients with HES.

Differential Diagnoses

Diagnostic Considerations

Intrinsic eosinophilic syndromes, including chronic eosinophilic pneumonia (CEP), and hypereosinophilic syndrome (HES), become more likely in the differential diagnosis once extrinsic etiologies have been excluded.

Differential Diagnoses

- [Ascariasis](#)
- [Aspergillosis](#)
- [Asthma](#)
- [Eosinophilic Granulomatosis with Polyangiitis \(Churg-Strauss Syndrome\)](#)
- [Dirofilariasis](#)
- [Echinococcosis Hydatid Cyst](#)
- [Eosinophilia](#)
- [Eosinophilia-Myalgia Syndrome](#)
- [Eosinophilic Fasciitis](#)
- [Eosinophilic Granuloma \(Histiocytosis X\)](#)
- [Eosinophilic Pneumonia](#)
- [Filariasis](#)
- [Food Allergies](#)
- [Fungal Pneumonia](#)
- [Hodgkin Lymphoma](#)
- [Hookworm Disease](#)
- [Hypereosinophilic Syndrome](#)
- [Hypersensitivity Pneumonitis](#)
- [Idiopathic Pulmonary Fibrosis \(IPF\)](#)
- [Interstitial \(Nonidiopathic\) Pulmonary Fibrosis](#)
- [Intestinal Flukes](#)
- [Mediastinal Lymphoma](#)
- [Mucormycosis \(Zygomycosis\)](#)
- [Nematode Infections](#)
- [Pneumocystis jiroveci Pneumonia \(PJP\)](#)
- [Respiratory Failure](#)
- [Restrictive Lung Disease](#)
- [Rheumatoid Arthritis \(RA\)](#)
- [Sarcoidosis](#)
- [Scleroderma](#)
- [Pulmonary Arterial Hypertension](#)
- [Tuberculosis \(TB\)](#)
- [Zygomycosis](#)

Workup

Approach Considerations

The workup should start with the history and physical examination. Pertinent history of travel, evidence of collagen vascular disease, status of the immune system, usage of medications, duration of symptoms, and evidence of airway obstruction are essential elements to consider. The final diagnosis always rests with the response to treatment, even with infectious syndromes. Rule out infectious etiologies based on the travel history, regardless of how remote.

Pulmonary function testing may be useful in the initial evaluation to help narrow the differential diagnosis. Note the following:

- Pulmonary function is helpful as an initial test to distinguish between obstructive and restrictive diseases and to assess the severity of airway obstruction or parenchymal restriction.
- An obstructive pattern may be seen in persons with asthma, allergic

bronchopulmonary aspergillosis (ABPA), bronchocentric granulomatosis, eosinophilic granuloma (EG), bronchiolitis obliterans organizing pneumonia (BOOP), eosinophilic granulomatosis with polyangiitis (EGPA), and, occasionally, hypereosinophilic syndrome (HES).

- A restrictive pattern may be seen in persons with tropical pulmonary eosinophilia (TPE), intrinsic eosinophilic syndromes, and interstitial lung diseases.

Skin prick testing and intradermal testing can be performed for an immediate hypersensitivity response to *Aspergillus* infection. Avoid skin testing if the patient has significant wheezing.

Laboratory Studies

Initially, examine stool for ova and parasites. Specimens may be negative if intestinal infection is not established. Multiple specimens should be sent and examined by experienced laboratory personnel. Stool or gastric aspirate examination is generally useful for detecting *Strongyloides* species, *Schistosoma* species, and *C. sinensis*; is often less useful for detecting *Paragonimus*, *Ancylostoma*, *Necator*, and *Ascaris* infection; and is usually not helpful for detecting *Toxocara*, *Trichinella*, and *Echinococcus* species and tropical pulmonary eosinophilia (TPE)–associated filariae. IgE should always be performed to rule out/ in TPE. **Blood leukocyte count with differential is necessary.** Leukocytosis is common in all of these syndromes. **The upper limit of normal for the range of eosinophils** in the peripheral blood is 3%-5% with a corresponding absolute eosinophil count (AEC) of 350–500/ μ L. The severity of eosinophilia has been arbitrarily divided into mild (AEC from the upper limit of normal to 1500/ μ L), moderate (AEC 1500–5000/ μ L) and severe (AEC >5000/ μ L). The eosinophil percentage is less sensitive than the absolute eosinophil count (AEC). CBC count and AEC should be monitored to assess the course of illness and response to treatment when appropriate. **Blood and pulmonary eosinophilia are generally present together in persons with Loeffler syndrome**, parasitic and fungal infections, CEP, allergic bronchopulmonary aspergillosis (ABPA), EGPA, and HES. **Isolated pulmonary eosinophilia may be observed in persons with AEP, medication-related syndromes, *P. carinii* pneumonia, BOOP, tuberculosis, and eosinophilic granuloma (EG) (Langerhans cell).** **Microbiologic studies, rarely, may show evidence of infection with *Mycobacterium tuberculosis*, *P. carinii*, or fungi.** Make additional efforts to exclude parasitic or other fungal co-infection. Parasitic infections may be detected by examining stool, urine, and sputum or BAL fluid. Urine examination may be useful in cases of schistosomiasis. Sputum or BAL fluid examination may be useful for detecting *Paragonimus*, *Ascaris*, *Strongyloides*, and, rarely, *Schistosoma* infections. Fungal infection may be detected by examining respiratory secretions. ABPA is supported by growth of *Aspergillus* species from respiratory secretions. *Coccidioides* species may be cultured from respiratory secretions. **Immunologic studies, ie, serologic testing, may be useful in persons with ABPA, parasitic infection, and EGPA.** Serologic testing may obviate the need for invasive testing in the case of parasitic infections. Use a targeted approach to serologic testing, bolstered by clinical information.

Total IgE values are often elevated in persons with these syndromes, and this finding has no specific diagnostic value. The following general trends may be noted:

- Levels of less than 1000 ng/mL are usually observed in association with asthma and low-intensity infections.

- ABPA and parasitic infections are typically associated with high levels, often greater than 2000 ng/mL.

The diagnosis of ABPA is supported by an elevated IgE level, an elevated *Aspergillus*-specific IgE level, a positive result for *Aspergillus* precipitins, and an immediate skin hypersensitivity response to *Aspergillus*. Levels correlate with the activity of ABPA. If levels are within the reference range in a patient with respiratory symptoms, ABPA can usually be excluded. **Some parasitic infections may be diagnosed based on serological results.** These include TPE-associated filarial infection (eg, *B malayi*, *W bancrofti*); echinococcal infection (serology results are positive in 60-90% of cases); and toxocariasis, with best results obtained by enzyme-linked immunosorbent assay (ELISA). A variety of sensitive and specific serologic tests, including complement fixation, ELISA, and immunoblot, have been developed to detect *Paragonimus* infection.

Tests with limited value are available for *Strongyloides* and *Ascaris* infections. In EGPA, perinuclear antineutrophil cytoplasmic antibody results are positive in at least 60% of cases. In CEP, check antinuclear antibody or rheumatoid factor levels because CEP may be associated with connective tissue diseases. **In 2009, Velthove et al report on possible biomarkers (neutrophilia, eosinophilia) for inflammation in obstructive lung disease.** Based on the results of their case-control study, they suggested both neutrophil counts and eosinophil counts may be useful biomarkers for exacerbations in obstructive lung disease. Additionally, Hillas et al suggest eosinophil counts are the future direction of focus for a noninvasive method of assessing airway inflammation in clinical practice and not just research settings.

Imaging Studies

Chest radiography

Extrinsic syndromes

The following findings may be noted on chest radiography studies in patients with extrinsic syndromes:

- Loeffler syndrome: Fleeting interstitial infiltrates may be evident.
- Acute eosinophilic pneumonia (AEP): Interstitial infiltrates progress to alveolar-filling infiltrates. Small pleural effusions and Kerley B lines may be present.
- Parasitic infections: These typically manifest as interstitial or indistinct nodular densities, usually in the middle and/or basilar lung fields. Infiltrates may be migratory. Chest x-ray films may yield normal findings in many individuals.
- Tropical pulmonary eosinophilia (TPE): Fibrosis may be evident in persons with chronic disease.
- *Echinococcus* infection: This manifests as large, smooth-edged, masslike densities, with or without calcification.
- Chronic schistosomiasis: Patients with chronic schistosomiasis may have hilar enlargement and right ventricular enlargement as a consequence of pulmonary hypertension.
- Allergic bronchopulmonary aspergillosis (ABPA): Fleeting infiltrates, atelectasis, pneumonitis, and bronchiectasis may be evident.

Intrinsic syndromes

The following findings may be noted on chest radiography studies in patients with intrinsic syndromes:

- Chronic eosinophilic pneumonia (CEP): Peripheral alveolar infiltrates may be migratory, and they have the classic appearance of the photographic negative of pulmonary edema in one fourth of

cases.

- Hypereosinophilic syndrome (HES): Interstitial infiltrates, pleural effusions, pulmonary edema, pulmonary infarct, and fibrosis may be present.
- Eosinophilic granulomatosis with polyangiitis (EGPA): Interstitial infiltrates, alveolar infiltrates, and nodular opacities may be present. Cavitory, small, patchy irregularities are not usually present.
- Eosinophilic granuloma (EG): Reticulonodular infiltrates, increased lung volumes, cystic changes, coalescing nodules, and pneumothorax may be seen.

Chest CT scanning

Computed tomography (CT) scanning of the chest helps define the extent and distribution of the disease; helps distinguish between predominantly interstitial or alveolar infiltrates; helps detect lymphadenopathy, fibrosis, and bronchiectasis; may be helpful in distinguishing between malignancy and other etiologies; and may be needed if biopsy is contemplated. High-resolution CT scanning is preferred to enhance the evaluation of the pulmonary parenchyma. Note the following:

- ABPA: Fleeting infiltrates, atelectasis, pneumonitis, and bronchiectasis may be evident. High attenuation mucoid impaction is associated with higher IgE levels, eosinophilia, *Aspergillus*-specific titers, and a greater probability of relapse.
- Parasitic diseases: CT scanning images provide finer detail of nodules and interstitial infiltrates. In schistosomiasis and echinococcal diseases, additional cysts may be seen in the liver.
- AEP: Ground-glass infiltrates are commonly seen, but dense consolidation, nodules, and septal thickening may also be revealed.
- CEP: Alveolar ground-glass infiltrates in a peripheral distribution are highly characteristic of CEP.
- HES: Nodules and effusions may be seen.
- EGPA: In addition to abnormalities seen on plain radiographs, irregular pulmonary arteries may be seen.
- Bronchiolitis obliterans organizing pneumonia (BOOP): Peripheral triangular-shaped infiltrates are classic, but alveolar filling may be evident.
- EG: Cystic changes, nodules, and fibrosis are seen.
- Idiopathic pulmonary fibrosis: Interstitial infiltrates, a ground-glass alveolar pattern, nodules, and fibrosis are seen.

Positron-emission tomography (PET) scanning

Patients with pulmonary eosinophilia have been reported to have F-18 fluorodeoxyglucose (FDG)-avid uptake on positron emission scans.

Echocardiography

Establishing an estimation of right ventricular, left ventricular, and valvular function is indicated in individuals with certain intrinsic syndromes (eg, EGPA, HES) or in individuals with sustained high-level eosinophilia in which cardiac complications are relatively common. **Establishing an estimation of pulmonary systolic pressure** and right ventricle function is indicated in persons with chronic schistosomiasis because pulmonary hypertension is common.

Ventilation/perfusion scanning

This scan may be useful in some patients with HES in the appropriate clinical setting who have a propensity to develop pulmonary emboli. Schistosomiasis and other parasitic diseases may result in matched and unmatched defects.

Procedures

Fiberoptic bronchoscopy with bronchoalveolar lavage

Bronchoalveolar lavage (BAL) is often necessary to obtain adequate specimens to help rule out infection, particularly in the instance of CEP and other intrinsic syndromes. Note the following:

- BAL fluid leukocyte and differential cell counts may provide the presenting or only sign of eosinophilic pulmonary syndrome. Normally, few eosinophils are obtained from BAL fluid. The presence of more than 20% suggests Loeffler syndrome, AEP, CEP, or HES.
- Pulmonary eosinophilia alone may be present in persons with AEP, medication-related syndromes, *P carinii* pneumonia, BOOP, tuberculosis, and EG (Langerhans cell).
- BAL examination may be useful for detecting *Paragonimus*, *Ascaris*, *Strongyloides*, and, rarely, *Schistosoma* infections.
- BAL fluid cytology findings may be useful for excluding malignancy.
- BAL cytology findings may also be useful for detecting EG, for which immunohistochemical staining for the S-100 antigen or electron microscopy (demonstrating the pentilaminar Birbeck granule) can be diagnostic.

Transbronchial biopsy

Transbronchial biopsy may be performed to help determine if an invasive fungal infection is present. The size of the tissue specimens obtained is generally insufficient to reliably provide the histopathologic information for the syndromes discussed.

Transthoracic needle aspiration/biopsy

Transthoracic needle aspiration/biopsy occasionally may be used to help distinguish infection from malignancy when the results of other, less-invasive studies have been unrevealing. Dirofilariasis, which is difficult to diagnose with noninvasive methods, has been diagnosed based on findings from this method. Avoid aspiration of echinococcal cysts because of the risk posed by dissemination, resulting in a massive hypersensitivity reaction.

Open lung biopsy

Open lung biopsy is rarely necessary, but it is usually performed if EGPA, interstitial lung disease, or malignancy is suggested. For AEP and CEP, BAL is usually performed. Once infection is excluded, the rapid response to therapy contributes to a clinical diagnosis.

Other biopsies

Other biopsies are indicated based on clinical presentation as follows:

- Liver biopsy is performed for chronic schistosomiasis with cor pulmonale. It rarely is performed for TPE (which is usually confirmed based on serology findings) and toxocariasis.
- Lymph node biopsy is occasionally used in cases of TPE.
- Skin biopsy is performed for trichinosis, and it is occasionally performed for toxocariasis or when skin manifestations of other diseases are prominent.
- Rectal biopsy is occasionally pursued in persons with schistosomiasis.
- Muscle biopsy findings may indicate trichinosis.

Histologic Findings

Histologic findings may include the following:

- Parasitic diseases: Findings include increased histiocytes, eosinophilic and lymphocytic infiltration of airspaces, eosinophilic abscesses, granulomas, and areas of fibrosis.

- Allergic bronchopulmonary aspergillosis (ABPA): Findings include eosinophilic, lymphocytic, plasmacytic, and monocytic infiltration around bronchi; granulomas; fibrosis; microabscesses; and bronchiectasis.
- Acute eosinophilic pneumonia (AEP): Findings include eosinophilic infiltration of airspaces and airway walls and edema, but not vasculitis.
- Chronic eosinophilic pneumonia (CEP): Findings include eosinophilic and lymphocytic accumulation in alveoli, eosinophilic abscess formation, bronchiolitis, and fibrosis. Granulomas are not seen. Occasionally, mild vasculitis is seen.
- Eosinophilic granulomatosis with polyangiitis (EGPA): Eosinophilic necrotizing vasculitis of small vessels and granulomas are common.
- Hypereosinophilic syndrome (HES): Findings include eosinophilic infiltration of interstitium and airways and intravascular thrombi.
- Eosinophilic granuloma (EG): Findings include Langerhans cell proliferation and granulomas, lymphocytic and monocytic infiltration, desquamative interstitial pneumonitis, granulomatous vasculitis, lymphoid follicles, S-100 antigen staining of Langerhans cells, and, with electron microscopy, the Birbeck (X-body) within cytoplasm of Langerhans cells.

Treatment & Management

Approach Considerations

With extrinsic diseases, the priority is to establish the diagnosis, assure adequate oxygenation, and provide bronchodilator therapy, with or without steroids as indicated. Note the following:

- Acute eosinophilic pneumonia (AEP): Patients may deteriorate rapidly to respiratory failure and require mechanical ventilation, but they generally respond well to high-dose steroids.
- Fungal infections: For allergic bronchopulmonary aspergillosis (ABPA), assure clinical improvement. For coccidioidomycosis, patients who are immunocompromised may develop disseminated infection if steroids are administered.
- Parasitic diseases: Patients may develop a Mazzotti reaction, in which the death of parasites releases new antigens, with resultant fever, urticaria, pruritus, bronchospasm, and associated gastrointestinal symptoms. Patients who are immunocompromised and have strongyloidiasis may develop hyperinfection syndrome with use of steroids (see Medication).

With intrinsic syndromes, make aggressive attempts to exclude infections. Note the following:

- Chronic eosinophilic pneumonia (CEP): CT scanning and bronchoscopy are generally performed. If no infection is present, the patient is treated with prednisone. Rapid clinical and radiologic improvement occurs within 24-72 hours.
- Eosinophilic granulomatosis with polyangiitis (EGPA): If significant end organ damage results from vasculitis and if the damage is rapidly advancing, the urgency of treatment may be increased.
- Hypereosinophilic syndrome (HES): Patients tend to respond slowly, and only 50% respond to steroids. Patients may develop deep venous thrombosis and pulmonary emboli.

INTERPRETATION

UNDERSTANDING Nephelometry and Turbidimetry:

Nephelometry and turbidimetry, in analytical chemistry, methods for determining the amount of cloudiness, or turbidity, in a solution based upon measurement of the effect of this turbidity upon the transmission and scattering of light. **Turbidity in a liquid is caused by** the presence of finely divided suspended particles. **If a beam of light is passed through a turbid sample**, its intensity is reduced by scattering, and the quantity of light scattered is dependent upon the concentration and size distribution of the particles. **In nephelometry the intensity of the scattered light is measured**, while, in turbidimetry, the intensity of light transmitted through the sample is measured. **Nephelometric and turbidimetric measurements** are used in the determination of suspended material in natural waters and in processing streams.

Scattering: The redirection of radiation out of the original direction of propagation, usually due to interaction with molecules and particles.

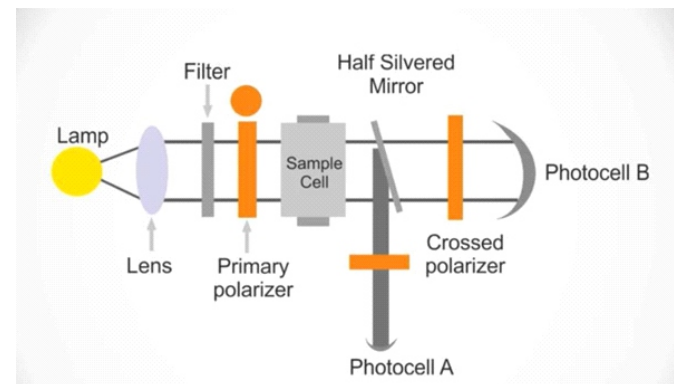
- Reflection
- Refraction
- Diffraction

Light Scattering is a physical character and depends on following parameters:

- Particle size
- Distance of observation
- Concentration of solution
- Molecular weight of particles
- Agitation of solution containing particulate matter
- Temperature of solution
- Viscosity of medium
- Presence and absence of protective colloids
- Number of particulate matters suspended
- Dimension of particulate matter
- Wavelength of radiation beam
- Refractive index of medium

Turbidimeters:

Ordinary calorimeter or spectrophotometer can be used. Any photometer (visual or photoelectric) can be a Turbidimeter.



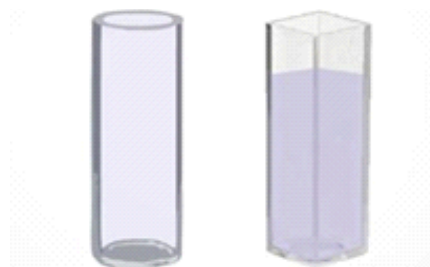
Source: Mercury lamp or Laser Light

Tungstun lamp

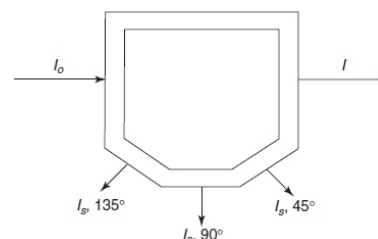
Filters: Converts polychromatic light to mono chromatic light.

- 1) absorption filters
- 2) Interference filters

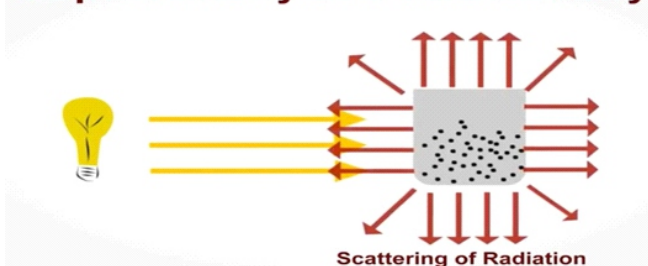
Sample Cells:



In general cells with rectangle cross section is preferred where measurements can be made at angles more than 90°

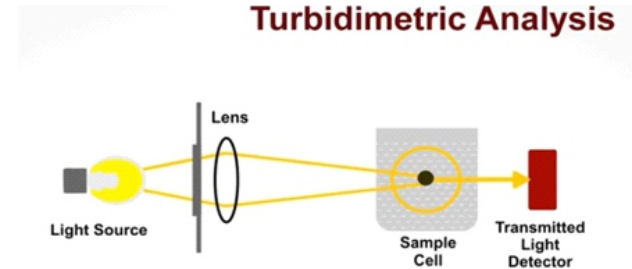


Nephelometry and Turbidimetry



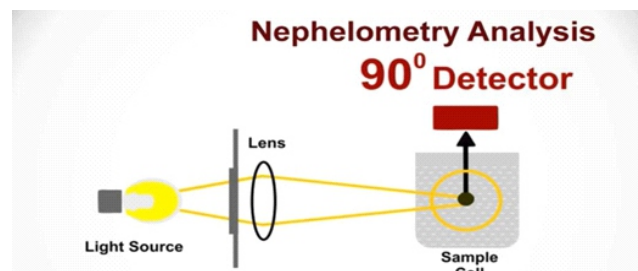
Scattering, Reflection and Refraction of Radiation

Turbidimetric Analysis



Measurement of Intensity of transmitted light is a function of concentration of suspended particles.

Nephelometry Analysis 90° Detector



Measurement of Intensity of scattered light as a function of concentration of dispersed phase. Source and detector as a right angle to each other.

Detector:

- Photovoltaic cells and Phototubes are suitable for Turbidimetric analysis.
- While sensitive photomultiplier tubes are suitable for Nephelometric analysis

Sensitivity of methods:

- Addition of water-soluble polymers
- Gives stability to immune complex

Differentiation:

	Turbidimetry	Nephelometry
Definition	Light passes through a medium with dispersed particles, so the intensity of light transmitted is measured	Measurement of intensity of scattered light at right angle to the direction of the incident light as a function of the concentration of the dispersed phase. It is most sensitive for dilute suspensions (100mg/L)
Instrument used	Spectrophotometer	Nephelometry machine
Type of light measured	Transmitted light	Scattered light
Arrangement of photometer	Made in the same direction as the propagation of light source.	Measure the light scattered at right angle to the direction of propagation of the light from the source.

Uses:

- The technique is also used for determination of sulphur in coal, oil, and other organic materials; the sulphur is precipitated as barium sulphate
- The main uses of nephelometers relate to air quality measurement for pollution monitoring, climate monitoring, and visibility. Airborne particles are commonly either biological contaminants, particulate contaminants, gaseous contaminants, or dust.
- Biological contaminants include mold, fungus, bacteria, viruses, animal dander, dust mites, pollen, human skin cells, cockroach parts, or anything alive or living at one time. They are the biggest enemy of indoor air quality specialists because they are contaminants that cause health problems. Levels of biological contamination depend on humidity and temperature that supports the livelihood of micro-organisms. The presence of pets, plants, rodents, and insects will raise the level of biological contamination.
- Sheath air is clean filtered air that surrounds the aerosol stream to prevent particulates from circulating or depositing within the optic chamber. Sheath air prevents contamination caused by build-up and deposits, improves response time by containing the sample, and improves maintenance by keeping the optic chamber clean. The nephelometer creates the sheath air by passing air through a zero filter before beginning the sample.
- Nephelometers are also used in global warming studies, specifically measuring the global radiation balance. Three wavelength nephelometers fitted with a backscatter shutter can determine the amount of solar radiation that is reflected back into

- Reduced reaction concentration

End point detection:

Nephelometry is a modification of photo-optical end-point detection in which 90-degree or forward-angle light scatter, rather than OD, is measured. A light-emitting diode produces incident light at approximately 600 nm, and a photodetector detects variations in light scatter at 90 degrees (side scatter) and 180 degrees (forward- angle scatter).

space by dust and particulate matter. This reflected light influences the amount of radiation reaching the earth's lower atmosphere and warming the planet.

- Nephelometers are also used for measurement of visibility with simple one-wavelength nephelometers used throughout the world by many EPAs. Nephelometers, through the measurement of light scattering, can determine visibility in distance through the application of a conversion factor called Koschmieder's formula.
- In medicine, nephelometry is used to measure immune function.
- Gas-phase nephelometers are also used in the detection of smoke and other particles of combustion. In such use, the apparatus is referred to as an aspirated smoke detector.

Application:

- Nephelometry has been applied to the quantitative determination of various protein and other antigens in blood serum, urine or cerebrospinal fluid such as lipoproteins, immunoglobulins, complement factors, rheumatoid factors and immune complexes.
- Measurement of light scattering has also been used for the determination of cell size
- Determination of benzene percentage in alcohol
- Amount of amino acids, vitamins and antibiotics
- Determination of proteins
- Air and water pollution
- Turbidity titration
- Determination of Molecular weight

TROUBLESHOOTING

TURBIDIMETRY

Turbidity has long been one of the key indicators in determining water quality. However, it is well recognised within the industry that because of the effect of instrument design on readings, different instruments can give different results on the same sample. There are a number of reasons for this, some to do with the instruments incident light and scattered light detection angle, and some to do with how the sample is presented to the instrument. [Turbidity can be a complex measurement to do, especially at the very low levels required in UK drinking water production.](#) Measurement can be affected by the size and shape of the material scattering the light, the sample colour and then the distribution of the material in the sample. [To overcome these issues, a new turbidity instrument has been developed,](#) created by an expert team led by world-renowned turbidity expert Mike Sadar. The online instrument they designed sought to address the common issues with the presentation of the sample to the instrument.

The challenges of turbidity measurement:

Cause	Effect
Bubbles	High results
Sample cell variations	High or Low results. The impact of this issues is most severe when measuring low level turbidity.
Stray light	High results
Contamination	High results. Results from the build-up of particles/scale within the instrument, or from microbiological fouling.
Instrument optical aspects	High or low results. Degradation of the optical components within the instrument and the effect of calibration.
Absorbing coloured particles	Low results
Sample colour	Low results.(If using a wavelength in the visible region)
Particle Size	High or low results (wavelength dependent) Large particles scatter longer wavelengths of light more readily than small particles. Small particles scatter shorter wavelengths more efficiently than longer wavelengths
Particle settling	High or low results. Tends to be an issue with portable instrumentation rather than online.
Particle Density	Low results

A new way of measuring turbidity has been developed by tulip Diagnostics.

Bubbles

Bubbles are the bane of turbidity measurement and a number of methods of removing them from the sample prior to measurement have been attempted by manufacturers over the years. To eliminate bubbles from entering the measurement chamber, the new instrument design incorporates an integral patented bubble trap mechanism, using both horizontal and vertical flow to trap and remove even microbubbles from the instrument prior to measurement.

Sample cell

Any surface that comes between the incident light and the detector is not ideal, bench-top turbidity measurement is inherently prone to defects on the cell caused by cleaning and use, these cause false positive turbidity results, so why use them in online instrumentation if you don't need to. Glass cells are prone to scratching and fouling. [Added to this is the issue of condensation,](#) a particular problem when using glass cells but also effects online instruments that don't when condensation builds up around the light source. [To avoid these issues,](#) the experts simply didn't use glass cells and incorporated a temperature controlled light source to prevent condensation on the optics.

Stray light

Stray light is another problem which can be reduced by a well thought out instrument design. Essentially, it is the light that is detected by the instrument that isn't associated with the scattering by the particles in the sample at that moment. Again, very low-level turbidity measurement is prone to error due to even the tiniest amounts of light bouncing around the sample chamber. [The new instrument has been designed to channel stray light downwards,](#) away from the detector and towards a 'stray light dump'. This specially developed component captures stray light and prevents it from bouncing around the measurement chamber and causing false positive results.

Contamination

Specially designed wetted parts are used and the measurement chamber design is completely smooth to minimise any places where sediment can build up. Additionally, the measurement chamber is designed to simple to access as making cleaning easy for operators is the key to avoiding contamination issues.

Instrument optical aspects

By using a LED light source, the instrument offers long and stable performance over time. In order to verify the optical system, a solid standard has been developed to enable operators to check their system, but the expert team wanted to go one step further and enable calibration on the primary calibration solution for turbidity instrumentation, formazin. Turbidity calibration is all based around the response of the instrument to formazin. Formazin was specially developed for the calibration of turbidity instruments and is a polymer which has relatively consistent light scattering properties. It and is the **ONLY** real primary calibration standard available, every other standard you can get for a turbidity instrument is a secondary standard which relates back to formazin and should only really be used for verification. Unfortunately, formazin has two major drawbacks in that it's not very nice to handle and secondly, it isn't terribly stable in dilute solution. Given that drinking water works are working below 1NTU then the solutions you would use to calibrate would

have to be made up fresh before use.

Sample colour/coloured absorbing particles

There is little that can be done about the absorption of light by colour, however as it tends to affect instruments using a wavelength below 800nm. As most turbidity instruments in use in the UK are designed to comply with the ISO 7027 standard which specifies at near infra red wavelength should be used, it is less of an issue.

Particle Size / density

Again, not a lot can be done about the instruments handling of the different scattering properties of particles of different size and density. The user must decide whether they want to be able to detect smaller particles by using a shorter wavelength (and hence run the risk of colour interference) or use the longer wavelength ISO compliant version of the instrument. The new instrument comes in both forms. With respect to

particle settling, again, not a lot can be done in the instrument design but it is worth noting when online and portable instrumentation results are compared.

Conclusion

In conclusion, a new way of measuring turbidity has been developed, from TDPL which incorporates the expertise of a team with over 2 decades of experience in turbidity measurement. [Whilst overcoming many of the technical issues associated with turbidity measurement](#), the team also designed it with the water treatment works in mind. This meant ensuring only small volumes of sample were required to reduce water consumption and introducing an App based interface for operation on a smart device where this is desirable. [A new standard for turbidity measurement](#) has been developed.

BOUQUET

In Lighter Vein



When a woman says "What?", it's not because she didn't hear you.

She's giving you a chance to change what you said.

Husband:
Call ambulance, fast!
I am having heart attack...

Wife: (took his mobile)
Quick!! Tell me the password

Husband:
It's ok! I am feeling
Better now.



This is the first time in english literature question and answer both are same

Q: Who declared Corona as a pandemic?

A: WHO declared Corona as a pandemic .



Wisdom Whispers

IF YOU WANT
SOMETHING YOU'VE
NEVER HAD,
THEN YOU'VE
GOT TO DO
SOMETHING YOU'VE
NEVER DONE.

“Never allow
someone to be
your priority
while allowing
yourself to be
their option.”

YOU CAN'T HAVE
A BETTER
TOMORROW IF YOU'RE
STILL THINKING
ABOUT
YESTERDAY.

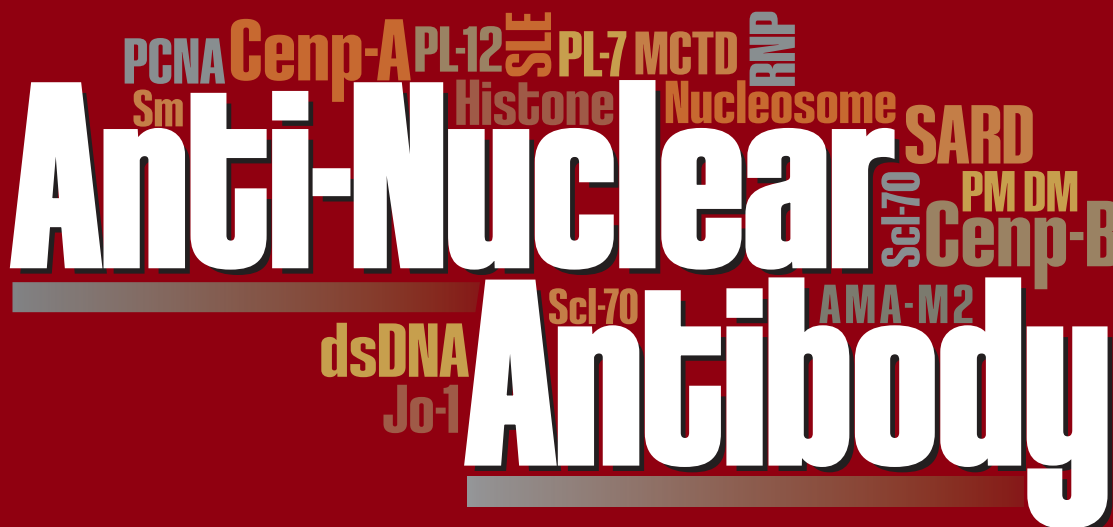
JUST WHEN THE
CATERPILLAR
THOUGHT THE
WORLD WAS
OVER, IT
BECAME A

butterfly.



Brain Teasers

- What does E stand for in TPE, CEP, HES and EGP
 - Eosinophilia
 - Early
 - Elevated
 - None of the above
- Which of the following is an Intrinsic eosinophilic syndrome
 - Tropical pulmonary Eosinophilia
 - Loeffler Syndrome
 - DRESS Syndrome
 - Eosinophilic granuloma
- Which Immunoglobulin would you estimate in TPE?
 - IgE
 - IgD
 - IgA
 - IgG
- Which of the following can be responsible for Eosinophilia
 - Ascaris lumbricoides
 - Ancylostoma duodenale
 - Visceral larva migrans
 - All of the above



Anti-Nuclear Antibody

Anti- Nuclear Antibodies (ANAs) refer to a collection of autoantibodies that target a variety of nuclear and cytoplasmic antigens. Anti- Nuclear Antibodies are responsible for most of the autoimmune disorders which are affecting more than 100 million people worldwide. Screening of these antibodies is a must for detecting the associated autoimmune diseases.

For screening of ANAs Enzyme Linked Immunoassay (ELISA) is the most preferred and widely accepted technique.

Characteristics of an Ideal ANA Elisa

- ▶ Detection of all major ENAs.
- ▶ High Specificity and Sensitivity against Coated ENAs.

Introducing

Qualisa ANA:

- ▶ Detection of All Major ENAs (SS DNA, dsDNA, Nucleosomes, Histones, Jo-1, SSA, SSB, Sci-70, SM, SM/RNP)
- ▶ 100% specific with sensitivity of 95.2%
- ▶ Turn Around Time of only **50 minutes**.
- ▶ Ready to use reagents.
- ▶ Standardized and Harmonised on Indian Ethnic population.

Available in 96 Test

***Better Testing Systems & Products
For Better Diagnostics & Preventive Health***

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