A system for the identification, investigation & management of medical conditions caused by the new identified infectious disease Paill Spectrum

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Abstract

A system for the identification, investigation and management of medical conditions caused by the newly identified infectious disease: Paill Spectrum (aka "PaillSpectrum"). It appears to be due to an infectious organism.

The most common pattern of Paill Spectrum illness has mood swings as the common symptom. If questioned people will mention attacks of jitters and panics as well as memory loss.

A clinically distinctive pattern of illness: is fatigue and pain. Many of these people have the classical symptoms of chronic fatigue, sweaty hands, loss of balance and soreness/tendon pains.
Title:
A System for the Identification, Investigation and Management of Medical Conditions Caused by the Newly Identified Infectious Disease: Paill Spectrum

Technical Field:
Health / Medicine

Essential Features:
Symptoms and Recognized Syndromes, which are identifiable features of the Paill Spectrum Syndrome.
Tests and reference Ranges used to identify the presence of the Paill Spectrum Syndrome/ Disease.
Treatment protocols for the management of the Paill Spectrum Syndrome.

Description:
This application forms a "system" for the
- Identification,
- Investigation &
- Management
of a medical condition which has a range of symptomatic presentations.

The medical condition has been called "Paill Spectrum" (aka "PaillSpectrum"). It appears to be due to an infectious organism. The Paill Spectrum infection can be diagnosed using the criteria as specified and can be treated using the system as specified.

The symptoms can be variably present and combinations of the specified symptoms may be found in affected patients.

The presence of the infection is characterized by the presence of positive infective markers. Other tests, as specified may or may not be done to assist diagnosis, exclude other medical conditions unrelated to Paill Spectrum infection or to guide treatment.

Therapy may involve any treatment or combinations of treatment, to a variable extent as dictated by symptomatic response or pathology test assessed response. Therapy may involve other antibiotics in the classes of medications as specified. Currently unknown therapies may be assessed for effectiveness against Paill Spectrum using the clinical criteria as specified.

The Paill Spectrum infection can be identified by the presence of characteristic symptoms.

The most common pattern of Paill Spectrum illness has mood swings as the common symptom. If questioned people will mention attacks of jitters and panics as well as memory loss.

A clinically distinctive pattern of illness: is fatigue and pain." Many of these people have the classical symptoms of chronic fatigue, sweaty hands, loss of balance and soreness / tendon pains.
Other common patterns of Paill Spectrum infection may be characterised by single symptoms or combinations of symptoms and the characterisable Paill Spectrum blood inflammatory markers. These conditions will all respond to the treatment principles as specified by the Paill Spectrum treatment program.
Identification Of Paill Spectrum

Some "Paill Spectrum": Presentations

**Mood / Temper Group**
- Don't Feel Well
- I don't think I am depressed
- Anger, Irritability, Snappiness
- Maybe: Attacks of Jitters & Panics
- Memory getting Worse

**Fatigue / Pain Group**
- Don't Feel Well
- Some Aches and Pains
- Chronic fatigue
- Sweaty Hands
- Loss of Balance: Static/Dynamic
- Tendon Pains

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**Paill Spectrum**

*Sick & Tired?*

- Mood Swings
- Angry
- Irritable
- Memory Loss
- Jitters & Panics
- Sweaty Hands
- Chronic Fatigue > Weight Gain
- Dizziness or Loss Of Balance

**Sore / Tendons**

- Sore Chest
- Sore Elbows
- Sore Stomach
- Sore Knees
- Sore Ankles & Feet

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Identification Of Paill Spectrum

Paill Spectrum Symptoms: The group headings form a systematised “memory aid” rather than an exclusive grouping. Group headings are intended to be generally descriptive only.

Tiredness Cluster of Symptoms:
- Chronic persistent fatigue or tiredness, (Typically lasting over three months).
- Excessive sleepiness or napping
- Loss of activity or a reduction in normal activity levels
- Cessation of a preferred activity
- Weight gain (Weight loss may occur in some sub-groups).

Hand Symptom Cluster
- Sweaty Hands and/ or night sweats (may affect the entire body)
- Hand discomfort in early morning.
- Tingles as well as pins and needles
- Carpal tunnel syndrome
- Symptom response to heating, typically most aching in the morning, but easing rapidly with activity.
- The feet may also experience all these symptoms.

Ear Related Cluster
- Dizziness and/or Unsteadiness: short episodes occur or may present as clumsiness. The patient may fail a standard sobriety test.
- Balance Problems
- Instability in standing or walking, Dizziness, vertigo, or mild loss of balance.

There are three basic tests in assessment.
- Standing still with feet together and eyes closed. Try not to sway at all. Movements of over one inch are not normal.
  - Walking heel toe across a room. Instability Movements of over one inch are not normal.
  - Walking heel toe across a room with the patient's eyes closed. Keep a hand on their upper front chest and their back to guard stability.

- Instability Movements of over one inch are not normal.
- Movements of over one inch are not normal. If the movement swings are of the order of one inch or 2-3 cm, I label them as faint.
- Swings double this are labelled as +½. (ie two inches or five cm).
- Progressively worsening balance is recorded as +1 for 7 cm (3 inches) of swing and +2 for 10 cm (4 inches) of swing.
- +3 is reserved for people who almost fall over.

- Clumsiness
- Instability in standing or walking, Dizziness, vertigo, or mild loss of balance
- Meniere's Disease
• Hearing loss

Easy Bruising Cluster
• Skin hematomas, skin bruising: Particularly on the arms and thighs, (usually without remembering the incident that put them there). The bruises are often typical fingermark bruises or about the same size as fingermark bruises.
• Mouth Blood Blisters

Pain Syndromes and Tenderness Cluster
• Need for Painkillers: characteristic of Paill Spectrum Pain Syndromes.
• Short sharp jabbing pains in the chest or other parts of the body. These may be felt as burning.
• Fibromyalgia:
• Predominantly giving upper body and shoulder aches: deltoid and trapezius muscle distributions.
• Soreness in the chest
  o Next to the breastbone area: extreme soreness in all four quadrants of the parasternal area is an important sign
• Episodes of short sharp stabbing pains in the chest or other sites: typically being described as chest wall pain (Typically of very short or fleeting duration)

The tendon points are tender to a degree that a bit of mild blunt pressure that should not be tender, elicits a noticeable degree of tenderness. Often, the patients have surprisingly not noticed this tenderness themselves. Many are surprised to find how uncomfortable they are. Often the patients jerk in painful surprise when these areas are pressed.

• Sore tennis elbows, sore golfers’ elbows
• Tender Lateral Epicondyles: "Tennis" elbows
• Tender Medial Epicondyles: "Golfers" elbows
• Achilles Tendonitis
• Tender Achilles tendons
• Tender Metatarsal V bases at the lateral sides of the foot
• Symphysis Pubis: There can be tender areas in the symphysis pubis as well areas such as behind the knee.

The tender areas can occur in any pattern and do not need to be symmetrical. Month on month testing can reveal some left / right fluctuation in tenderness. Tenderness may vary in location between assessments, but tends to stay roughly constant in terms of number of sore points and intensity of tenderness, if the Paill Spectrum disease is unaltered.

• Shoulder tenderness in the shoulder rotator cuff, bicipital tendons,
periscapular muscle and tendons,

- Symphyseal Pubic Tenderness

- Mid-Abdominal Soreness
  - Symptom represents a probable Para-ganglionitis, with tenderness following the line of the aorta to the bifurcation.
  - Then continuing, the right iliac branch is more usually found as tender than the left iliac branch.

There may be associated pancreatitis, characterised by mild elevations of lipase or amylase.

**Pain Treatment Failures Group**
- Failure of tendon pain syndromes to respond to standard therapy or to improve "spontaneously."
- Similar treatment failures exist in the abdominal soreness group.

**Neuropathy Cluster**
- Mononeuropathies
- Tingles
- Footnumbness or Loss of Sensation
- Foot burning, Burning areas in the skin, often very temporary
- Jabbing sharp fleeting pains in any part of the body.
- Weakness
- Wasting

**Autonomic Neuropathy**
- Cardiovascular Instability
- Fluctuant Hypertension
- Syncope
- Cardiac Rhythm Disturbances: VPCs and Supraventricular Tachycardias

- Raynaud's Phenomena
- Microangiopathic circulatory changes:
- ? Buerger's disease or
- ? Thromboangiitis obliterans:
- Cold feet, cold peripheral circulation.

- Bowel and bladder dysfunction
- Erectile dysfunction

**Nasal Cluster:**
- Blocked Nose
- Sinusitis especially where there is a progressive worsening of sinus symptoms over several years.
- Asthma with long term exacerbation with increasing steroid usage.

"Third Wave: Paill Spectrum Infective Disorders"
- "Idiopathic" Hypertension
- Type 2 Diabetes Mellitus
- Abdominal Endocrine organ failure
- Autoimmune disorders
- Mild pancreatitis
- Peripheral Nerve dysfunction / mononeuropathy

Frontal Lobe Symptoms (Primary or Stage 1 Brain Infection).
- JAimi
- Judgement difficulties
- Aggression & anger, Violence
- Irritability
- Mood changes especially Depression
- Impulsiveness

FRAME
- Flattened Facies (Characteristic Appearance in many but not all): suggests often a depressive element.
- Restlessness
- Anxiety and Panic Attacks
- Memory Disturbance, predominantly of short-term memory
- Energy disturbances: some patients withdraw from their family, friends, and begin to do little and communicate little.
- Associative Deficits: narrow spectrum thinking with little realisation of consequences of actions or immediate indirect associations of behaviour. Typically, the person affected just never seems to think of related issues to whatever they are thinking of. If you talk to someone with associative deficits who is concentrating on something else, they may not realise that you are talking to them, even though there may be no-one else in the room.

Other Frontal Lobe Symptoms/ Mixed frontal / Deep Dysfunction Symptoms
- Episodes of anger, violence, or poor judgement, Not typical of that person's usual behaviour.
- Weird Things, Funny in head, "Delirium" in the head is one description given me.
- Blanking Syndromes
- Process Dyslexia is probably a mixed frontal and deep brain (Stage 2
brain infection) syndrome. These patients have a “deficient planning and sequencing function” evident in their behaviour. These patients still are capable of correct number recall and correct spelling abilities. Where chains of "processes " are needed to complete a complex task, these patients just have no chance.

- Blanking Syndromes:
  These people look like a curtain has been pulled over their brain.

Secondary Brain Syndromes (Stage 2)
- Thought Thread: Intense or inappropriate thoughts, which may be associated with language deficits or thought deficits / abnormalities.
- Cross-linked memories
- Process Dyslexia: This is extremely difficult to assess by any but the patients' closest confidants and co-habitants. Memory processing difficulties such as revisits, substitutions, flips, mirrors and drops are typical of Paill Spectrum infection in the symbolic speech processing area of the brain. These symptoms are more easily characterised in concrete from in children with the condition who have Paill Spectrum Dyslexia.
- Fluctuant Temporary Psychosis: A variable loss of reality functioning, with the patient still capable of forcing themselves to deal with publicly acceptable reality.

Specific Secondary Syndromes: usually are diseases in their own right as the appearance is characteristic. Many of these types of syndromes are commonly known by specific names as the clinical features and ages of the affected persons form a classical pattern).

- Mental Retardation from birth
- Developmental Delay
- Delayed Speech & Language develop
- Communication Disorders
- Learning Disorder
- Developmental Coordination Disorder
- Autism
- Autism Spectrum Disorders
- Asperger's Syndrome
- Asperger's Syndrome Traits
- Slow speech development in kids who just seem to have a bit of trouble getting started in life,
- Dyslexia
- Tic Disorders
- Attention Deficit Disorders
- Stereotypic Movement Disorders
- Catatonic States unrelated to drugs or other acute illness
• Dementia
• Amnestic Disorders
• Personality Disorders
• Increased drug inc use esp. narcotics

• Anorexia,
  • The intense beliefs and feelings that seem to define the teenage
  • years.

• Schizophrenia
• Schizoaffective Disorder
• Delusional Disorder
• Psychosis
• Multiple personality disorder,
• Other schizoid type disorders

• People with strange judgement and thought processes who seem
  incapable of learning from experience.

• Mood Disorders
• Endogenous Depression
• Bipolar depressions with psychotic symptoms and irritability
• Disorders of Mood Variation
• Anxiety Disorders

• Conversion Disorders
• Hypochondriasis
• Doctors who are convinced “their patients are nuts” Disorders
• Dissociative Disorders

These form a general description of the brain disorders that are caused by Paill Spectrum (PaillSpectrum). There are many subtypes of each of these categories that can be implied from the group heading, using generally accepted standards of disease naming in taxonomy.

**Other Possible Paill Spectrum Syndromes:**
• Black intense depressions with no obvious cause
• People with scattered disordered thoughts
• Bizarre unrealistic beliefs,
• Insensate violence from criminals, terrorists, and the strange people
  next door,
• Paranoia
• The strange things that “grandma” says.

• Restlessness and fidgets
• Insomnia: predominantly a restless type
• (Insomnia associated with flu like symptoms in germ killing reactions associated with antibiotic or nutritional therapy).
• Nightmares
• Sleep Terrors
• Crying out or talking in sleep where pronounced and frequent
• Sleep Volition Disturbances: sleepwalking
• Sleep time disoriented thinking and disturbed consciousness.
• Sleep Disturbance can be related to fibromyalgic like symptoms in some patients

• Hypersomnia
• Unusual Ideas, often translating into unusual actions
• Adjustment disorders
• PTSD and flashbacks, (may be thought to be drug related).

Learning Deficits
• Discrepancies between maths and English scores in older children.
• Poor learning in general in younger children.
• Dyslexia
• Dyspraxia
• Memory processing difficulties such as revisits, substitutions, flips, mirrors and drops are typical of Paill Spectrum infection in the "symbolic speech processing area" of the brain.

Skin Accessory Problems
Vitiligo
Illness pattern hair loss
Alopecia
These may be related to autoimmunity

Eye Problems
• Iridocyclitis
• Conjunctivitis: Many patients develop slightly red eyes. They seem to respond readily enough to chloramphenicol eyedrops in repetitive dosage. The condition is recurrent and often has no identifiable underlying “trauma” or “allergy” or “irritation” cause associated.
• ? Cataracts
• ? Macular degeneration

Sore throat and enlarged glands: occur as an “associated” phenomenon of Paill Spectrum infection, but usually respond to long courses of penicillin antibiotics.

Weird Events:
• Abnormal drug reactions to immune stimulant medications, other
medications, or antibiotics.
  - Eg tendon rupture with Quinolones
  - Eg Inflammatory reactions and sweatiness reactions such as night sweats with antibiotic therapy.
  - Eg myalgia, Arthralgia
  - Eg Uveitis
  - Eg Paill Spectrum disease flares when high dose hypolipidemic drugs such as the "statins" are used.

- Flu like reactions to antibiotics (Ciprofloxacin, minocycline or rifampicin),
- The occasional flu like reactions documented to Cell mediated immune stimulants such as Imiquimod or Levamisole,

LIR variants of Paill Spectrum will have minimal symptoms of reaction to antibiotics.

- ? Periungual erythema: not a paronychial pattern.
- Arthritis that responds to hand warming at night
- ? Balanitis xerotica obliterans:
- Any tissue condition with substantial T cell involvement and polyclonal lymphocyte proliferation, especially when lymphocyte numbers are very high, should be suspected.

**Hyperviscosity Syndromes or Ig Syndromes**
- Any event that could be attributable to a hyperviscosity syndrome e.g. bony infarct, other infarcts, clots, or emboli in certain circumstances
- Amyloidosis (Secondary)
- Progressive renal dysfunction : esp "stepped" renal deterioration in middle age

**Macro Syndromes**
Macro damage is not a typical Paill Spectrum pattern of tissue damage.
- The syndromes would appear stroke like. The disseminated foci of infection would progress, flare, and then regress over a period of time.
- Epilepsy may be suspected as due to Paill Spectrum if no other biochemical or trauma related cause can be identified.
- Patients who have shown abnormal EEG tracings if no other biochemical or trauma related cause can be identified.
- Patients whose brains on imaging have shown either white "macro" spots on MRI or other functional imaging scan.
- Multiple Sclerosis (MS),

Strangely, these macro lesions may fade or change in the long term.

**Disease resistance**
- Increased fungal infections esp. nail bed tinea.
- Accelerated gum recession, with exposure of subgingival dentine.
**Investigation Of Paill Spectrum & DD**

*My basic group of general tiredness tests embrace:*

- Nutritional Factors: B12, Iron,
- Occasional deficiency states such as vitamin C,
- Gluten sensitivity.
- Hormonal: Thyroid, Oestrogen, or testosterone deficiency.
- Chronic Disease: Renal disease,
- Other: Sleep problems such as Sleep Apnoea
- Connective Tissue Disease ANF, Anti DS DNA, and Rheumatoid Factor.
- Chronic carbon monoxide exposure: carboxyhemoglobin

**Other tests are:**

- Sleep studies.
- FBC/ ESR: normal in Paill Spectrum.
- Assess diabetes " Blood sugar level, GTT, Fructosamine, HBA1c or variants, (insulin antibodies may be important), C-peptide levels
- Myeloid Screen for immunoproliferative disease.

**Summary of Hormonal Tests for assessment of Chronic Fatigue**

- Serum FSH/ Oestrogen in women. The doctor can do Progesterone levels and LH hormone levels as well to give some more information on the patient's clinical condition.
- Oestrogen Deficiency Score
  This is one of my favourite questionnaires. It provides an objective score that gives an "average" of the amount of oestrogen hormone "effect" in the body. It focuses on Mood Symptoms (eg depression, unloved feelings), Body Discomforts (eg sweats, itches, dry skin and flushes) and Genital Symptoms (eg poor lubrication, discomfort with sex, urinary tract infections). Use this questionnaire to monitor the effect of hormone therapy on patients.
- Thyroid Function Tests especially Serum T4 and TSH.
  If any thyroid manipulation is undertaken, care must be taken to keep thyroid status within safe reference range boundaries. A free T3 assay may be useful if aggressive over replacement has been instituted.
- Serum Testosterone (in men)
- Rarely in women: an androgen assessment eg DHEA

**Nutritional Assessments:**

- Iron Studies: Serum Iron, TIBC, % Sat, Serum Ferritin
  Iron studies are important to exclude collateral sources of tiredness.

- Serum B12
- Red Blood Cell Folate
• Serum Zinc
• Anti Gliaden Antibodies: I find Antigliaden IgG and Antigliaden IgA to be adequate for purposes of assessing the need for a trial of wheat free diet. Trial of diet is adequate to assess the need to undertake a wheat free or gluten free diet in most adult patients.

• Schilling Test
  o I have my own standard criteria for the Schilling test result. If your absorption is:
  o <5%: give injection monthly
  o 5-8%: give injection two monthly
  o 9-11%: give injection three monthly
  o 12 or more %: give oral B12 supplements

Do the Paill Spectrum Blood tests Group:
• E&LFTs
• C3,
• ANF
• Se B12,
• RBC Fol,
• Se Zinc,
• Antigliaden IgA, Antigliaden IgG
• IgG IgA IgM (sometimes called GAM)

Reference ranges for immunoglobulins EPP.
• Ig Gamma Band: 10 or higher: always abnormal, high probability of diagnosing Paill Spectrum.
• Ig Gamma Band 8-9: Suspicious of early Paill Spectrum disease. I believe you do not see brain lesions except in patients with a Gamma Band of 10 or more. (Usually).

The association of the clinical syndrome and IgG/ IgA/ IgM or EPP Gamma Band semi quantitative assay will usually result in the making of a diagnosis that will mostly be confirmed by clinical response to treatment.

• An increase of IgG of two g/l or more over time suggests an active immune process underway.

• A decrease of Gamma Band of 1g/l in response to treatment, confirms a likely diagnosis of Paill Spectrum infection. A fall in Gamma Band in response to a course of treatment with a tetracycline is diagnostic. This is further confirmed when the gamma rises over the 3-9 months following cessation of the antibiotic.

These criteria must be more loosely interpreted in patients
• With hypogammaglobulinemia;
• With depressed white cell counts, especially if predominantly
lymphocyte counts affected (I believe this may occur with some heavy metal exposures).
With immune dysfunction
With exposure to medical immune suppressing agents such as chemotherapeutic or cytotoxic agents.

Always check Paill Spectrum marker levels in patients with any immune dysfunctions:
- Steroid using patients including patients using asthma steroid treatments or nasal allergy treatments.
- Cytotoxic immunosuppressants using patients
- Downs Syndrome patients
- Very Young and Very Old patients

Connective Tissue Antibodies & Autoantibodies:
- ANF Anti Nuclear Factor = ANA Anti Nuclear Antibody
- Rheumatoid Factor or Rheumatoid Protein
Rises often occur in post acute tissue damage events in Paill Spectrum and usually fall over the ensuing months. A component of the antibody rise may remain long term.
- Anti skeletal muscle antibodies
- Anti acetylcholine receptor antibody
- Anti adrenocortical antibody
These may often be found elevated in Paill spectrum infections.
Rises often occur in post acute tissue damage events in Paill Spectrum and usually fall over the ensuing months. A component of the antibody rise may remain long term.

Principles of Paill Spectrum Management
The condition is not hard to treat, just slow to treat

1. Manage conditions or treatments causing immune suppression:
- Stop or reduce substantially Cytotoxics or bone marrow suppressing agents.
- Stop or reduce steroids or prednisone.
- Nasal steroids must be reduced or preferably stopped.
- Control baseline medical conditions such as: diabetes, asthma, allergies, congestive cardiac failure with dependent peripheral limb swelling (oedema), and parasitic infestations.
- Investigate marrow hypo function and manage if possible. Especially beware of heavy metal toxicity. Identify the patient whose white cell count remains remarkably stable, in different clinical situations.

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2. Ensure GIT function
   - There must be no persisting malabsorption, even if very mild
   - Sort out GIT complaints such as irritable bowel disease or giardia.
   - Celiac Diets where patients have blood antibodies > 25% of reference range, calibrated against endoscopically proven Celiac disease. Exclude Wheat Protein Allergy (++++ critical).
   If wheat allergy confirmed, begin a diet to minimize exposure to wheat proteins.

3. Fix Nutrients affecting Immune Function
   - B12: I prefer a level of over 300 ng/l in all patients. Any patient with a low B12 level as well as being over 50 years of age, requires an absorption test for B12. Such a test is the Schilling test, where available. If a Schilling test is unavailable, time to drop B12 level to threshold adequate levels will dictate the replacement interval.
   - Folic Acid levels adequate over 250 mcg/ml, preferred over 300 mcg/ml.

Vitamins are best managed using supplements such as bioavailability weighted "Multivitamin and Multi-Mineral" tablets. Children will require a similar liquid or a soluble/ chewable tablet.

My criteria for vitamin supplements are that they must contain at least:
   - 3-4 mcg of Vitamin B12
   - 200-250 mcg of folic acid (Folate)
   - 50-75 mg of Vitamin C
   - 3-4 mg Zinc

In addition, they must contain a broad range of minerals and a general broad list of B group vitamin ingredients.

**Omega 3 & Omega 6 fatty acid supplements** are advisable.

**Serum Zinc:** I prefer levels of over 20 (RR 12-30) micro Molar
RBC Zinc or white cell zinc levels may also be used as a therapeutic guide.
   - Aim for 44 mg elemental zinc once daily for most patients.
   - If the patient is especially at risk, initiate therapy with 44 mg twice daily.
   - Patients with wheat allergies generally need at least six months of Zinc supplementation at high doses.

Beware extended dosage with zinc in Patients with hemochromatosis these patients.
Patients losing weight can appear to have artificially elevated zinc levels.
Germ killing reactions may occur with rising serum zinc.

Standard advice for taking zinc is:
- Take with food or before bed
- Encouraging patients to comply with long-term therapy means that the doctor needs to take care to maximise treatment "comfort."

Preferably, check the zinc level after each four months of therapy. Do not take the blood test within 12 hours of taking the last zinc tablet. I prefer to use zinc supplements such as tablets rather than diet, as the elevation in body zinc levels is more reliable.

4. Physical therapies, Heat therapy, Booster therapies & Other Medications

- Heat therapies
  - (The body is kept warm by the application of heat in part or in full).
  - Cover elbows, use gloves, and keep hands under bed covers at night.
  - Generally keep the body warmer for more hours per day.

- Thyroid or testosterone hormone
- Immune stimulant medications eg levamisole

Other Medications

- Avoid treatments with undocumented cell mediated immune effects.
- Many home herbal remedies have anti-inflammatory effects.

- If possible, check that the medication does not have an anti-inflammatory effect mediated by suppression of:
  - Interferon esp. Gamma
  - TNF
  - Cytokines such as Interleukin 2.
Therapy therapy: Considerations in Management

Before considering antibiotics, set goals for therapy: Suggestions include:

1. IgG+igA+lgM targets:
   - I prefer to see a 1.0 g/l Immunoglobulin fall as a response to treatment. In the long term,
   - I prefer to see Immunoglobulin levels fall to: IgG+igA+lgM-1.0 < 9.0. Higher levels indicate continued immune response to infection.
   - There must be a completed IgG/IgM pattern immune response in the short term. (See 3). These criteria may be unable to be achieved in HIR variant individuals.

2. Clinical symptom response must be achieved

3. IgG/IgM plotting to assess that a maturing immune response is occurring. The key pattern is a rising then falling IgG profile, following a similar IgM profile.

4. Diagnose LIR variant disease or Pail Spectrum in an Immunodepressed patient.
   - It will meet clinical disease criteria only. i.e. Immune markers will be relatively or even absolutely normal.
   - Immunodepressed patients may have a very prolonged or delayed immune response to antibiotic therapy, occurring a number of months more slowly than in the typical patient of any of the variant subtypes. Immunodepressed patients are far more likely to be LIR variant cases.

5. Consider Antibiotic therapy for all brain lesions early, but use
   - Rifampicin as first line ONLY where there are specific clinical indications that make the risk justifiable.
   - Use a low-grade antibiotic inhibitor such as:
     - Tetracyclines: the main members are minocycline, doxycycline and ordinary tetracyclines. Minocycline as the tetracycline of choice in Pail Spectrum infection.
     - Macrolides: clarithromycin, roxithromycin

6. Consider the appropriateness of particular antibiotics and possible complication scenarios with particular antibiotics.
   - I prefer not to use bactericidal drugs like the quinolones (eg ciprofloxacin) as first line therapies. Clinical circumstances may dictate the opposite strategy.
   - I prefer to avoid long acting drugs such as azithromycin in first phase treatment in view of the impossibility of stopping therapy to reduce
"germ killing reactions". Clinical circumstances may dictate the opposite strategy.

- Quinolones and tetracyclines may not be appropriate for children of particular ages or in pregnancy.
- Alternative antibiotics can be used if indicated. (For example, if a patient is allergic to one of the antibiotics). Alternate drugs from within the same family of antibiotics will usually be adequate for therapy though may not be preferred.
- Roxithromycin (macrolide class antibiotic) as the oral dispersible tablet is useful and easy for children, as long courses can be given without the need for preservation of the antibiotic syrup.
- Clarithromycin (Klacid) is effective, but needs to be given more often per day to achieve 24-hour cover.
- Azithromycin (macrolide class) is more important where LIR variant Pill Spectrum disease exists. It is also useful where compliance with therapy is likely to be an issue. It is more suited for use in maintenance therapy, where its long half-life is an advantage, rather than a source of risk for germ killing reactions, as in early treatment initiation regimes.
- Ciprofloxacin has better tissue penetration especially through the blood brain barrier. "Bacterial Killing Reactions" may be more pronounced with this antibiotic though.
- Available medical supervisory time is a likely limiting factor.
- Patient compliance and tolerance of therapy is another major factor limiting treatment.

7. Probiotics

- Probiotic supplements with Bifidobacteria, Lactobacilli, and propionobacteria may be necessary. They are important in controlling bowel upsets with the extensive powerful antibiotic therapy. Bowel Upsets will occur where multiple powerful antibiotics are used. As little as a single dose of these probiotic germs may remove bubbling, cramps, or low-grade diarrhoea. Other probiotic supplements may also be effective in controlling bowel "upset" symptoms.

- I believe preparing the patient for a bowel flora reaction with triple antibiotic therapy, is essential.

Management: What follows is my preferred method for initiating treatment.

All doses in children are reduced by a weight or surface area formula as appropriate at all stages of therapy.
All therapies may be modified by patient clinical circumstances, but the general patient principles remain.

1. **Pre-antibiotic Counselling** must be undertaken. Patient relationship building needs to be well established at this stage.
   - The patient needs to be convinced that they are ill. I have found that only people who are certain that they have an illness will be motivated to comply with a treatment regime.
   - There must be “Trust” in the doctor’s decisions.
   - Nutritional therapies need to be considered at every stage of Paill Spectrum therapy.

2. **Antibiotic Usage Schedule**
   - Some patients respond extremely well to dietary and nutritional therapies alone. I still believe that even these patients should undergo antibiotic therapy. Clinical deficits in behaviour and mental functioning can be subtle with Paill Spectrum damage syndromes. It may be difficult to determine when a treatment response begins to become a disease relapse.
   - One month to three months of treatment with a standard inhibitor should be initiated.
     - eg Minocycline 100 mg daily,
     - eg Clarithromycin
     - eg Roxithromycin
   - (These inhibitors are preferred to be 24/7 agents). I prefer three months of these therapies to precede Rifampicin initiation.
   - These therapies may be prescribed for shorter or longer periods as clinical circumstances dictate.
   - A number of patients may respond very well to a single antibiotic and be unwilling to continue with further therapy. I prefer every patient to have completed three antibiotics for a minimum of two weeks. Many patients will clinically respond well to single antibiotic schedules or to double antibiotic schedules only.
     - 200 mg daily of minocycline can be initiated if the risk of complications is low. If there is an active brain lesion due to Paill Spectrum disease, lower antibiotic doses of minocycline are safer, as an initiation regime. Clinical imperatives may dictate higher antibiotic doses.

Generally, if brain infection is suspected, lower antibiotic doses are advisable. Lower antibiotic doses in the triple antibiotic therapy are also advisable. Brain infections generally respond well to the first antibiotic inhibitor initiated.

3. **Monitor Treatment Response and Treatment Complications**
   Note that initially there is an immune response to antigen released by germ killing reactions that increases antibody levels in the first three months.
IgG/ IgA / IgM
Renal function assessments in treatment. (Remember Amyloidosis).
(Use of Allopurinol (short term), may be indicted if the urate level rises in the first few
days of therapy.)
IgG/ IgM response to confirm diagnosis, confirm immune response, and confirm therapy
effectiveness.

C3 or C4
Assessment of Autoantibody Titres: ANF, Rheumatoid Factor,
Blood Sugar or glucose levels need to be monitored carefully in patients who have
symptoms of hypoglycemia
Blood sugar levels need to be monitored carefully at two to four months into antibiotic
therapy.

Abnormal Blood counts or ESRs are not typical of pure Paill Spectrum.

4. Rifampicin Initiation

- Once or twice daily Rifampicin dosage for adults:
  300 mg daily or twice daily for a typical adult.
- Introduce Rifampicin in conjoint with the standard antibiotic inhibitor
  for two weeks.

- Rifampicin may be initiated in an intermittent format eg twice weekly
dosing in early disease treatment until 3-4 weeks have gone by. I
often do this in any patient who has noticeable symptoms on day 3 of
treatment.

- Rifampicin dosage is in the range of 300-600 mg daily. The higher
dose is often needed in LIR variant patients.

5. "Germ Killing" Reactions:
Antibiotic counselling must be very intense prior to initiating this therapy.
Generally, start low and go, more so with this stage of Paill Spectrum therapy than with
any other stage of Paill Spectrum therapy.

Always have an escape plan for therapy: do not initiate with long half-
life and very potent therapies.
I prefer to maintain improvements by maintaining a well-tolerated
background inhibiting antibiotics for the Paill Spectrum organism, if a germ killing reaction
to minocycline has occurred.

The counselling session carefully warns the patient what to expect in
terms of "Reactions" with the use of this antibiotic. Common clinical events include:
- Weird sweats
- Tremor
- Tremulousness that can extend into the head: ie to cause feelings of
  anxiety or panic
- Severe Malaise or generally a feeling of illness
- Movement disorders

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• Severe restlessness and Insomnia
• Akathisia, restlessness, and movement disorders

• Frontal lobe reactions would expect to include more fuzziness in the head, memory disturbance or forgetfulness, headaches, confusion, anxiety or panic attacks, worsening agitation, sleeplessness, and symptoms such as flaring depressive state or blanking phenomena.

• Use the germ killing extinction formula in the Paill Spectrum CDs.
• Alternatively, cease treatment until the germ killing reaction subsides, then reinitiate therapy at a lower dose eg three times weekly dosing. After several weeks of intermittent therapy with no germ killing reaction occurring, rest full therapy.
• Alternatively, reduce intensity of therapy or change to a less potent or less penetrating drug.
• (Clinical circumstances and clinical urgency will dictate most beneficial course of action.

6. Treatment of Germ Killing Reactions

- Treatment of "germ death" reactions is not for the faint hearted and some very unusual and very distressing reactions commonly occur. The patient is ordered to return between Days 2-7 of treatment after rifampicin is initiated. At this time, treatment reactions are assessed. Reactions can be very mild.
- Anti-inflammatory medications may be useful in limiting distressing anti-inflammatory reactions.
  - Simple antibiotic medication cessation may be a simple reaction limiting strategy. Continuing pre-rifampicin inhibitors for several months longer before reinitiating rifampicin may also be a safer option for some patients.
  - Oral prednisone or similar class steroids may be useful.
  - Other possibles: antihistamines, anti-5HT agents, leukotriene inhibitors, major tranquillisers, benzodiazepines, and sedative medications of any type.
- Effectiveness of these anti-inflammatory medications is limited.

The easiest and moist effective management of a Rifampicin germ killing reaction is simply to stop therapy until the reaction subsides, usually within one week post antibiotic cessation.

The patient returns at the end of triple antibiotic therapy (i.e. 2 weeks later), for dose adjustment. Any germ killing reaction has generally faded completely by two to three weeks from start of therapy.

7. Once regular Rifampicin antibiotic therapy is established,
Aim for triple drug therapy for all patients for a minimum two-week burst.
I prefer to see every patient given two weeks of triple drug therapy if
possible or if accepted by the patient.

If the patient is unwilling or unable to initiate an initial burst of triple antibiotic therapy, single or double antibiotic therapy may be continued, with a reasonable clinical result.

Patients often cease therapy. Paill Spectrum disease recurrence may recur at 3 – 9 months after cessation of therapy.

Patients may drop back to single or double antibiotic therapy following a clinical response or pathology test response after a burst of multiple drug therapy. This is not ideal but may need to be accepted due to patient resistance.

**Typical Paill Spectrum antibiotic “initial triple kill” regime drugs are:**
- Rifampicin 300 mg +
- Minocycline 100 mg +
- Ciprofloxacin 500 mg
All as a single daily dose.

In LIR variant Paill Spectrum infection or difficult to control disease:
- Double the doses of Rifampicin and Ciproxin:
  - Typical drugs are
  - Rifampicin 300 mg twice daily +
  - Minocycline 100 mg daily +
  - Ciprofloxacin 500 mg twice daily.
  - Twice daily medication regimes are more effective for disease control.

**8. Long Term Maintenance Therapy**

- Match the treatment regime to the disease burden. Some patients will respond on once weekly therapy. Some patients very definitely will need daily double or triple antibiotic drug therapy. Simple treatment options are not a preferred treatment but may be dictated by clinical circumstances.
- I Prefer: Minocycline to be continued at 100 mg daily. Other antibiotics such as macrolide or quinolone class antibiotics can be used in long-term therapy as an alternate choice to minocycline.
- Avoid use a single drug for long-term therapy.

- Some patients may achieve symptom resolution on a single medication. Use of single antibiotics for limited times may achieve symptom resolution but is not a preferred therapy.
- Long-term treatment should preferably involve a *minimum* of two drugs in a once weekly dose.

- When using antibiotics in long term therapy: a 24/7 inhibitor is advisable in the mix. I strongly prefer using a 24-hour a day acting inhibitor. Patients may insist on single antibiotic therapy or even cease treatment following a clinical response. The patient should preferably be advised as to the risks associated with ceasing therapy.
• My preferred maintenance therapy is for a daily dose of macrolide or tetracycline for 24/7 plus a weekly dose of Rifampicin. This therapy is suitable only for simple uncomplicated patients with no significant brain lesions and no severe disease symptoms.

• In patients with brain lesions or symptoms persisting or breaking through on the above regimen:
  Daily macrolide or tetracycline inhibitor +
  Daily 300 mg Rifampicin long-term.

• LIR variant disease with patients with underlying immune disturbances may require triple antibiotic therapy for up to months.

• Dose reduction to weekly doses may result in the patient "hitting the wall." The patient's symptoms may recur. Match treatment to the patient need and response. A simple burst of triple antibiotic therapy followed by more maintenance therapy will usually regain control of the Paill Spectrum infection.

• The best drugs in LIR disease involve a combination of Rifabutin and azithromycin. I would normally complete a cycle of at least two weeks of Rifampicin/ minocycline and ciprofloxacin therapy, before changing to the more powerful drug combination. Bowel flora upsets are more common with triple antibiotic therapy.

• Ciprofloxacin 375 mg twice-daily minimum for an adult. 750 mg can be initiated twice daily if tolerated. Ciprofloxacin has a high incidence of bowel flora upsets. Ciprofloxacin has high intraneural penetration and is very useful for long term therapy failure or symptom escape, probably related to failure of standard medications to penetrate intraneural protected sites.

The Paill Spectrum disease does not disappear even if there has been a marked response to treatment. A disease response does not equate with cure in Paill Spectrum therapy. If the immune status of the patient deteriorates, so will the clinical symptoms patient

Issues In Second Phase & Maintenance Therapy

• Many people, who have a defined or substantial elevation of IgG with Paill Spectrum, do not have many symptoms associated with this antibody rise.

• Complications can occur in people with minimal symptoms. Patients may deteriorate rapidly, especially if their circumstances deteriorate. Eg with dieting,

• An antibody rise (IGG IgA IgM), C3 fall often will indicate the acute deterioration in clinical circumstances, before a recognisable brain injury event may occur.

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I would use higher dose antibiotics long term in LIR variant Paill Spectrum disease or in patients with many symptoms. Many Fibromyalgia patients or LIR patients without brain disease require high dose antibiotic treatment. Many fibromyalgia or LIR variant patients will require long-term double antibiotic therapy, as a minimum.

My preference is for every patient with LIR disease to have two or three months of triple antibiotic therapy. Use the blood marker tests to guide treatment intensity and duration.

This should then be followed by extended double drug therapy.

Well patients usually achieve effective disease control with minimal therapy: ie two weeks of triple antibiotics and then three months of double therapy. I believe weekly therapy with two antibiotics is then an absolute minimum requirement for at least 12 months.

In some patients, especially those with myalgias, Dose reduction to weekly doses only, often results in the patient "hitting the wall." Long term treatment for years with multiple antibiotics, may be required to control disease activity.

Extra treatment bursts may help to regain control of the disease in the long term.

My preferred long term medication regime is as follows:

- Rifampicin is prescribed on a regular daily schedule. (300 mg daily) plus minocycline 100 mg daily. Ciprofloxacin is ceased.

- There is good potency and good tolerability. Most patients stay very well with minimal risk of relapse on this treatment regime long-term. Generally, immunoglobulin levels fall after three months of antibiotic therapy.

- EPP gamma checking or immunoglobulin checking should document falls in immunoglobulin levels with therapy. If this is not occurring, higher dose antibiotics may be indicated.

- There are a number of choices for therapy after this. Long-term treatment intensity depends on disease burden and disease responsiveness to therapy.

Possible maintenance treatments include:

- 600 mg Rifampicin weekly plus minocycline 200 mg weekly.
- 600 mg Rifampicin weekly plus 100 mg minocycline daily.
- 300 mg Rifampicin daily plus 100 mg minocycline daily.
- Two week burst of triple antibiotic therapy each six months in addition to the daily rifampicin / minocycline combination.
- Upgrade to Rifabutin Azithromycin \ Ciprofloxacin combination until an IgM response occurs and an IgG drop is noticed. Drop back to usual double drug combination when clinical circumstances allow.
The basic principles are: use a 24-hour a day inhibitor always.
- This would include either minocycline or ciprofloxacin or macrolide antibiotics interchangeably. Other antibiotics in the same class as minocycline (i.e. tetracyclines) are not as useful as minocycline.
- Any of the macrolide antibiotics are OK.
- Use Rifampicin at least weekly and always in combination with the Inhibitor.

9. LIR Variant Disease
Special Immune markers are required for LIR variant disease, namely longitudinal IgG/IgM quantitation and follow up.
Long-term daily presence of an inhibitor and at least weekly use of a high potency killers are the preferred minimum level treatments.
A patient with LIR disease needs to have check ups done at least twice a year if well and at any time they may feel unwell. Symptoms are a good guide to a flare.
Management: Treating Paill Spectrum is a lifelong goal.

Instruction for Doctors for: Patients with Chronic Fatigue Seeking Treatment: “A suggested model”

Assess / Write Down Symptoms: eg

- Chronic fatigue
- Loss of balance or Dizziness
- Sweaty Hands
- Soreness:
- Elbows
- Chest in sharp twinges here
- Stomach
- Pubic Bone
- Knees
- Achilles Tendon
- Base 1st metatarsal
- Fibromyalgic ache in Upper Trapezius and Upper Deltoid
- Mood, Anger, Irritability
- Memory changes
- Short attacks of Jitters, shakes, and anxiety
- Other:

It is important to map symptoms, as they are useful to map treatment response to Paill Spectrum Treatment. They also help with follow up of treatment progress.

A doctor then does these blood tests.

- E&LFTs: Inc urate / dec chol
- Serum B12: should be over 300 ng/ml (220nM)
- RBC Folate: prefer over 250 mcg/ml (570 uM)
- Serum Zinc (RBC Zinc can also be used): prefer over 16-17, but not too high (>25)
- Antigliaden IgG and Antigliaden IgA: normal is less than 20-25% of reference range: assess clinical response to diet
- Serum: IgG IgA IgM: (Add these up and subtract one)
  Normal IgG + IgA + IgM – 1.0 < 10.0 (GAM1),
  Below this can still be unwell
- C3 and C4: C3 esp. must be above reference range, below 1000 implies acute tissue damage
- ANF: appears late after damage: usually low levels that disappear over months, similar for many other autoantibodies

These form a basic Paill Spectrum Blood Test assessment group.
Basic Treatment is Over the Counter:

- Multivitamins e.g. Centrum 50+: One daily
- Gluten Free Diet: If Appropriate, Useful for even mildly allergic patients
- Zinc 22mg elemental: a maximum of three months at 50mg daily. A blood test should be used to guide treatment after this time frame. Aim for a level of zinc in the mid to upper reference range at the completion of treatment. (Zinc is the icing on the cake. Don't get too worried about it early).

Medications

- Check for tetracycline allergies. Macrolides are also suitable: in particular Rulide for children. Germ killing reactions are common: always call the patients in and assess them, but do not panic.
- Give a script for the antibiotic Minocycline for 60 Rpt 2 enough for three months@ two tablets daily (once daily is OK).

Get a dosage box for your treatment doses.