CURRICULUM VITAE

PERSONAL DETAILS

NAME   :   DR. BAHOU YACOUB

NATIONALITY   :   JORDANIAN

MARITAL STATUS :   MARRIED

DATE OF BIRTH :   1952

EDUCATION
1.   Elementary and Secondary School Education in the Brothers' College in Amman, Jordan
2.   Diploma of General Medicine from Toulouse University, France in 1979
3.   Certificate of special studies in Neurology (C.E.S) from the University of Montpellier, France in December 1984.
4.   Jordanian Board (Jordanian Medical Council Certificate) in 1985.

EMPLOYMENT HISTORY
1.   One year training at King Hussein Medical Centre, prior to presentation of Jordanian Board. (December 1984-December 1985)
2.   Consultant Neurologist in Queen Alia Hospital, Amman – Jordan, prior to its transfer to the Armed Forces. (February 1986 – February 1987)
3.   Consultant Neurologist in Bahrain International Hospital.
      (February 1987 – February 1988)
4.   Senior Registrar in Neurology at Riyadh Armed Forces Hospital between August 1988 and January 1995.
5.   Consultant Neurologist at the Consulting Clinics in Riyadh from January 1995 to April 1999
6.   Actual position = Assistant Professor in Neurology at Jordan University Hospital Since April 1999

PUBLICTIONS:
1. Symposium Abstracts
1. Y Bahou, S M AI Deeb, Biary
   Retrospective study of 19 patients will myasthenia gravis observed at Riyadh Armad Forces Hospital since 1983.
   Annals of Saudi Medicine, Volume 10; Number 61, November 1990, page 684

2. N Biary, SMAI Deeb, Y Bahou, M Jaberi
   Essential tremor at Riyadh Al Kharj Hospital
   Annals of Saudi Medicine Volume 10, Number 61, November 1990, page 687

3. N Biary, SM Al Deeb, Y Bahou
   Long term therapy of essential tremor with flunarizine. Neurology, suppl. 2, 1993; 43:385

4. S M AL Deeb, <u>Y Bahou</u>, B A Yaqub, N Biary, S Khan
    Pattern of Neurological diseases in Saudis. XVth World Congress of Neurology.
    Vancouver, Canada, 5-10 September 1993.

5. N Biary, B Singh, S Shahwan<u>, Y Bahou</u>, S M Al Deeb, S Kalman
   Neurophysiologic Findings in patients with sub acute sclerosing panencephalitis
   American Electroencephalographic Society. Annual meeting. New Orleans, U.S.A
   10-12 October 1993.

6. <u>Y Bahou</u>, S M Al Deeb, N Biary
    Retrospective study of 97 cases of bacterial meningitis observed at RAFH since 1983
    8th Annual Neurosciences symposium, 26-28 January 1992

2.   **Publications**
  1. <u>Y. Bahou</u>, S M Al Deeb, N Biary
      Bacterial Meningitis: Series observed in Riyadh Armed Forces Hospital 1983 – 1990
      Journal of Tropical and Geographical Neurology, Volume 2, Number 2, 1992.
  2. <u>Y. Bahou</u>, N. Biary, Sl. Al Deeb
     Guillain – Barre Syndrome: a series observed at Riyadh Armed Forces Hospital:
     January 1984 – January 1994.   J Neurol (1996) 243: 147-152
  3. <u>Y. Bahou</u>, Saleh M Al Deeb, Nabil Biary
     Myasthenia Gravis – A seven year Hospital – based review. Neurosciences 1998;
     Vol 3 (2): 53-56.
  4. S M Al Deeb, <u>Y Bahou</u>
     A new neurocutaneous syndrome possible related to OTA's nevus. Journal of
     Neurological Sciences 118 (1993); 92-96
  5. N Biary, B Singh, Y <u>Bahou</u>, S M Al Deeb, H Sharif
     A case of post traumatic paroxysmal hemidystonia. Journal of movement disorders,
     1993
  6. N Biary, S M Al Deeb, <u>Y Bahou</u>
      Long term therapy with Flunarizine in essential tremor. Journal of Neurology,
      Neurosurgery and Psychiatry
  7.   N Biary, S M Al Deeb. <u>Y Bahou</u>
       Flunarizine in migraine: a double-blind placebo controlled study
       (in a Saudi Population) Headache 1992; 32 (9): 461-462
  8. N. Biary; <u>Y. Bahou</u>: M.A. Sofi; W. Thomas and S.M. Al-Deeb.
     The effect of nimodipine on essential tremor. Neurology 1995; 45: 1523-1525
  9. <u>Y. Bahou</u>
     Multiple sclerosis at Jordan University Hospital. Neurosciences 2002; Vol 7 (2):
     105-108.
  10. <u>Y. Bahou</u>
     Carpal tunnel syndrome: A series observed at Jordan University Hospital, Clinical
     Neurology and Neurosurgery 104 (2001); 49-53.

IN HOSPITAL STROKE

INTRODUCTION:
.   Success of thrombolytics (NINDS, NEJM 1995) and new studies of
        antiplatelet (Davalos, Cerebrovas Dis 2003) and neuro- protective agents
        (Davalos, stroke 2002).

.   Narrow time window thus applicable to 2-15% (Grotta, Katzan 2001-2000)
.   Potential candidates: stroke while already in hospital for reasons other than
        stroke or TIA

1.   Magnitude of in-hospital stroke:
        . One population-based study (Schoenberg, Neurology 1983):
          6.5% of all first strokes
        . Hospital-based registries (Foulkes 1988, Walker 1981, Kelley 1986): 7-
        15%
         . Some researchers (Alberts, stroke 1993): 35000 to 75000 cases/year in
        USA
        . Most are perioperative or related to coronary ischemia
          (Alberts, Alvaro 2003).
        . Because stroke complicates 2-5% of cardiac operations (Naylor, 2002)
        and about 300000 CABGs were done in USA in   1993 (National Heart
        Institute, 1995) thus 15000 cases annually.
        . One study (Nadar, Cerebrovasc Dis 2002): 3.5% of stroke patients; not
          related to surgical procedures.

2.   Characteristics of in-hospital stroke (table 1)
        . Predominance of ischemic strokes
        . Hemorrhagic strokes in bone marrow transplants (39%, Coplin, Brain
        2001) due to coagulopathy or thrombocytopenia
        . About ½ in surgical or cardiology patients (Alberts, Alvaro,

1993, 2003).

. Well-recognized complication of carotid endarterectomy (Perler, J vasc surg. 1998; Hannan, stroke 1998) and cardiac surgery, particularly intracardiac procedures (Wolman, Anesth Analg 1994).
. Less frequent complication of general surgery (Parikh 1993, Larsen 1988, Limburg 1998)
. Cardiac and cerebral angiography carry a small but well- recognised risk of stroke (Leker 1999, Brown 1993, Heiserman 1994, Gryska 1990)
. Ivlg=possible precipitant of stroke (Carsess, Neurology 2003)
. Various risk factors associated with cardiac surgery (Naylor, 2002): old age, long-duration C-Pulm bypass, recent MI , left mainstem CAD, repeat cardiac surgery, Vent. Thrombus, post MI angina, CHF, DM, smoking, RF.

. Most consistent risk of perioperative stroke is a previous H/O stroke (Parikh, Limburg, Landercasper 1990)
. One study (Landercasper 1990): 2.9% of patients with H/O stroke had recurrent stroke following general surgery, compared to 0.08-0.2% in other series (Parikh, Larsen)
. Following CABG, H/O stroke or TIA increased perioperative stroke rate to 8.5% compared with an overall risk of 2%(NHI, 1995)
. Other factors: post op. arrhythmias (Parikh 1993,) peripheral vascular disease (Mickleborough 1996, Salasidis 1993), and COPD (Limburg)
. One study of 80 patients of CVA not related to surgery: role of fever, leucocytosis, high diastolic BP, unstable BP, dehydration, H/O MI (Nadav, 2002)
. Mortality of in-hospital stroke can be high (54%) (Walker, 1981) due to comorbidities
. May be a factor in changing from interventional to palliative treatment

3. **MECHANISMS**:
. Distribution of subtypes similar to that in the general stroke population (Kelly 1986, Alvaro 2003)
. Cardio embolism is a major mechanism (36%) (Naylor 2002)
. Among postop strokes, esp. cardiac surgery, role of AF or aortic arch atheroma predominates (Naylor 2002)
. Large-artery disease reported in 30% of one series (Alvaro 2003) (table2)

. Aside from procedures (Angio), Inadvertent ligation of carotid artery during radical neck dissection (Kelley 1986) or carotid damage during insertion of CV catheter (Bohlega 1997, Wang 2000)
. Embolic mechanism following cardiac surgery; fat embolism following orthopedic injuries (Johnson 1996) and paradoxical embolism in immobilized patients with DVT and PFO (Ofori 1995)

Cerebral hypoperfusion, global or focal:
Global hypoxia after cardiac arrest or other states of hypoperfusion (severe outcome, deVreede 1997)

    * Hypotension with large-artery stenosis $\rightarrow$ focal stroke (not supported by Hart 1982)

    * One study (Kelley, stroke 1986): 8/26 due to hypotension (in 4 due to medications)

    * Another study (Blacker, stroke 2003): intra op hypotension $\rightarrow$ 6% post op stroke in patients with previous VBI.

    * Another study (Tattle born, Neurology 1993): compression of extracranial VA due to neck positioning in drowsy patients $\rightarrow$ local thrombus$\rightarrow$embolism after moving about.

    * One study of dynamic MRA (Weintraub, Neurology 2001): $\downarrow$basilar flow when one hypoplastic VA following neck extension .

* Carotid bruits and stenosis increase risk of stroke following CABG (less than ½) and 3.6% risk following general surgery if previous cerebral ischemia
* Carotid bruits alone and symptomless carotid stenosis on U/S: No increased perioperative stroke risk (Gerraty, stroke 1993; Ropper, NEJM 1982).

* Hematological factors:
    . Higher concentrations of procoagulant proteins in critically ill patients (Rem, 1981)
    . Post op changes in clotting factors (Dahl 1993)
    . Dehydration (clinical and lab) (Nadav 2002)
    . Infections (Nieto 1998, Mattila 1998)
    . Hemorrhagic stroke due to bone marrow transplantation (Coplin, 2001)
    . ICH as cause of death in leukemia (Rogers, 1994)

* Manipulation of antiplatelet and anticoagulant medications :
    . Anecdotal reports of stroke due to treatment adjustment prior to invasive procedures (Bachman 2001)
    . Better to continue antiplatelets in perioperative period (Kovich 2003, Neilipovitz 2001, Mangano 2002, Mayo Clin Proc 1992.
    . One study (Mangano): More thrombotic events post CABG after stopping ASA.
    . Another study (Mayo clinic 1992): More MI following endarterectomy after stopping ASA prior to surgery
    . Risk of stroke is 0.05-0.3% if 4-6 days off oral anticoagulant in periprocedural period (Higher if complex medical illnesses or age >80 yrs. or previous stroke (Blacker 2003)
    . Review of 31 reports (Dunn 2003): 1.6% of thromboembolic events (0.4% stroke) following various surgical procedures when manipulating anticoagulants
    . Continue anticoagulants during dental procedures (Wahl 1998).

4. ### Recognition and assessment:
  . More feasible than in those with strokes elsewhere

. Need for trained staff, available records and recent lab results
. One study (Alberts, cerebrovasc Dis 2003): Substantial delay in recognition and assessment; delay in referral to stroke physicians; less than 30% assessed by neurology staff within 90 min. and >25% within 12 hr. of symptom recognition; mean and median time for complete assessment=14.5h and 2.5h (thus non receipt of interventional therapy)
. Another study (Naylor 2002): emergency referral to a stroke specialist in <10%.

- **Factors impeding recognition and assessment (table):**
  . Unable to recognize stroke by staff outside neurology wards
  . Judicious use of opioid and benzodiazepine antagonists
  . Junior neurology staff are slower to respond to referrals "confusion" than to "stroke" (Alberts, 1993)
  . In Multitrauma patients, presence of fractured limbs on the side of hemiparesis →delayed recognition of in-hospital stroke (Blacker, 2002)
  . Referring physicians are not aware about interventional treatment (medical patients deserve assessment for Thrombolysis)
  . In-hospital stroke should be high on the list of priorities

5.   **Treatment:**
  . In medical patients: No barriers for IV Thrombolysis unless there has been a recent invasive procedure (upper age limit= 80yrs)
  . In postoperative patients, IV alteplase in contraindicated. According to NINDS (NEJM 1995) and other guidelines (Adams, stroke 2003): treatment should not be used within 14 days of major surgery, head injury in previous 3 months, GI or urinary-tract bleeding within 21 days, MI within 3 months (cardiac tamponade due to hemopericardium) (Kasner 1998).
  . The number of reports on intra-arterial Thrombolysis in post op , esp. cardiac setting, is increasing (chalela, Katzan, Moazami 2001). Risk of hemorrhage at operative wound site in 25% of cases (Chalela, stroke 2001)
  . Patients with global ischemia after cardiac arrest might be candidates for hypothermic techniques (Bernard, NEJM 2002; Holzer NEJM 2002)
  . Clotting-factor replacement for ICH (Mayer, stroke 2003)
  . Control of hyperthermia and hyperglycemia (Baird, 2002)
  . Control of BP, hydration, body positioning
  . Neuroprotective agents can be trialled prophylactically in patients undergoing procedures with high risk of stroke, such as CABG or carortid endarterectomy (Fisher, stroke 1994; Andrews 1999).

TUBERCULOUS MENINGITIS

I. <u>**INTRODUCTION:**</u>
  * **Postmortem observations of Green (Lancet 1836) described distinct pathological features (DD: other causes of acute hydrocephalus).**

* **Challenge=distinguishing disease before death and delivering grave prognosis**
* **Fatal before advent of anti TB, therefore diagnosis became a priority after streptomycin was found to reduce mortality by 1/3 (MRC 1948)**
* **Rapid progress over next 5 years:**
- **addition of PAS to streptomycin →reduction of mortality to 30%**
- **Addition of INH→↓mortality to 20%**
- **Since 1952: no change because of decline in TB in developed world**
- **In 2002:**
  - **optimum drug regimen has not changed since discovery of Rifampicin and pyrazinamide 30 years ago**
  - **Best rapid diagnostic method is still Zeil and Neelsen stain (1883)**
* **Impediments for reviewing diagnosis and treatment**
1. **Much of literature predates 1966 (Not in med line)**
2. **Only small numbers of patients included in trials**
3. **Few randomized trials**

II. DIAGNOSIS
- **Difficult**
- **Need for a rapid and sensitive diagnostic test because delayed treatment → poor outcome (no such method is available at present)**

1. CLINICAL DIAGNOSTIC METODS
- **Extensively described; similar to many sub acute meningoem cephalitides**
- **Diagnostic uncertainly if comatose patient with a few days of headache, fever and neck stiffness; undefined treatment in the community and a lymphocytic CSF with a low glucose: ? immediate anti TB.**
- **Predictive features:**
  5 presenting features in one study of 232 children
  . Prodnomant stage $\geq$ 7 days
  . Optic atrophy
  . Focal neurological deficit
  . Abnormal movements
  . CSF leucocytes < 50% polymorphs
  If one feature: diagnostic sensitivity is 98% and specificity is 44%
  If 3 or more features: sensitivity is 55% but specificity is 98%

  - **Another study of 251 Vietnamese adults 5 features were predictive :**
    - **Age**
    - **Length of history**
    - **WBC count**
    - **Total CSF WBC Count**
    - **CSF neutrophil percentage 88% sensitive and 79% specific when applied to a further 75 adults (table)**
    - **These tests may be of benefit to clinicians working with limited microbiological diagnostic facilities**

2. LABORATORY DIAGNOSTIC METHODS
  a) **Direct CSF exam for acid-alcohol fast bacilli**
  - **Remained the cornerstone of diagnosis ever since Robert Koch first saw the tubercle bacillus in 1882.**

- Demonstration in CSF requires diligence and time (fig)
- <u>Stewart</u> (1953) demonstrated AFB in 91 of 100 patients of TB meningitis confirmed by culture
- Kennedy (1979) found AFB in CSF of 45/52 (87%) patient with clinical diagnosis of TB meningitis
- <u>? source of difficulty</u>
1. Sensitivity of direct smear depends on volume of CSF: 10-20mil examined by Stewart and as many as 4 specimens by Kennedy
2. Lab should undertake meticulous search for AFB (30 to 120 minutes; Stewart). Therefore better take 5-10ml of CS and with careful microscopy diagnostic sensitivity might be increased (10-70%)

b) <u>CSF culture for Mycobacterium tuberculosis</u>
- Diagnostic gold standard but it takes long for early diagnosis and treatment.
- Large volumes of CSF-greater numbers of positive cultures
- Helpful in patients started on anti TB on clinical grounds alone
- Sensitivity ad specificity exceeds that of direct smear but fully quickly once treatment has been started.
- <u>In Vietnam</u>: only 5-10% positive cultures before treatment will have positive cultures after 72 hours of 4 anti TB drugs
- Although AFB (pressured died) can be found in CSF some days after start of treatment, they will not grow in culture

c) CSF adenosine deaminase activity
- ↑ activity of adenosine deaminase in CSF (enzyme produced by CD4+ lymphocytes and monocytes) [table]
- Cut off value 4-10 IU/ml
- Sensitivity 44-100%; specificity 71-99%
- 3 problems:
  - No accepted diagnostic cut-off for levels
  - Not evaluated in HIV which depletes adenosine deaminanse producing T-lymphocytes
  - High levels in lymphoma, malaria, brucellosis, pyogenic meningitis (partially treated)

d) <u>Detection of Mycobacterium tuberculosis (MT) nucleic acid in the CSF</u>
  - Amplification and detection of Mycobacterium tuberculosis nucleic acid
  - Specificity dependent on selecting a region of genome unique to MT, while sensitivity is enhanced by amplification of selected region
  - Suitable when few AFB in CSF and a low chance of contamination but no consistent diagnostic performance
  - Table: sensitivity and specificity from no studies evaluating PCR (sensitivity of CSF smear is similar to PCR)
  - PCR is helpful once treatment has began (↓ sensitivity of smear and culture) when my cobacterial DNA remains detectable for one month.
  - Variable specificity due to cross-reaction with other mycobacteria and contamination of DNA in the lab, thus a positive result should be placed within the clinical context before starting treatment.

e) <u>Tuberculin skin test:</u>
   - **Value varies according to age, vaccination with BCG, nutritional status, HIV infection and prevalence of TB**
   - **Sensitivity compromised by energy=failure of those with known infection with MT to respond to ID injection of tuberculin (elderly, malnourished with disseminated TB and HIV)**
   - **Only 20% have positive test (more useful in children); one South African series=86% >15mm induration with 5 units**
   - **Positive results should be seen in the context of TB prevalence in the area.**
   - **Never diagnostic of TB meningitis**

3. <u>Chest X-Ray and brain imaging</u>
   a. <u>Chest X-Ray</u>
      - **50% active or previous pulmonary TB**
      - **In high prevalence areas = evidence of previous pulmonary infection**
      - **5 to 10% military TB**

   b. **CT Brain**
      - **Hydrocephalus and contrast enhancing exudates in the basal cisterns**
      - **Hydrocephalus is more common in children (87% of children and 12% of adults)**
      - <u>**Kuma and Kohli**</u>
        - **94 children with TB meningitis compared with 52 with pyogenic meningitis**
        - **Basal meningeal enhancement or tuberculoma or both = 89% sensitive and 100% specific**

      - <u>**Recent series**</u>
        - <u>**Normal CT**</u> **in 35 of 289 (12%) patients with TB meningitis and not all were fully conscious.**
        - <u>**Abnormalities:**</u> **hydrocephalus (80% children, 43% adults), parenchymal enhancement *26% children, 8% adults), contrast enhancement of basal cisterns (15% children 23% adults), cerebral infarct and focal or diffuse brain, edema (14% children, 13% adults)**

   c) <u>**MRI Brain**</u>
      - **More information when assessing S.O.L. infarcts and extent of inflammatory exudates but limited studies**
      - **More sensitive for diverse intracranial pathology of TB meningitis**
      - **Neither CT nor MRI are specific i.e DD=cryptococcal meningitis, CMV encephalitis, sarcodiosis, meningeal metastases and lymphoma**

III   MANAGEMENT
   - **Poor outcome despite effective chemotherapy against pulmonary TB**
   - **Recent series: mortality>20% and severe neurological sequalae in 30% of survivors**

- **Importance of early treatment before coma**
- **Retrospective study of 434 Turkish adults: convulsions, coma, delayed or interrupted treatment=predictors of mortality**
- **Extramemingeal TB, CN palsies, focal weakness, neurological abnormalities and drowsiness=predictors of later neurological disability**
- **THUS we should not delay treatment even before diagnostic confirmation**

1. **ANTI-TB chemotherapy**
   - **Short course chemotherapy as far pulmonary TB: Intensive phase followed by a continuation phase**
   - **Unlike pulmonary TB: optimal drug regimen and duration of each phase are uncertain**
   - **According to BTS (1998), Infectious diseases society of American and ATS (1994):**
     - **INH+Rifampicin + Pyrazinamide (Rif and Pyr do not improve outcome or ↓ treatment duration)**
     - **INH is critical because if penetrates CSF freely and has potent early bactericidal activity**
     - **?4ᵗʰ →streptomycin or Ethambotol**
       * **Neither penetrate CSF in absence of inflammation**
       * **No streptomycin if pregnancy or renal impairment**
       * **Intrathecal streptomycin in MDR cases**
       * **South Africa: Ethionamide (penetrates healthy and inflamed meninges)**
       * **Vietnam: Streptomycin resistance therefore Ethambotol**
     - **Contimation phase = INH+Rifampicin (+Pyr according to some because of high CSF noncentrations throughout the whole course)**
   - **If resistance to INH and Rifampicin MOR)**
     - **In pulmonary TB: according to WHO aminoglycoside (Kanamycin, amikacin or capremycin) ethiomaide, pyrazinamide and ofloxacin for initial phase.**
     - **In resistant TB meningitis**
     * **No equivalent recommendations**
     * **Ethionamide, prothionamide and cycloserine →penetrate BBB and may be effective**
     * **Guided by drug resistance profiles in individual patients and predicted CSF penetration of drugs.**

   - **DOSE (BTS: table)**
     INH at standard doses achieves CSF levels 10-15 times the MIC of Mycobacterium tuberculosis (higher doses do not improve outcome or shorten treatment in adults).

   - **DURATION:**
     - **At least 6 months (?more prolonged)**

- **BTS: 12 months in uncomplicated cases, extending to 18 months if pyrazinamide is omitted (BTS, 1998)**
- **I2 months may be an overestimation (shorter courses are effective)**
- **Recent review (2001):**
  6 months of anti TB is sufficient provided that drug resistance is low
- **Consider: disease severity, drug toxicity and patient compliance**
- **In Vietnam: 4 anti TB for 3 months followed by 3 drugs for 6 months, extended if intolerance to first-line drugs, if persistent symptoms, signs and inflammatory CSF changes after 9 month of treatment .**

2. <u>Adjunctive CORTICOSTEROIDS</u>
   Cochrane review including 6 randomized trials (595 patients)
   - **those receiving steroids had a lower death rate and a reduced risk of death or severe neurological sequelae**
   - **Beneficial effect on mortality in children (inconclusive in adults)**
   - **May be of benefit in TB meningitis but still small studies**
   - **?which corticosteroid and ? dose**
   - **Dexamethasone for at least first 3 weeks of anti TB chemotherapy followed by tapering over 3 weeks**
   - **In children: 4mg/kg/day of Prednisolone or 12 mg/day of Dexamethasone**
   - **In adults: 16mg/day of Dexamethasone**

3. <u>Response to treatment</u>
   - **90% of deaths in first month of treatment**
   - **Usually slow and fluctuating response: if rapid and sustained response over a few days=wrong diagnosis**
   - **Headache persists for many weeks; fever lingers for 6-8 weeks; neck stiffness takes 4-6 weeks to resolve**
   - **CSF cell counts are raised for 1-2 months, glucose remains low for a similar period and total CSF protein can rise before falling slowly over many months.**
   - **Transient episodes of high fever, headache and increasing neck stiffness during first 2 months of treatment**
   - **Brain imaging if new clinical signs**
   - **Acute deterioration due to hydrocephalus, cerebral infarction, expansion of intracranial tuberculoma and poor adherence to treatment.**

4. **Replace, paradoxical treatment reactions and adverse drug events:**
   - **Reasons for deterioration (table)**
   - **Paradoxical treatment reactions: ?pathogenesis; intense inflammatory response? Timing in TB meningitis**

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STATUS EPILEPTICUS