

Chronic Cough :A Marker for Silent Diseases

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Abbreviations and key words:

ACE = Angiotensin converting enzyme

C Ch = Chronic cough

GERD = Gastro Esophageal Reflux Disease

NAEB = Non Asthmatic Eosinophilic Bronchitis

PNDS = Post Nasal Drip Syndrome

PPI = Proton Pump Inhibitor

UACS = Upper Airway Cough Syndrome

Chronic cough (cch) is very frequent in clinical practice. The cause is not always obvious. (C Ch.) may be the main manifestation of important and common group of diseases or syndromes as (GERD), (UCSA) or asthma where its usual cardinal symptom or signs are not evident and cough in fact is the main marker for many entities. To think of these entities and to treat them may solve the problem in sizable bulk of patients, publication in English from 1980 until 2008 were reviewed and relevant information is referred to lengthy, costly, and repeated investigations may be needed.

(ACE) inhibitors should be inquired about from the beginning of the workup, and (NAEB) should be thought of. Diagnosis of psychogenic cough is overused and this should only settled at after excluding all organic cases.

Appropriate treatments may achieve relieve or cure as treating (GERD) with lifestyle, (PPI) and prokinetics or even surgery. On similar ground treating (C Ch.) in asthma variant treating as a conventional case of asthma may terminate the patients suffering.

Chronic cough in this communication is defined as persistent cough for over eight weeks duration without obvious discernible cause with an almost normal chest radiogram in a non immune compromised adult.

Chronic cough is a frequent complaint which faces the family doctors, practitioners, consultants and respiratory specialists. In the last three decades, lot of work and publication which could pin point the diagnosis in about 95% of the cases^(1,2) yet (C Ch.) may remain as dilemma in some cases. It is estimated that between 6-49% of case fall either in a

miscellaneous or in the undiagnosed group among eleven series of patients⁽³⁾. I see no gain or benefit in dividing cough into: sub acute and chronic clinically, therapeutically or academically and what is called or labeled sub acute^(1,2) is in fact mostly are post infective, viral, bacterial or rarely fungal, it is part of long convalescing process from a nasty agents⁽⁴⁾.

The history and physical examination remain to be the first basic step in evaluating (C Ch.) as in any condition in clinical medicine.

Although the characteristics of cough show no reflection on etiology^(1,2,5), yet it could be of help in some cases as the “whoop” and vomiting as described by the patient, relatives or observer indicating the infection with pertusis⁽⁴⁾ however pertusis in not mentioned in many articles concerning (C Ch.) yet it may exist in a cluster gathering and in certain geographical areas⁽⁶⁻⁹⁾. On the same token purulent sputum usually make the physician lean toward infective process. (C Ch.) in special position may point to (GERD) as a cause but this is not consistent⁽¹⁾.

Chronic smoking remains to be an important cause of (C Ch.) whether primary or secondary with almost normal chest x ray, the easiest approach is to stop smoking and watch for improvement⁽²⁾. Chronic smoking should not be used an umbrella to miss a small bronchogenic and its high association with smoking⁽¹⁾.

The main bulk of (C Ch.) fall under four major categories of diseases though they are well defined and known in medical practice but in good number of (C Ch.) could be the only manifestation and the rest of their signs and symptoms remain dormant since the adjective of “silent” disease or syndromes is assigned to them.

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Heading these groups is (UACS) which is used to be called (PNDS), this include a variety of conditions as sinus disease, allergic rhinitis, the cause is either extrensie due to exposure to an irritant or intrinsic^(1, 2, 3).

The history of throat clearing, hawking cough or cobble stone appearance of the throat are not necessary for a diagnosis of (UACS). One should look at home and the work condition of the patient hoping to find an offending agent to remove and cure the condition^(1, 5). If this end to no avail treating the case empirically by first generation antihistaminics, decongestants and nasal inhaler

with good response may put the physician closer to the diagnosis of (UACS). If infective sinusitis suspected a good course of antibacterial covering aerobe, anaerobe, hemphilus influenzae, for 2-3 weeks should be started and may resolve the issue⁽¹⁰⁾.

Sinus x ray could help in great number of cases⁽²⁾ and one may need CT scan⁽⁴⁾ rarely. When allergy is suspected than skin testing and immunological studies could be referred to.

The next large group of chronic cough is attributed to silent (GERD), it is so common and may account to 75% of (C Ch.) cases⁽¹⁾.

Table : Summary of Studies of Common Causes of Cough Reported in the Literature*

Study/ Year	Patients, No.	Country	PNDS/BA/GERD, †%	E	PI, %	CB (COPD)	Misc or No. Dx
Irwin et al ² /1981	49	US	82	0	0	12	6
Poe et al ¹⁸ /1982	109	US	44	0	25	12	19
Puolijoki and Lahdensuo ¹⁹ /1989	198	Finland	34	0	15	4	47
Irwin et al ³ /1990	102	US	86	0	0	5	9
Pratter et al ⁴ /1993	45	US	96	0	0	0	4
O' Connell et al ²¹ /1994	87	Ireland	40	0	10	0	49
Mello et al ⁶ /1996	88	US	92	0	0	0	8
McGarvey et al ²⁰ /1998	43	Ireland	81	0	0	0	19
Brightling et al ¹³ /1999	91	UK	47	13	13	7	20
Palombini et al ⁷ /1999	78	Brazil	94	0	0	0	6
Ayik et al ¹⁴ /2003	39	Turkey	44	31	5	0	20

*BA = bronchi al asthma; CB = chronic bronchitis; EB = eosinophilic bronchitis; PI = postinfectious; Misc = miscellaneous; Dx = diagnosis.

† One, two, or all three diagnoses are present

The mechanism of cough in (GERD) is probably mediated by a reflex through vagus nerve, beside possible multiple micro aspiration^(1, 2, 3).

It is not necessary to have gastro intestinal symptoms such as heartburns or eructation, chest discomfort or non cardiac chest pain to make the diagnosis or (GERD) as a cause of (C Ch.).

The diagnosis is usually settled by aggressive treatment when suspected and this achieved first by the style of life, diet, weight reduction, to avoid smoking and alcohol excess tea, coffee, and minerals, with elevation of head during sleep. Secondly by ample administration of (PPI) two or three doses may be required per day, the target is to

keep the Ph of the stomach and esophagus under control for about 24 hours a day, for adequate period of time which may last 3-6 months^(1, 11).

Thirdly prokinetic agents could help as metchlpromide before each meal. The reader may be surprised to start aggressive treatment before further investigations my view is that this approach is more practical, convenient, easy and cost effective.

The ph monitoring of the stomach and esophagus with pressure measurement is most dependable presently but it is not 100% reliable, it could be normal, it is inconvenient, and costly beside it is not

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available in small centers or every city. Esophagoscopy and barium study is likewise may not give definitive diagnosis.

If all investigations were not helpful and the aggressive treatment for (GERD) has failed and other conditions have been excluded one may revert to the surgical intervention for (GERD) ^(1, 11, 12, and 13).

Repeated surgery may be attempted after the failure of the first attempt where excellent results are claimed ⁽¹⁴⁾.

The third large group of (C Ch.) is "the silent asthma" of the "asthma variant". This group constitutes about 53% of (C Ch.) and the chronic cough may be the only presentation, patients show no evidence of obstruction as wheezing ^(2, 15).

If silent asthma is suspect confirmation is needed by performing methicholine challenge testing. A negative test is of great value to exclude asthma as a cause of (C Ch.) since its predictive value is 100%. However this test is not specific because its positive predictive value is only 62-80% ^(1, 16, 17, and 19).

If asthma is suspected on the bases of positive methicholine testing, the patient is to be treated as ordinary case of asthma ⁽²⁰⁾, if this fails to clear the cough, one have to presume the test was a false positive and to seek an alternative possible diagnosis ^(1, 20).

A rather new entity is coming into view as a cause of (C Ch.) and this is "Non Asthmatic Eosinophilic Bronchitis". It was first described in the mid eighties: characterized by chronic cough, without evidence of respiratory obstruction, a normal sprriometry, and the persence of 3% or over of eosinophil among sequmus cells in the sputum or bronchial washout, in addition of infiltration of bronchial wall by eosinophils. In asthmatic patients sputum also contain eosinophils as well as in the bronchial wall but there is slight deference in (NAEB)⁽³⁰⁾ that there is increase number of the mast cells in the bronchial washout in (NAEB) compared with asthma while mast cells are more in the smooth muscles in asthma compared with (NAEB) ⁽³⁾.

The incidence of (NAEB) among (C Ch.) patient vary from 13-33% depending on geographical area as report by deferent authors ^(1, 3, 21). Its response is favorable to oral corticosteroid ^(1, 3). It is a curable disease except some cases may end in airway narrowing or irreversible obstruction due to late diagnosis and treatment ^(21, 22).

Physicians and family practitioners should not forget or miss an important cause for (C Ch.) and this is the intake of (ACE) inhibitor, it affects 5-20% of its user, female are affected more. The cough is not dose related and neither affected by the brand nor the class where its number is proliferating to a large number. Changing the brand will rarely affect the outcome of the cough. Stopping the (ACE) will terminate the cough which may take few days or in an average period of 26 days ⁽¹²⁾.

Since (ACE) inhibitor is so useful in clinical medicine as in hypertension, congestive heart failure, kidney protection and improving endothelial function. It could be replaced by angiotensin II receptor inhibitor ⁽¹⁾.

As was shown, the main bulk of (C Ch.) will fall in the pathogenic triangle which is composed of (UACS), (PNDS), (GERD) and asthma variant. The new entity of (NAEB) will add to this volume. It is estimated that those will account anywhere in between 40-96% of all cases of (C Ch.) ⁽³⁾ (See the table).

Two causes of the pathogenic triangle are found together in 53% of the case and all the three causes combined are found in 35% ^(1, 2, and 23). It is surprising to see in the table ⁽³⁾ that the incidence of (NAEB) was 0% in nine out of the eleven series. Two of them only were written before the description of the entity (NAEB).

Finally it is impossible to end discussing a medical condition without touching on the "PSYCH and the SOMA". Psychogenic (C Ch.) does exist but it is way over estimated, in a study it turned up that 23% of cases referred to a specialist returned to be a missed diagnosis ⁽¹⁾.

As happen sometime in chronic headache labeled as psychogenic than it turn into full blown up tragic picture of brain tumor where it is too late to help. Psychogenic headache should only be a diagnosis by exclusion of other causes. There is nothing specific for this entity as the cough is absent during sleep is not hawking in type, neither there is special character as all these could occur in organic diseases as in (GERD) ⁽¹⁾.

But a personality background, the presence of circumstantial evidences, the absence of cough during enjoyable time as during vacation may all be suggestive of psychological element ^(1, 2, 10, 22) but again emphasizing the exclusion or the causes one could make the diagnosis of psychogenic headache, this is strengthen if favorable response follow the

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administration of an anxiolytic agent and or psychotherapy.

There are few unusual cause of chronic cough which should be kept in mind such as sarcoidosis, endobronchial tuberculosis, hidden small Bronchogenic carcinoma, disseminated carcinomatosis, histoplasmosis, coccidiomycosis, pharyngeal dysfunction, aspiration, scleroderma, foreign body, left ventricular failure, or certain neurological disorder^(1, 25), where more sophisticated investigation are needed such as high resolution CT scan, repeated Ph monitoring with pressure measurement of the of the esophagus, bronchoscopy with endobronchial biopsy, wash out and bacteriological and fungal studies and esophogram. The repeated studies may give positive result which were negative earlier either missed or the pathological process was in an early stage of cooking⁽¹⁾.

The term "suppurative process" referred to, we would rather not use this term and use instead "infective or inflammatory process"⁽¹⁾. Although an overt case of bronchiectasis as an example could take or present as a suppurative course than in such case it should not be a diagnostic problem. In the rare occasions of persisting (C Ch.) due to infective process and after thorough investigation is to be treated with a very wide umbrella of antibacterial for a period of 3 weeks⁽¹⁾.

After all these comprehensive, time, and cost consuming tests very few cases of chronic cough will remain undiagnosed and one is justified to revert to symptomatic therapy⁽⁴⁾.

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