What is the Tropical Splenomegaly Syndrome?

“Everyone has a palpable spleen in Uganda”. Well, that is not quite true but splenomegaly is certainly very common. One cause is the tropical splenomegaly syndrome or, as it is now called, hyperactive malarious splenomegaly (HMS). Can the diagnosis be made on clinical grounds alone when there are so many causes of splenomegaly in the tropics? There are features that make the diagnosis of HMS more likely:

- Young to middle-aged male,
- Complaint of abdominal swelling and pain from
- A huge spleen associated with hepatomegaly but
- No lymphadenopathy.

In addition the patient may have
- Recurrent infections,
- Moderate to severe anaemia,
- Jaundice.

Laboratory investigations may show
- Normochromic normocytic anaemia,  
- Leucopenia,  
- Thrombocytopenia,  
- Serum IgM markedly raised (this assay not widely available).

Even with all of these features, which make HMS very likely, a differential diagnosis list must be considered and the important conditions include:

- Leukaemia,
- Lymphoma,
- Thalassaemia,
- Haemoglobinopathies,
- Visceral leishmaniasis,
- Schistosomiasis,
- Myelofibrosis.

If these latter conditions have been reasonably excluded and HMS rises to the top of the list then action should be taken. If the spleen is huge then mortality may approach 90% within five years. Death occurs as a result of severe infection.

Treatment is not by Splenectomy as this leads to a high operative mortality. Lifelong antimalariais are much more effective. In Africa proguanil is perhaps the best: the spleen gradually reduces and immunocompetence improves. In the absence of a satisfactory response then the following should be considered:

- Poor compliance with treatment,
- Resistant malaria,
- The diagnosis is not HMS.

So the answer to the question “can we make a clinical diagnosis?” is “yes” provided we are aware of the differential diagnosis. It is important to attempt to make the diagnosis because much morbidity and mortality can be avoided.

*** *** ***

What to record on the out-patient card when a patient is discharged from hospital.

As is the arrangement in many hospitals in Uganda, patients attending Kitovu Hospital (Masaka) keep their own out-patient records. This has great advantages

- Patients rarely (in the Editor’s experience) fail to bring these records to the out-patient clinic so
- These records are immediately available to the clinician
• Even if the patient attends an alternative health unit.
• No need for a separate records department in the hospital with all of the additional work that would be created in locating and making the records available and subsequently refilling them.
• Waiting times in the out-patient clinic is reduced.

Accepting the value of these records it is important that they contain adequate information. This becomes especially important if the patient sees a new clinician and / or attends a different health unit. When a patient has had an in-patient stay a short summary of the essential information should be recorded. Always ask yourself “What information would I wish to see if I saw this patient for the first time in the out-patient clinic after discharge?” There are certain pieces of clinical information that are important and here are two examples:

<table>
<thead>
<tr>
<th>KITOVO HOSPITAL (MASAKA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:……………………… Age: 20 Sex: F</td>
</tr>
<tr>
<td>Address:………………………</td>
</tr>
<tr>
<td>Out-patient No: 435/05 In-patient No: 721/05</td>
</tr>
<tr>
<td>Date of admission: 10.11.05 Date of discharge: 13.11.05</td>
</tr>
<tr>
<td>Diagnosis: Malaria (blood slide ++ve for P. falciparum). Anaemia (4.5G/dl: hypochromic, microcytic)</td>
</tr>
<tr>
<td>Management: IV then oral quinine. Transfused 1 unit of blood (Group ARh+ve). Hg. rose to 5.6G/dl. Rapid resolution of fever and clinical recovery.</td>
</tr>
<tr>
<td>Treatment at discharge: Quinine 600mg 8 hourly (4 days) Ferrous sulphate 200mg bd (2 months) Folic acid 5mg daily (2 months)</td>
</tr>
<tr>
<td>Out-patient follow-up: Nil</td>
</tr>
</tbody>
</table>

From this example it can be seen that the detail is not great but the essential information is there. The in-patient record number could be helpful on a future occasion should more data required. The “diagnosis” states the evidence. The blood slide is often negative if the patient has received antimalarial treatment prior to admission: if that is the case then it should be stated so. The type of anaemia and the latest haemoglobin level: a note of the patient’s blood group could be useful should a future transfusion be needed. The treatment prescribed and provided at discharge is essential.

<table>
<thead>
<tr>
<th>KITOVO HOSPITAL (MASAKA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:……………………… Age: 32 Sex: M</td>
</tr>
<tr>
<td>Address:………………………</td>
</tr>
<tr>
<td>Out-patient No: 772/05 In-patient No: 555/05</td>
</tr>
<tr>
<td>Date of admission: 09.07.05 Date of discharge: 19.07.05</td>
</tr>
<tr>
<td>Diagnosis: Pulmonary TB (sputum negative X3). Immunosuppression syndrome.</td>
</tr>
<tr>
<td>Management: Presented with fever, night sweats, cough, haemoptysis and weight loss for 2 months. Weight: 55.0. CXR (No. 775/05): right mid-zone soft infiltration with nodules. Hb 10.0G/dl, ESR 77. Treatment started, on the basis of a clinical diagnosis, with EHRZ. Fever settled within one week.</td>
</tr>
<tr>
<td>Treatment at discharge: EHRZ tabs 3 daily Pyridoxine 50mg daily Co-trimoxazole tabs 2 daily 2 weeks’ supply</td>
</tr>
<tr>
<td>District TB forms for DOTS completed Referral arrangements to Mobile Home Care and consideration for onward referral for ARV’s.</td>
</tr>
<tr>
<td>Out-patient follow-up: 02.08.05</td>
</tr>
</tbody>
</table>

This patient is more complex than the first example. The sputa were negative for acid fast bacilli on microscopy. So it was important to record the CXR number so that this can be reviewed in future as a guide to progress. Equally the note of the patient’s body weight and ESR are useful baseline data.

It will be seen from these brief examples that the essential clinical information to record in the discharge summary is
• The diagnosis and the evidence.

1 EHRZ (sometimes abbreviated to RIPE): ethambutol (E), isoniazid (H), rifampicin (R), pyrazinamide (Z).
• Other data, clinical (e.g. body weight) and laboratory (e.g. Hb., white cell count, ESR), that may help with future monitoring of progress. These should include the most recent data whilst an in-patient.
• The nature (including complications) of the clinical progress.
• Treatment (including duration) prescribed on discharge.
• Post-discharge plans (e.g. DOTS).
• Out-patient follow-up date.

It only takes a few minutes to handwrite these brief summaries. This is time well worth spending and the doctor (including you!) seeing the patient on a future occasion will be very grateful.

***   ***   ***

Arcus cornealis: a pointer to hyperlipidaemia in Uganda?

David Tibbutt, DM, FRCP (Visiting Consultant Physician) and Nursing Staff of the Out-patient Clinic at Kitovu Hospital, Masaka.

Introduction

Non-communicable vascular diseases, hypertension and diabetes mellitus are increasing in frequency in Uganda. Stroke is common although myocardial infarction still remains unusual in the indigenous population especially in rural areas. With the increasing habit of smoking and incidence of hypertension and diabetes (i.e. three major risk factors for arteriosclerosis) it is likely that, in time, coronary artery disease will become a significant disease burden. There is a further risk factor: hyperlipidaemia (cholesterol and triglycerides). The incidence of hyperlipidaemia in Uganda is unknown\(^2\). However there are physical signs that can be used to point to its occurrence? These include: arcus cornealis, xantholasmata (yellowish deposits around the palpable fissure), tuberoeruptive xanthomata (lumpy deposits over pressure points such as knees, elbows and buttocks) and palmar xanthomata (yellowish deposits in the palmar creases).

Arcus cornealis is “an opaque, greyish ring at the periphery of the cornea just within the sclero-corneal junction. It results from deposits of fatty granules in, or hyaline degeneration of, the lamellae and cells of the cornea”. We have heard it said that arcus cornealis is uncommon in Uganda. The purpose of this small study was to assess the occurrence of this physical sign among the patients attending the medical out-patient clinic at Kitovu Hospital.

Method

Consecutive patients attending the medical out-patient clinic were observed: Sex, age and grade of arcus cornealis were recorded. The grade of arcus was conveniently placed into one of four categories:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>No arcus</td>
<td>0</td>
</tr>
<tr>
<td>Faint arcus</td>
<td>1</td>
</tr>
<tr>
<td>Definite arcus but not around the whole circumference of the cornea</td>
<td>2</td>
</tr>
<tr>
<td>Definite arcus around the whole circumference of the cornea</td>
<td>3</td>
</tr>
</tbody>
</table>

Results

Three hundred and four patients (133 males and 171 females) were included in the study. The mean age of the males was 48 years (range 10 – 89 years) and of the females 52 years (range 13 – 90 years). One hundred and fifty two (50%) patients were hypertensive and / or diabetic. The age distributions for males and females within each arcus grade are shown in figures 1 and 2 and Table 1. The main findings are:

• There is a similar trend for an increasing degree (grade) of arcus cornealis with aging in males and females although
• In grade 3 the females tended to be about nine years younger than the males.

\(^2\) If anyone is aware of any information please let us know.
Figure 1: Distribution of ages (males) in each of the arcus grades 0 – 3 (see text) (the intermediate numbers on the “grade” scale should be ignored). The line is that of “best fit” (straight line formula is stated).

Figure 2: Distribution of ages (females) in each of the arcus grades 0 – 3 (see text) (the intermediate numbers on the “grade” scale should be ignored). The line is that of “best fit” (straight line formula is stated).
Further analyses of the data (Table 2) showed that less than 2% of patients under aged 30 years had an arcus cornealis but 25% in the age group 30 – 49 years. From age 50 the figure rose to 88%. There was no clear difference between the sexes although women in the Grade 3 group were on average nine years younger than the men. Eleven (55%) of the 20 patients with an arcus in the age group 30 – 49 years were diabetic (8), hypertensive (2) or both (1).

<table>
<thead>
<tr>
<th>Age range</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>= / &lt; 29 years</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>1 of 34</td>
<td>8 of 35</td>
<td></td>
</tr>
<tr>
<td>30 – 49 years</td>
<td>23%</td>
<td>27%</td>
</tr>
<tr>
<td>8 of 35</td>
<td>12 of 44</td>
<td></td>
</tr>
<tr>
<td>86%</td>
<td>89%</td>
<td></td>
</tr>
<tr>
<td>55 of 64</td>
<td>91 of 102</td>
<td></td>
</tr>
<tr>
<td>= / &gt; 50 years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Proportion of patients in three age ranges with an arcus cornealis (grades 1, 2 or 3)

Is there a relationship between the development of an arcus cornealis and the existence of hypertension and / or diabetes mellitus? The group of patients aged 30 – 49 years was analysed for this purpose (Table 3). There was no statistically significant difference.

<table>
<thead>
<tr>
<th>Hypertension and / or diabetes mellitus</th>
<th>No hypertension and / or diabetes mellitus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arcus cornealis</td>
<td>11</td>
</tr>
<tr>
<td>No arcus cornealis</td>
<td>23</td>
</tr>
</tbody>
</table>

Table 3: Patients aged 30 – 49 years: relationship between hypertension and / or diabetes and the existence of an arcus cornealis. Chi-squared = 0.985 (using Yates correction for small numbers), p<0.5

None of the 304 patients had evidence of cutaneous lipid deposits (xantholasmata or xanthomata).

Comment

This study refutes the notion that arcus cornealis is a rare physical sign in Uganda: 55% of our medical out-patients had this physical sign and in those over 29 years old the proportion was 68%. However it was very uncommon (less than 2%) in those under the age of 30 years. The grade of arcus was also closely related to age.

Does this high incidence of arcus cornealis have any clinical importance? The arcus contains cholesterol, cholesterol esters, phospholipids and triglycerides so it would not be surprising if there were a relationship with blood cholesterol levels. However this is difficult to show given the very high incidence of arcus cornealis in the older patients: in this study 88% in those over aged 50. A large study (4,000 men and 2,000 women in USA and Canada) by Chambless et al. (Ref.) was published in 1990. It is interesting to note that there was a “low prevalence” of arcus cornealis among the women that “precluded analysis”. Men with clinical evidence of coronary artery disease at the beginning of the research were excluded and then it was found that “arcus cornealis was strongly associated with coronary artery diseases and cardiovascular disease in men aged 30 – 49 years with hyperlipidaemia”. In addition further analysis showed that arcus cornealis was “a useful prognostic factor for coronary artery disease and cardiovascular disease in men aged 30 – 49 years, independent of an association with hyperlipidaemia”. Surprisingly it was found that this easily observed physical sign was “a prognostic factor of the same magnitude of importance for coronary disease as smoking and other common risk factors in this age group.”

This study by Chambless et al. was carried out in a Western environment although the patients included “represented wide ethnic, socioeconomic….. groups.” We need further epidemiological
investigations to determine the significance of lipid levels in our Ugandan patients and also the significance of the physical signs including arcus cornealis. Studies could be centred on those aged 30 – 49 years where we found a 25% incidence of arcus cornealis perhaps looking at the following:

- Lipid levels and the association with arcus cornealis.
- Association with other risk factors especially obesity, hypertension, diabetes mellitus, tobacco smoking, urban versus rural life style, socio-economic factors.
- Long term observation of the occurrence of myocardial infarction, stroke and other vascular problems.

Reference


*** *** ***

Palsy of the third cranial nerve.

The third (oculomotor) cranial nerve has two main functions:
1. It supplies motor function to all of the external ocular muscles except the superior oblique and the lateral rectus. These latter are supplied by the fourth (trochlear) and sixth (abducens) cranial nerves respectively.
2. It supplies the parasympathetic autonomic nerve fibres to the pupilloconstrictor muscles of the iris.

So from this knowledge it is easy to work out what physical signs should result from a complete third nerve palsy:

- Pupil is dilated and unreactive,
- Ptosis,
- The eye looks (is deviated) downwards and laterally because of the unopposed action of the muscles supplied by the fourth (superior oblique) and sixth (lateral rectus) cranial nerves and
- If the eye lid is held up the patient complains of diplopia.

Hence the recognition of an isolated third nerve palsy should be straightforward.

What are the possible causes of a third nerve palsy? The nerve is a long one and there are a many points along its course where damage may occur:

- Within the brain stem,
- Base of brain before it reaches the cavernous sinus,
- Within the cavernous sinus,
- At the tentorial hiatus,
- Within the orbit.

Causes within the brain stem.

- Vascular disease,
- Tumours,
- Encephalitis,
- Poliomyelitis,
- Multiple sclerosis (rare in sub-Saharan Africa)
- Trauma.
- Moebius syndrome: this is a rare congenital problem where the nerve nuclei of the third, sixth and seventh cranial nerves are absent: there is bilateral facial palsy and ptosis, the eyes cannot be elevated and there is lateral rectus palsy sometimes with facial pain. Eighth nerve and mental disorders may also occur.

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3 PJ MOEBIUS (1853 – 1907) was a German neurologist: he worked in Leipzig and Heidelberg.
Before it reaches the cavernous sinus.

After leaving the brain the nerve passes forwards between the posterior cerebral and superior cerebellar arteries and is also close to the posterior communicating artery. An aneurysm of any of these adjacent arteries may compress the third nerve.

As the nerves (third, fourth and sixth) cross the base of the skull they may become in meningeal infiltration caused by extension of a tumour from the nasopharynx or metastases arising from cancers of e.g. lung, breast, stomach and prostate.

Inflammatory processes of any cause may involve the third (and / or sixth) nerves: pyogenic meningitis, syphilis, tuberculous and cryptococcal meningitis.

Cavernous sinus.

An aneurysm of the internal carotid artery within the cavernous sinus may compress the third nerve. In addition the fourth and sixth cranial nerves and the first division of the fifth (trigeminal) cranial nerve may be similarly compressed. Involvement of the fifth nerve is likely to give rise to pain in the supplied facial dermatome. Thrombosis of the cavernous sinus may have similar effects.

Tentorial hiatus.

If the brain stem is displaced as a result of pressure from a supratentorial mass (e.g. tumour or abscess) the third nerve becomes compressed: sometimes known as producing a “false localising sign”.

Orbit.

Tumour extension into the superior orbital fissure may produce a total ophthalmoplegia. In addition pain and sensory loss in the distribution of the first division of the fifth cranial nerve should be expected. Within the orbit any of the third, fourth or sixth cranial nerves may be affected by tumour or granulomata. The eye may also be proptosed because of obstruction of the ophthalmic vein.

Other causes of damage to the third nerve (and the others) at any point along its course include:

- Diabetes mellitus (the pupil is usually not dilated) and especially in those with hypertension and arteriosclerosis: recovery may be spontaneous within three to six months.
- Any of the polyneuropathies especially Guillain-Barre syndrome and diphtheria.
- Sarcoidosis,
- Lyme disease,
- Syphilis.

If the pupil dilates early then a compressive lesion should be suspected.

The diagnosis.

In order to make a precise diagnosis special imaging (CT scan and / or MRI scan) is often required: these facilities are not widely available. Nevertheless it is still possible to make a working diagnosis in many (perhaps most) of the patients we see in Uganda. The key (as always!) is the taking of an adequate history and carrying out a careful clinical examination bearing in mind all that has been described above and what is most likely to occur in our area.

Diabetes mellitus, often with hypertension, is probably the most important cause in those over 50 years old and should always be excluded: if there is a third nerve palsy without a dilated pupil then diabetes is highly likely. It is a treatable condition and the nerve palsy may well resolve in three to six months.

Infections, by the nature of their frequency, ease of diagnosis and being treatable, should be vigorously sought. These should include:

4 Lyme Disease was first recognised in Lyme, Connecticut, USA. It is caused by the tick-borne spirochaete Borrelia burgdorferi. The disease is mainly characterised by an annular skin lesion (erythema chronicum migrans) followed by short episodes of asymmetric pain and swelling in the large joints. Occasionally there is a migratory polyarthritis that affects small and large joints. In addition there may be neurological involvement (e.g. third cranial nerve palsy) and cardiac conduction defects.
- Syphilis: appropriate serological tests will help here.
- Diphtheria.
- Tubercular meningitis.
- Cryptococcal meningitis especially in HIV infected patients.
- Pyogenic bacterial meningitis.

The clinician should carefully look for the pattern of signs characteristic of these underlying causes.

Polyneuropathies such as Guillain-Barre syndrome is always worth bearing in mind. The key features include limb weakness progressing over less than four weeks, distal paraesthesiae, occasionally back and limb pain, other cranial nerve palsies (especially the seventh) and autonomic nervous system disturbances. With careful management (over weeks to months) most patients will survive. Respiratory arrest occurring without warning is a constant risk and respiratory function must be constantly monitored: the simple measurement of the peak flow rate is probably the easiest.

Malignant tumours must be sort and many can be detected (or suspected) on clinical grounds: nasopharynx, breast, lung, prostate and stomach.

Learning points:
- Determine the features of a possible third nerve palsy then
- Look for features that might suggest other cranial nerve palsies and other neurological abnormalities: this will give a clue as to the location of the causative lesion.
- Thorough general physical examination looking for the primary cause (e.g. breast cancer in women and prostate cancer in men: do not omit a rectal examination!!)

***   ***   ***

Drug interactions: do they matter?

When more than one drug is prescribed they may interact in such a way to modify the effects of each other:
- An effect may be increased (potentiated),
- Reduced (antagonised),
- A completely new effect may occur.

The answer to the question in the title is “some do and some do not”. We can predict a likely interaction in many cases e.g.
- Two antihypertensive drugs (e.g. bendroflumethiazide and atenolol) are likely to produce a greater antihypertensive effect than one drug alone. This is usually a desirable effect from a planned prescription. However there are drugs which have an antihypertensive effect (e.g. chlorpromazine) which are not commonly used as antihypertensives. So if to one of these drugs is added another antihypertensive the resultant fall in blood pressure may be greater than that intended.

If the clinician is in doubt he / she should consult a formulary. The British National Formulary (BNF) has a whole appendix (44 pages!!) on interactions. Here are some examples:

<table>
<thead>
<tr>
<th>Drug 1</th>
<th>Drug 2</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiotensin converting enzyme (ACE) inhibitors (e.g. captopril)</td>
<td>Non-steroidal anti-inflammatory drugs (e.g. ibuprofen)</td>
<td>Antagonism of the effect of the ACE inhibitor and also a separate risk of renal damage.</td>
</tr>
<tr>
<td>Angiotensin converting enzyme (ACE) inhibitors (e.g. captopril)</td>
<td>Antacids (e.g. magnesium trisilicate)</td>
<td>Reduced absorption of ACE inhibitor and hence possible reduced effect.</td>
</tr>
<tr>
<td>Angiotensin converting enzyme (ACE) inhibitors (e.g. captopril)</td>
<td>Spironolactone</td>
<td>Increased risk of hyperkalaemia. This risk will be greater in the presence of any degree of renal impairment.</td>
</tr>
<tr>
<td>Drug 1</td>
<td>Drug 2</td>
<td>Interaction</td>
</tr>
<tr>
<td>------------------------</td>
<td>------------------------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>Sulphonylureas (e.g. chlorpropamide)</td>
<td>Chloramphenicol, Fluconazole, Cimetidine.</td>
<td>Antidiabetic effect increased hence producing a risk of hypoglycaemia.</td>
</tr>
<tr>
<td>Phenytion</td>
<td>Chloramphenicol, Fluconazole.</td>
<td>Effect of phenytion increased with a risk of toxicity.</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Erythromycin, Quinine, Diuretics (non-potassium-sparing)</td>
<td>Effect of digoxin increased with risk of toxicity. Any hypokalaemia will increase the risk of digoxin toxicity.</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>Phenytoin, Carbamazepine, Rifampicin.</td>
<td>Effect of oral contraceptive reduced: patients should be warned and advised to use barrier methods of contraception.</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Ciprofloxacin, Fluconazole, Cimetidine.</td>
<td>Risk of theophylline toxicity.</td>
</tr>
</tbody>
</table>

This list is not comprehensive but is meant to highlight some of the more common drug combinations and where we should be especially careful.

***   ***   ***

**National Pharmacovigilance**

The National Drug Authority of Uganda has launched the National Pharmacovigilance initiative. Sensitisation presentations have been given around the country. For the purposes of this initiative it is important to understand what is meant by the term “drug”. The definition is “*Any substance administered to a human being or an animal for the prophylaxis, diagnosis or therapy of a disease or for the modification of physiological function*”. Within this definition should be included any drugs / medicines bought “over the counter” at a pharmacist, herbal and “traditional” medicines and any blood products (e.g. whole blood, plasma and extracts).

Adverse drug reactions (ADR’s) produce a significant clinical problem throughout the world. With greater knowledge of the occurrence and distribution of these ADR’s we give ourselves the opportunity to minimise their impact on our patients (clinically and economically) and the overall health economy. This in turn should free resources to be used for the greater benefit of the population. In addition we may gain information about the quality of drugs on the Ugandan market: this requires careful recording of the reports (see below).

So how will the information on ADR’s be collected? All healthcare professionals in Uganda can (and indeed should) report an ADR directly to the National Drug Authority (NDA). Even if you only suspect an ADR then this should be reported. As much information as possible about the patient (age, sex, diagnoses, etc.) and all medication that the patient is taking (and has recently taken) should be gathered and reported. Reporting forms can be obtained from the NDA Office, the DDHS or NDA Regional Office. They are easy to use, just follow the instructions, fill in the details and forward to the National Pharmacovigilence Centre at the NDA Head Office at

**Drug Information department,**  
**Plot 46/48, Lumumba Avenue,**  
**PO Box 23096,**  
**Kampala**  
**Telephone +256 41 255665 / 347391 / 347392; Hotline +256 41 344052;**  
**Fax. +256 41 255758 / 342921**  
**E-mail : nda@nda.or.ug**  
**Web site: www.nda.or.ug**

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5 e.g. a vaccine.  
6 e.g. barium as a gastrointestinal Xray contrast medium.  
7 e.g. an antibiotic.  
8 e.g. an oral contraceptive.
The information that you provide will be put into a database, analysed and evaluated. There will also be international collaboration with the World Health Organisation Monitoring Centre in Uppsala in Sweden. These data accumulated from the whole nation should give a much clearer idea of the problem. By sharing this knowledge we can learn valuable lessons and hence modify and improve our prescribing habits. For your own interest it is a good idea to keep a copy of the information you send to the Centre. This locally collected information could be used for CME discussions in your own hospital or other health unit. Particularly interesting ADR’s could be reported (as “Case Reports”) for publication in this “Uganda CME Newsletter”.

***   ***   ***

Pericardial disease in the Tropics.

A 25 years-old lady presented with a one day of acute epigastric pain and sweating. She had a low grade fever, a regular tachycardia of 100 / minute and hypotension (BP70/30). No other abnormal signs were detected although in retrospect it was felt that her heart sounds were rather feint. It was thought that she may have an abdominal problem so an ultrasound scan was carried out. The scan was normal until the ultrasonographer looked at the heart from below and found a large pericardial effusion. It was then realised that the patient was suffering from cardiac tamponade. Indeed when the blood pressure was recorded whilst the patient inspired the systolic pressure approached zero and the jugular venous pressure rose (Kussmaul’s sign). An urgent drainage of the effusion was performed using the xiphisternal route. A litre of heavily blood-stained fluid was removed with a dramatic clinical improvement and rise in blood pressure. The fluid did not contain tubercle bacilli on appropriate staining and there was no other indication of a pyogenic bacterial infection. However the patient was found to be HIV-positive. Antituberculous treatment was started and within a week there was a further marked clinical improvement. Six months later the patient was well.

This case exemplifies one of the commonest causes of pericardial disease in Africa namely tuberculosis. It also teaches us once again the importance of a careful clinical examination!!

So what should alert us to pericardial disease with or without a pericardial effusion?

Pericarditis:
• Constant sternal pain that may
• Radiate in any direction especially to the arms and the abdomen (as in the patient just described).
• The pain may be eased by leaning forwards and may be
• Exacerbated by deep inspiration, coughing and lying down.
• A pericardial friction rub (in time with cardiac activity) is often (but not always!) heard over the praecordium especially when the patient sits up, leans forward and is in the expiration phase of respiration.

Pericardial effusion:
When an effusion collects in the pericardial sac the signs change and the friction rub disappears. If the effusion collects rapidly the pericardium has not had time to stretch and tamponade develops and
• the blood pressure falls as the cardiac stroke volume falls,
• central (jugular) venous pressure (CVP) rises because venous inflow to the right side of the heart is impaired.
• The CVP rises further during inspiration (Kussmaul’s sign).
• The heart rate increases as a response to maintain cardiac output.
• The amplitude of the arterial pulse falls on inspiration (pulsus paradoxus): this is detected also by taking the systolic blood pressure and noting the measurement during inspiration and expiration.

* A. KUSSMAUL (1822 – 1922) was a German physician. Apart from describing what has become known as the Kussmaul sign, he achieved many other things. He was the first to describe periarteritis nodosa, progressive bulbar palsy and mesenteric embolism. In addition he was the first to attempt oesophagoscopy and gastroscopy. He became Professor of Medicine successively in four different German cities first at the age of 35 years in Heidelberg.
10 Ethambutol, rifampicin, isoniazid and pyrazinamide.
• The apex of the heart becomes less easily defined and may be impalpable.
• The heart sounds are less audible.

If the effusion collects slowly the pericardial sac stretches and the main clinical features are
• Ascites,
• Hepatomegaly,
• Splenomegaly.

However less marked signs of cardiac compression (as described above) should be sought. The pericardium may become fibrosed, and later calcified, (as in tuberculous pericarditis) leading to constrictive pericarditis: low amplitude pulse, pulsus paradoxus and a high venous pulse wave.

In Uganda and other tropical countries the commonest causes of pericardial disease are:
• Tuberculous pericarditis.
• Pyogenic pericarditis.

HIV infection has increased the occurrence of these conditions. The clinician should look for tuberculosis and pyogenic infection elsewhere as the primary foci. There are many other causes of pericardial disease:
• Malignant deposits (e.g. breast),
• Kidney failure,
• Kaposi sarcoma,
• Lymphoma,
• Virus infections (e.g. coxsackie),
• Post myocardial infarction: this may occur acutely as a result of the inflammatory process of infarction or at about two to three weeks (but up to ten weeks) post-myocardial infarction where there is an autoimmune response (Dressler’s11 syndrome12).
• Other bacteria (e.g. meningococcae).
• Entamoeba histolytica from a liver abscess.
• Trauma.
• Connective tissue diseases (e.g. rheumatoid arthritis, disseminated lupus erythematosus).
• Hypothyroidism.

The management of pericardial disease has three main aspects:
• The relief of life-threatening tamponade or constriction by the aspiration of pericardial fluid.
• Pain relief.
• Treatment of the underlying cause.

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CAUTION

Every effort has been made to ensure that drug doses quoted in all the papers in this Newsletter are correct. However the reader is advised always to check the doses before prescriptions are made. Unless otherwise stated the doses quoted are for adults.

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11 W. DRESSLER (1890 – 1969): An American physician although he was educated in Vienna (Austria). He went to the USA in 1938. He became head of the cardiac department at Marmonides Hospital, Brooklyn (New York).

12 Less commonly known as Harley Disease. G. HARLEY (1829 – 1896) was a Scottish physician. He went to the Edinburgh Medical School when he was only 17-years-old.