



Introduction:

Welcome to CUGH's bi-weekly clinical case-series, "Reasoning without Resources," by Prof. Gerald Paccione of the Albert Einstein College of Medicine. These teaching cases are based on Prof. Paccione's decades of teaching experience on the medical wards of Kisoro District Hospital in Uganda. They are designed for those practicing in low resource settings, Medicine and Family Medicine residents, and senior medical students interested in clinical global health. Each case is presented in two parts. First comes a case vignette (presenting symptoms, history, basic lab and physical exam findings) along with 6-10 discussion questions that direct clinical reasoning and/or highlight diagnostic issues. Two weeks later CUGH will post detailed instructors notes for the case along with a new case vignette. For a more detailed overview to this case-series and the teaching philosophy behind it, see [Introduction to "Reasoning without Resources"](#). Comments or question may be sent to Prof. Paccione at: gpaccion@montefiore.org

Note: If you would like to be notified when a new case is posted (along with instructor notes for the previous one), send your e-mail to Jillian Morgan at jmorgan@CUGH.org.

About the Author:

Dr. Gerald Paccione is a Professor of Clinical Medicine at the Albert Einstein College of Medicine in the Bronx, New York. His career has centered on medical education for the past 35 years – as a residency Program Director in Primary Care and Social Internal Medicine at Montefiore Hospital, and director of the Global Health Education Alliance at the school. He has served on the Boards of Directors of Doctors for Global Health, Doctors of the World USA, and the Global Health Education Consortium. Dr. Paccione spends about 3 months a year in Uganda working on the Medicine wards of Kisoro District Hospital where he draws examples for the case studies.

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CASE 40 – Common and Missed x 3

a) A 23 year old woman is admitted to the hospital with the chief complaint of 2 weeks of neck swelling. A farmer and mother of 2 children, she delivered her last child 3 months ago after a normal term pregnancy, and resumed working in the fields 2 months ago. She was in her usual state of fully functional health until two weeks ago when she noticed a painless swelling in the lower part of her neck associated with sweats and feeling “hot” all the time. She went to a clinic and received medications for malaria which didn’t help. The swelling has progressively increased and she now feels uncomfortable when swallowing. Her heart is “pumping fast” , she tires easily while working, and she hasn’t been sleeping well; she’s had loose bowel movements about 3-6 times a day for the past week days without nausea, vomiting or abdominal pain; and a headache, bitemporal and constant for 2 days. She’s noted no change in weight but an increased appetite, and was tested for HIV, negative, during her pregnancy. She’s had no skin changes, eye or visual problems, cough, shortness of breath, chest pain or joint pain.

Physical Exam:

In no distress, sitting up in bed; comfortable appearing

BP 90/40 lying, increased to 100/50 on standing; HR: 110 to 120 (lying to standing); T: 97 p.o.; RR 18;

Skin: normal texture, normal temperature in hands, hands moist, no rash;

Head normal; mouth: no thrush

ENT: no pharyngeal exudates or masses; normal TMs;

Eyes: no stare, no lid lag, no chemosis, proptosis, conjunctival icterus or petechiae;

Neck: supple; 8 (horizontal) x 6 (vertical) cm diameter thyroid, smooth without nodules; no bruit over thyroid;
2-3 cervical nodes bilaterally, 0.5-1.0 cm diameter, non-tender, mobile, non-fixed;

Lungs: clear

Heart: PMI in 5th ICS/mid-clavicular, 2 cm. hyperdynamic; S1, S2 normal, no S3, Gr 1/6 short SEM LSB without radiation

Abdomen: no hepato-splenomegaly, masses or tenderness

Neurologic: normal CN, motor, sensory, cerebellum; reflexes +3 diffusely; no tremor;

b) A 57 year old woman presents to the clinic complaining of 2-3 years of increasing weight loss and weakness despite a good appetite. Over the past few years she’s been tiring more easily while working in the fields, her arms and legs feel weak and her heart seems to “race” when she digs or climbs hills. She’s been more nervous, and for the past year has had bowel movements 3-5 times/day and recently at night, with watery diarrhea and crampy abdominal pain intermittently. She’s been de-wormed multiple times, and various antibiotics have had no effect. She’s had increased sweating but no fever, doesn’t have a temperature preference and was tested HIV negative last month. She’s had a swelling in her lower neck since adolescence, similar to other women in her family.

Physical Exam:

Thin, cachectic woman, fidgeting, looking uncomfortable sitting up, but in no acute distress

BP 130/82; HR: 118 and regular, lying down, 122 standing; RR 20; T 98.0 p.o.

Skin: warm hands, normal texture, dry, no rash;

Mouth: no thrush

Eyes: + lid lag; no chemosis, proptosis; no conjunctival icterus, pallor or petechiae;
Neck: supple; irregular nodular goiter prominent: 2 firm round nodules spanning 3-4 cm right lobe; 3 firm, round nodules 1-2 cm each, spanning 4 cm left lobe; non-fixed, non-tender, no transillumination; no bruit heard;
Lungs: clear
Heart: PMI in 5th ICS/mid-clavicular, 2 cm., normal; S1, S2 normal, no S3, Gr 1/6 short SEM LSB without radiation
Abdomen: no hepato-splenomegaly, masses or tenderness; increased bowel sounds
Neurologic: normal CN, sensory, cerebellum; motor: 5-/5 diffusely in arms and legs;
+ fine tremor of outstretched hands; reflexes +2 diffusely

c) A 28 year old woman presents to the hospital complaining of 4 months of “heart pains”. The pains started about 4 months ago, felt initially on climbing hills, and described (with her hand fluttering in the air) as her heart pounding very fast on mild exertion. The problem has progressed: now she’s experiencing the “pain” for hours even at rest - a rapid fluttering and vague discomfort in her chest. In addition, she always feels “hot”, even in the rainy season, is more comfortable at night than during the day, and always feels hungry - eating more than usual and gaining weight. She’s noted no change in her bowel or sleep habits, or mood. She’s had no joint pains, fevers, changes in her vision or eyes, but complains of her hair falling out. Upon direct questioning, she notes that there’s been an increased fullness in her lower neck region but is unsure of its duration. She continues to work in the fields, but feels “sick” when she does. She has 3 children, the last one delivered without problems 2 years ago.

Physical exam:

No distress, sitting on edge of bed, seeming jittery and shifting position frequently, clumsy disrobing for exam
BP 140/70; HR 110 at rest, 140 after walking 40 yards, regular; RR 16; T 97 p.o.
Skin: smooth; palms moist and warm;
Eyes: no lid lag, chemosis, proptosis; no conjunctival icterus, pallor or petechiae;
Neck: smooth, diffuse goiter without nodules, firm, non-tender, 3 cm (vertical) lobes bilaterally;
+ bruit over thyroid, systolic, no change with neck rotation or compression over internal jugular veins;
Lungs: clear
Heart: PMI in 5th ICS/mid-clavicular, 2 cm. hyperdynamic; S1, S2 normal, no S3, Gr 1/6 short SEM LSB without radiation
Abdomen: no hepato-splenomegaly, masses or tenderness; normal bowel sounds
Neurologic: normal CN, motor, sensory, cerebellum; + fine tremor accentuated by paper draped over outstretched hands; reflexes brisk, +2-3 diffusely

1. What symptoms are common to all 3 of these patient presentations? To at least 2 of the 3 presentations?

Common to all 3 presentations:

- heart “pumping fast/racing”
- neck swelling

To at least 2 of the 3:

- heart “pumping fast/racing”
- neck swelling
- temperature preference for cold, “hot feeling” persistently
- tired, weak

- diarrhea, loose BMs

2. What physical exam signs are common to all 3 of these patient presentations? To at least 2 of the 3 presentations?

Common to all 3 presentations:

- goiter
- tachycardia

To at least 2 of the 3:

- goiter
- tachycardia
- warm hands
- moist hands
- hyperdynamic PMI
- hyperreflexia
- fine tremor
- hyperkinetic movements at rest (jittery, fidgeting, clumsy)

3. What physiologic aberration explains all three illnesses? Explain.

Hyperthyroidism is the common theme.

The manifestations in multiple systems – cardiac, intestinal and neurologic – and the absence of overt signs of focal inflammation or neoplasm strongly suggest a chemically mediated chronic process induced by a circulating hormone, cytokine or drug. The type of clinical manifestations - hyper-metabolic symptoms and signs - and the goiters in these patients all indicate hyperthyroidism.

4. Which symptoms and signs are the most valuable/accurate in diagnosing this condition? (What are the sensitivity and specificity and/or likelihood ratios for the various clinical manifestations of this disease?)

In one of the earliest diagnostic clinical prediction rules (CPR), Crooks, Murray and Wayne (QJM 1959; 28 (no.110):211-234, April) applied statistics to the clinical diagnosis of thyrotoxicosis deriving a CPR on “definitely toxic and definitely non-toxic” patients in which symptoms and signs were weighted by their sensitivity and specificity for the diagnosis, and the weights further modified to increase the discriminate spread of the final rule. The scoring system was then applied to a series of 171 questionable cases in 5 hospitals, and both accuracy and observer variability tested. Overall accuracy was 85%: only 3% were errors, and 12% were in the equivocal range, and observer variability was likewise quite good.

<i>Symptoms</i>			<i>Signs</i>		
<i>Symptoms</i>	<i>Present (score)</i>	<i>Absent (score)</i>	<i>Signs</i>	<i>Present (score)</i>	<i>Absent (score)</i>
<i>Dyspnea on exertion</i>	+1		<i>Palpable thyroid</i>	+3	-3
<i>Palpitations</i>	+2		<i>Bruit over thyroid</i>	+2	-2
<i>Tiredness</i>	+2		<i>Exophthalmos</i>	+2	
<i>Preference for heat</i>		-5	<i>Lid retraction</i>	+2	
<i>Preference for cold</i>	+5		<i>Lid lag</i>	+2	
<i>Indifferent to temp</i>	0		<i>Hyperkinetic movements</i>	+4	-2
<i>Excessive sweats</i>	+3		<i>Fine finger tremor</i>	+1	
<i>Nervousness</i>	+2		<i>Hands: warm</i>	+2	-2
<i>Appetite increased</i>	+3		<i>Hands: moist</i>	+1	-1
<i>Appetite decreased</i>		-3	<i>HR: <80</i>		-3
<i>Weight increased</i>		-3	<i>80-90</i>	0	
<i>Weight decreased</i>	+3		<i>>90</i>	+3	
			<i>AFibrillation</i>	+4	

A patient is normal (non-hyperthyroid) with a score less than or equal to 10; hyperthyroid with a score of 20 or more.

All 3 patients in the vignettes above scored 20-25 on this CPR.

Odie and Boyd reported on the incidence of signs and symptoms in thyroid disease in the U.S. and Australia in 1972 from both summaries of old reports and their own data. (MedJAust 1972; 2:981-986). The results of the raw retrospective data permit calculations of sensitivity, specificity and LRs from these multiple cohorts of thyroid clinic patients with and without thyroid disease.

Approximate values of these indexes for some of the hyperthyroid findings, (approximately weighted among data sources by patient number (usually between 500-2000)), are below:

<i>Clinical Finding in Hyperthyroidism</i>	<i>Sensitivity (TP/TP+FN)</i>	<i>Specificity (TN/TN+FP)</i>	<i>Likelihood Ratio + (TP rate/FP rate)</i>	<i>Likelihood Ratio - (FN rate/TN rate)</i>
<i>HR > 90</i>	75	84	4.7	0.30
<i>Sweats more</i>	62	70	2.1	0.54
<i>Heat intolerance</i>	61	75	2.4	0.53
<i>Appetite increased</i>	37	87	2.8	0.72
<i>Weight loss (significant)</i>	53	85	3.5	0.55
<i>Diarrhea</i>	18	92	2.3	0.89
<i>Hyperkinetic movements</i>	53	92	6.6	0.51
<i>Fine Finger tremor</i>	77	83	4.5	0.28
<i>Skin warm, moist</i>	67	85	4.5	0.38
<i>"Eye signs" present</i>	47	80	2.4	0.66
<i>Thyroid bruit</i>	34	99	34.0	0.66
<i>Goiter</i>	86	60	2.2	0.23

A study by Nordyke, et.al (Arch Intern Med 1988;148:626-631) investigated the prevalence of clinical findings by age in patients with Graves disease who had thyroid nuclear scans in Hawaii. Overall, some of the most sensitive findings were goiter (80-98%); HR > 90 (75-84%) (LR+4.2); fine finger tremor (~68% in all ages) (LR+~14). Some of the most specific findings

were: increased appetite and weight loss (~25-50% sensitive, but 100% specific); lid lag (~15-20% sensitive, but 100% specific); increased bowel movements (~15-25% sensitive, ~98% specific); fine finger tremor (~95-98% specific). Results by age are discussed below (see #5).

The following points can be culled from studies on the clinical presentations of hyperthyroidism:

- *No clinical findings rule in or rule out hyperthyroidism. Most of the classic findings from the history or physical aren't very sensitive, i.e. seen in only 15-70% of patients with hyperthyroidism; and conversely, most are also quite non-specific with a low positive predictive value, i.e. as individual symptoms/signs they're found far more commonly in patients without than with hyperthyroidism. This, along with variability in performance and interpretation of history and exam, emphasizes the importance of analyzing the overall composite picture of the patient's illness and not relying on one or two findings.*

- *Almost all large studies on clinical observations are "old" and were based on patients referred to thyroid clinics. Most of them had symptoms. Although there are important points from these studies that can still be applied in the U.S. today, given better patient access to care nowadays and the availability, accuracy and low cost of the sensitive TSH assay, most patients with "hyperthyroidism" in the West are diagnosed earlier with many fewer symptoms.*

Ironically however, the weakness of these clinical prediction rules in the West nowadays may be their strong suit in Africa. Despite obvious ethnic differences between the patient populations in these Western studies and Africa, the "old" indexes are (probably) still very applicable in rural Africa where most diagnoses of hyperthyroidism remain clinical, diagnostic testing facilities are scarce, and the district hospital occupies the same place in the referral chain as the thyroid clinics of old.

- *Composite findings can be very helpful, as long as both positive and negative findings are evaluated. A few LRs of "independent" findings (i.e. independence implies different sensory observations and/or separate organ systems) can be multiplied in sequence to produce a "composite LR". Thus for example, a patient who has neither a fine tremor nor a HR>90, has a composite LR (-) of $0.3 \times 0.28 = \sim .09$ (which means that that particular combination of findings is ~ one-tenth as likely to come from someone who is hyperthyroid as someone who is euthyroid). Through shorthand Bayesian analysis, this combination of negative "tests" reduces the pretest (or pre-exam) probability of hyperthyroidism (guess-stimated from local prevalence and patient symptoms), by ~50%, effectively ruling out the majority of patients considered to have the disorder in routine practice.*

(N.B. LRs of 0.5, 0.2, and 0.1 effectively lower the probabilities of disease by 15, 30 and 45% and conversely LRs of 2, 5 and 10 raise the probabilities of disease by 15, 30 and 45%.)

5. How does the usual presentation of this condition vary with patient age?

What are the common pitfalls of clinical diagnosis to be aware of in this condition?

As noted above, Nordyke, et.al (Arch Intern Med 1988:148:626-631) investigated the prevalence of clinical findings by age in patients with Graves disease in Hawaii.

Many symptoms had both good sensitivities and specificities and were almost as common in the elderly as in the young: HR >90, fine tremor (signs); palpitations or rapid heartbeat. Other symptoms, although insensitive, maintained excellent specificity in both groups: lid lag/retraction, combination of increased appetite and weight loss, and increased BMs.

However, other findings varied with age:

- Skin findings - skin moist/warm, sweating - and heat intolerance markedly decreased with age >60 years old (y.o.)
- Appetite in those older than 60 with hyperthyroidism is as commonly decreased as it is increased (each ~20-30%) (versus far more commonly increased in those <40 y.o.)
- Young patients with hyperthyroidism frequently gained weight due to increased appetite overriding hyper-catabolism, while among patients >60 years old weight loss was seen in ~80% and weight gain in none.
- Goiter is less common in the elderly - absent in 25% of patients older than 70 in this study; but in other studies goiter was observed even less commonly, in only 50-60%. In one small study of 21 patients with hyperthyroidism and an average age 81, goiter was detectable in only 3 (Tibaldi, et.al AmJMed 1986; 81:620).
- Tachycardia: in some studies, tachycardia was absent in 40% of elderly Western patients with hyperthyroidism due to concomitant conduction system disease, while AF was far more common than in the young, up to 15-20% of hyperthyroid elderly patients vs 2-3% of young patients.

Commonly (i.e. up to a third of cases), the elderly with hyperthyroidism present with apathy and depression (apathetic hyperthyroidism) instead of the usual hyper-metabolic, hyperactive presentation in the young. As noted above, weight loss and/or atrial fibrillation are common in the elderly.

Common pitfalls in under-diagnosis are not considering hyperthyroidism in patients with depression and weight loss (since depression itself causes weight loss), and not appreciating that a goiter is often absent (possibly mediastinal in location) in the elderly, at least in the West. Unexplained tachycardia, tremor, and/or increased BMs are useful clues to the diagnosis. The temptation to over-diagnose can be held in check by appreciating that the combination of HR <90 AND absence of fine tremor lower the pre-exam probability of hyperthyroidism by an absolute 50% and thus rule it out in most cases. (N.B. In the elderly however, tachycardia is absent in as many as 40% of hyperthyroid patients.)

- 6. a) What other symptoms and signs, not mentioned above, might suggest the diagnosis?
b) How should an isolated symptom or sign, consistent with the diagnosis, be evaluated?**

- a) SKIN: (from D.Ross, UpToDate 2011)
- Onycholysis (loosening of the nails from the nail bed) and softening of the nails.
 - Hyperpigmentation in severe cases (It appears to be mediated by accelerated cortisol metabolism, leading to increased corticotropin (ACTH) secretion.)

- *Pruritus and hives are occasional findings, primarily in patients with Graves'.*
- *Vitiligo and alopecia areata can occur in association with autoimmune disorders.*
- *Thinning of the hair*
- *Graves dermatopathy (erythematous edematous plaques usually on the lower extremities of patients with Graves, with ophthalmopathy (pretibial myxedema).)*

EYE

- *Exophthalmus, proptosis in Graves', overt in 25% of patients but detectable by ultrasound or CT in >80%;*

BONE

- *Acropachy: clubbing, periosteal elevation*

MUSCLE

- *Weakness: proximal myopathy, easy fatigability*

CARDIO-PULMONARY

- *Dyspnea is common and multifactorial in hyperthyroidism, particularly in the elderly: cardiomyopathy, myopathy of respiratory muscles, increased O₂ consumption and CO₂ production, goiter compression trachea; bronchospasm;*
- *Wheezing: hyperthyroidism precipitates asthma (down-regulates B-receptors).*

b) Since thyroid hormone affects multiple organs by essentially revving up their normal level of metabolic function, the findings of hyperthyroidism are extremely common in normals too. In isolation, few findings of hyperthyroidism are specific for the diagnosis.

In a rural Ugandan patient with a finding suggestive of hyperthyroidism, look for more – clinical diagnosis is made by the company it keeps. Always evaluate multiple symptoms and signs, and assess the composite likelihood of disease. Using scores or likelihood ratios aids that assessment. If a clear-cut picture of disease emerges, treat, and if not, follow over time and consider B-blocker therapy for symptom control.

7. What does the history and physical exam tell you about the possible specific pathology underlying the physiology in each of the 3 patients?

The histories of these 3 women differ in the onset and duration of their illnesses and their goiters.

Patient A has been ill for 2 weeks and complains of the recent and rapid growth of a goiter; Patient B ill for 1-3 years, and has always had a neck mass as long as she can remember; and Patient C for about 4-6 months, and although she acknowledges a neck fullness on direct questioning, is unsure about its duration.

The timing of the illness and goiter in patient A, 2 weeks, strongly suggests an inflammatory process consistent with “thyroiditis”. The history also provides a (probably decisive) clue to the etiology of the disorder: her recent delivery 3 months ago - which makes this diagnosis likely to

be “*postpartum thyroiditis*” (PPT), a fairly common auto-immune process triggered by the post-partum hormonal-biochemical milieu.

The exam of the goiter, “10 (horizontal) x 7 (vertical) cm diameter thyroid, smooth without nodules; no bruit over thyroid” corroborates this suspected diagnosis: a diffusely enlarged gland (i.e. involved throughout by the inflammatory process), yet non-tender (characteristic of PPT, and other auto-immune processes affecting the thyroid such as Graves disease and Hashimoto’s thyroiditis), without evidence of hypervascularity (no bruit).

Although it’s common in rural Africa for patients with chronic diseases to present late and be unaware of timing details, the rough span of 1-3 years of illness in patient B suggests a pathologic process that’s insidious and chronic. The goiter in this 57 year old woman has been present her whole life, and other female family members have had it as well.

The physical exam is that of a multi-nodular goiter:

“irregular nodular goiter prominent: 2 firm round nodules spanning 3-4 cm right lobe; 3 firm, round nodules 1-2 cm each, spanning 4 cm left lobe; non-fixed, non-tender, no transillumination; no bruit heard” and the symptoms of hyperthyroidism are indicative of one or more of the nodules hyper-functioning independent of TSH regulation – a “*toxic multinodular goiter*”. These usually produce symptoms of variable duration and onset: most are chronic and insidious as in this patient, but some present after only a few weeks to months of symptoms.

Patient C is young, and has been sick for 4 months. Although this duration of illness can be seen, 4 months is long for most cases of thyroiditis in which the hyperthyroid phase usually lasts 2 to 8 weeks. On the other hand, the duration is quite consistent with the more insidious auto-immune etiology of *Graves Disease*, probably the most common cause of hyperthyroidism in most regions of the world, and usually presents after more than 2-3 months of symptoms. A common (auto-immune) competing cause, post-partum thyroiditis, is ruled out by history.

Despite the absence of exophthalmus, dermopathy or acropachy, all quite specific for the diagnosis of Graves, the exam of the thyroid cinches the diagnosis in this case:

“smooth, diffuse goiter without nodules, firm, non-tender, 3 cm (vertical) lobes bilaterally; (+) bruit over thyroid, systolic, no change with neck rotation or compression over internal jugular veins”.

Thus this is an exam of a diffusely enlarged gland (i.e. involved throughout by the inflammatory process and not nodular), non-tender (not sub-acute granulomatous thyroiditis); with a bruit (a sign of hyper-vascularity of a hyper-functioning gland, not one releasing thyroid hormone because its cells are lysing). The thyroid bruit of Graves is heard in about a third of cases, and should be differentiated from a venous hum which disappears with neck rotation, lying down, or compression of the internal jugular veins.

7. What is the pathogenesis and the significance of Uganda in these diseases?

Patient A likely has post-partum thyroiditis which is (somewhat paradoxically) considered a form of Hashimoto’s chronic autoimmune thyroiditis with high anti-thyroid peroxidase antibody concentrations early in pregnancy which decrease later in pregnancy only to rebound after delivery. Resulting thyroid inflammation damages thyroid follicles and releases large amounts of T4 with subsequent hyperthyroidism beginning 1-4 months after delivery and lasting 2-8 weeks.

There's no solid data on the incidence of PPT in Africa. However we do know that it's common worldwide, varying between 1 and 17% of pregnancies in different parts of the world, influenced by both genes and environment. Whatever the genetic predisposition is in Uganda, with one of the highest fertility rates in the world, PPT is likely to be a fairly common cause of thyroid dysfunction and likely to become more prevalent as the campaign to iodize salt throughout Uganda comes closer to its goals.

In this patient, the goiter is larger than most in PPT, more consistent with Graves Disease which also produces diffuse enlargement. To complicate matters, the incidence of Graves post-partum is increased three-fold. Nevertheless, studies suggest that in the post-partum period PPT is 20 times more common than Graves as a cause of hyperthyroidism. Whereas imaging, serology and the ratio of T4/T3 (higher in PPT) can help differentiate the two conditions in the West, in Uganda, follow-up will provide the definitive diagnosis.

Patient B has toxic multi-nodular goiter (TMNG) which is thought to be caused by mutations in the TSH receptor that lead to thyroid hormone production independent of TSH. It's one of the most prevalent causes of hyperthyroidism in iodine-deficient areas such as the Uganda highlands. Iodine deficiency induces TSH which stimulates thyroid follicle and nodular hyperplasia from an early age. In some patients the persistent stimulation leads to autonomous function and hyperthyroidism.

Kisoro, in SW Uganda, has a visible goiter prevalence of ~40%. Five years after a universal iodized salt law was passed in Uganda in 1993, Kisoro still had the lowest level of urinary iodine in its population of any Ugandan district studied.

As a greater number of iodine-deficient people with nodular goiters are exposed to increased dietary iodine, the incidence of TMNG will increase. Called the Jod-Basedow phenomenon, some autonomously functioning euthyroid goiters, newly exposed to increased iodine, overproduce thyroid hormone and frank thyrotoxicosis results. An increase in hyperthyroidism from the Jod-Basedow phenomenon triggered by iodine supplementation of salt has been seen in Zimbabwe and nearby eastern Congo. It may well be what stimulated the development of thyrotoxicosis in our patient.

Patient C has Graves Disease (GD) which remains the most common cause of hyperthyroidism in most of Africa. GD is an autoimmune disease with a strong genetic predisposition in which thyroid-stimulating immunoglobulins activate hormone production independent of TSH. Cytokine activation of fibroblasts (particularly orbital fibroblasts) and glycosaminoglycans which trap water is largely responsible for the extra-thyroid manifestations of the disease. It is more prevalent in iodine-sufficient areas, and is likely on the increase in areas like SW Uganda where iodized salt is being recently and rapidly introduced.

8. What is the natural history of these disorders, and how should they be treated?

Post-partum thyroiditis can first present with either hyper or hypo-thyroidism. About 20-30% go through both: initially within the first 4 months post-delivery with hyperthyroidism, which lasts usually 2-8 weeks, and then hypothyroidism, which lasts weeks to 6 months. However, 20-40% has only hyperthyroidism, and 30-50% only hypothyroidism. Symptoms are usually mild and full recovery is usual within a year. Recurrence with future pregnancies is the rule, and although

most recover, some remain persistently hypothyroid. Over the long term up to 30% may develop hypothyroidism.

Thus treatment of the hyperthyroid phase of PPT is symptomatic, with B-blockers (e.g. atenolol 25-50 mg/day). Therapy should be stopped to assess recovery after a month or so. This will also help differentiate PPT from GD, which won't spontaneously resolve within a few months. Long-term follow-up of patients, for the late development of hypothyroidism, is necessary.

TMNG won't resolve on its own. Symptomatic treatment with b-blockers is appropriate. In the U.S., radioactive iodine is the treatment of choice, but in rural Uganda definitive treatment is by thyroidectomy if available. Surgery carries risk, especially with large goiters, and usually necessitates permanent thyroid replacement - which also is hard to find (only in the capital, Kampala) and expensive.

Graves Disease has a 30-40% spontaneous remission rate on long-term follow-up, more likely with smaller goiters (and lower levels of circulating thyroid hormone). Control of symptoms by b-blockade is indicated. Long-term methimazole, a once-a-day anti-thyroid drug which blocks iodination (and can be found in the capital Kampala), is optimal. Symptoms usually improve within a month after initiation of the drug which should be continued for at least 1-2 years. After that, 30-50% will have entered permanent remission.

Suggested Readings: (in addition to references in the text)

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