THE NOVA SCOTIA MEDICAL BULLETIN

Scientific Fortune Telling

"What ye don't know won't hurt ye"
Old Nova Scotian Saying

Years ago mankind was content. Content to accept his lot despite the ravages of war, earthquakes, floods, pestilence, plagues and countless misfortunes which threatened his very existence. The disasters as well as the delights he experienced, were regarded as an inevitable will of the Gods who had to be placated. He had no other means to change his fortune.

Not long after the Garden of Eden, or soon after the first intelligent Ramapithecan conversation[1] (depending on how you look at evolution), the first semblance of scientific scepticism appeared in the quest of the unknown, and man tried to explain or even predict and control his own destiny. Very soon Pythagoras made logical conclusions about triangles, Gallileo disputed the fact that the sun rotated around the earth and the world was no longer regarded as a flat plate in the center of the Universe.

Darwin[2] after intense study of the flora and fauna of the Galapagos Islands shook the theological and scientific world by providing documented evidence of his theory of natural selection. Although to this day some still maintain that the Creation provided this globe with an almost infinite variety of living organisms in one grand sweep, most scientists have accepted the evolutionary emergence of homo sapiens as a consequence of his developing unrivaled intelligence, ingenuity, powers of conversation and remarkable manual dexterity.

In the past century medical science has eliminated many causes of premature death, and has been responsible for preserving some of the frail. It is remarkable, however, how steadfastily some inborn mechanism eliminates the imperfect products of conception before they are born. Most abnormal embroyos are spontaneously aborted. This process known as Tetrathanasia may actually be prevented by drugs such as Chlomiphene.[3] Without this interference, in the ordinary way, 50% of aborted embroyos have a significant chromosomal abnormality. In addition, 30% of stillborn babies have congenital abnormalities. Thus while 95% of infants born are healthy, 2% have major and 3% have minor abnormalities.[3]

Congenital abnormalities may be malformations found at birth or congenital defects — irreversible disturbances resulting from genetic disorder or a result of antenatal environment. Scrimgeour and Cockburn explain that for 65-70% of abnormalities the cause is unknown. Genetic or pre-conceptional causes account for 20%, chromosomal or conceptional causes 3-5% and a known environmental factors are responsible for 7-10%. When a precise diagnosis is known and the mode of inheritance established, parents can be given an accurate prediction of the risks of giving birth to an abnormal child.

During the past ten years, however, advances in medical techniques have made it possible to diagnose many foetal abnormalities in utero and thus allow the parents to decide whether they will allow their offspring to develope and bring fortune or burden into an unfriendly world. For some, this is a decision they do not wish to face; to others, amniocentesis and foetal exploration brings valuable information. Amniocentesis, biochemical microscopic examination and culture of amniotic fluid have been practiced for nearly ten years. We are pleased to publish Elizabeth Winsor's article on Prenatal Detection of Down's Syndrome from the Atlantic Research Centre for mental diseases.

In this process a sample of amniotic fluid is obtained by needle puncture, incubation and tissue culture and are examined for karotype. For constant results, amniocentesis requires the combined efforts of an expert team of physicians, technicians and consultants. A remarkable series of 3,000 consecutive amniocenteses reported by Mitchell Globus *et al.*[4] Amniotic fluid was obtained on first attempt of 99.3% of the last 1,000 cases. Chromosomal abnormalities were detected in 2.4% of the pregnancies monitored because of advance of maternal age. In 0.4% mosaicism was detected and unexpected translocations in 0.4%. Cultures were successful in 99% and Karotype had an error rate of 0.07%. The best time for the procedure seems to be 16 weeks from the time of the last menstrual period. Ultrasound is used by most exponents to localize the fetus and exclude multiple pregnancy. A size 21 needle is recommended.[5 6]

Elizabeth Winsor gives specific indications for amniocentesis including advanced maternal age and a history of chromosomal abnormalities. Nineteen percent of children with Down's Syndrome born in the Maritimes were born to mothers 35 years or older. Whilst the incidence of chromosomal abnormalities in children born to older mothers is well established there is a suggestion that an increased incidence of these defects may soon be prevalent in younger women.

Harlap[7] *et al.* reported three cases of *de novo* chromosomal abnormality in 814 mothers still taking oral contraceptives (pill failure group) — an increased incidence (3.69 per 1,000 compared with similar controls 1.28 per 1,000). The main problems from the patient's point of view must be the two-week delay before an answer is available and the mental worry while waiting to make up their decision about the outcome. All authors emphasize the importance of a wise counselling before the procedure is adopted. Indications for amniocentesis are expanding as new techniques develop. In some centres foetuscopic examination allows the sex to be determined as well as the study of uncontaminated fetal blood. Among the defects under scrutiny are chromosomal abnormalities, x-linked disorders, neural tube defects and biochemical and hematological conditions.

Requests for amniocentesis are rapidly increasing at the Atlantic Research Centre. It is hoped that this Centre will shortly report its findings of the study of alpha fetoprotein in neural tube defects.

Recent publications show promise that it will be possible to detect a hemophiliac in utero.[8] A son born to a mother who is a hemophiliac carrier has a 50% chance of inheriting the disease. Now, she can know whether he is affected or not before he is born. The implications of this finding are particularly significant in view of the Royal Associations of this historic disorder. With the possibility of genetic engineering in the future, this relentless march of scientific inquiry will bring searching ethical problems. For the present, it is reassuring to know that the Atlantic Research Centre is providing practical and reliable help to physicians and their patients who are confronted with the possibility of giving birth to defective offspring, particularly Down's Syndrome.

Meningitis and the Mind

Menigococcal meningitis remains an epidemic disease in Canada. Fortunately, the disease does not reach epidemic proportions. The paper by Bortolusi *et al.* emphasizes the severity of the disease which despite modern antibodies can still give rise to serious sequelae. Accurate and early diagnosis by lumbar puncture as essential and treatment must be started immediately. The authors stress the importance of accurate audiometric and psychological testing after recovery. Some 6-10% of children subsequently have a hearing defect or suffer mental retardation.

Unlike the old Nova Scotia adage, most patients nowadays want to know all that modern medicine can tell them about their future whether this knowledge hurts them or not. It is the way in which the physician dispenses this knowledge that marks his or her skill. □

B.J.S.G.

References on page 27.

An Appreciation

DR. W. J. PAYNE

Dr. Walter Joseph Payne of Sydney, Nova Scotia died in November 1979 following a prolonged illness.

Dr. Payne was a Graduate of Dublin University Medical School and took post graduate studies in Diagnostic Radiology at the Middlesex Hospital in London, England. He served as a consultant radiologist at St. John's General Hospital in Newfoundland from 1958 to 1965. From 1965 to 1968 he was staff radiologist at several hospitals in Harrow, England. He was appointed radiologist at the New Waterford Consolidated Hospital and consultant at St. Rita's Hospital in Sydney in 1968.

Dr. Payne was a member of many Medical Associations including the Royal College of Physicians and Surgeons of Canada, the British Medical Association, the Canadian Medical Association, the Nova Scotia Association of Radiologists and the Cape Breton Medical Society.

Walter was a family man, a devoted father always considerate for the welfare of his wife and children, anxious to give them every opportunity in life regardless of personal sacrifices. He was a very active person in medical circles and local cultural activities, and was a previous Director of the Sydney YMCA.

As a personal friend during his residence in the Cape Breton area, he was always available and rendered valuable advice, professional and otherwise. We have lost a true friend who will always be remembered by his associates in the medical profession.

He is survived by his wife, two sons and one daughter.

H. R. Corbett, M.D.

Prenatal Detection of Down Syndrome in the Maritimes

Elizabeth J. T. Winsor,* Ph.D., F.C.C.M.G.,
Halifax, N.S.

INTRODUCTION

Down syndrome ("mongolism") is the most common identifiable cause of mental retardation and is the result of an extra number 21 chromosome which can be identified in amniotic fluid cells. Prenatal diagnosis of chromosome abnormalities has been available in Halifax since the early 70's and the guidelines for testing have previously been discussed.[1,2,3] Amniocentesis for prenatal diagnosis is usually done at about 16 weeks gestation.

Although the number of pregnancies tested has increased yearly, only a small proportion of those women known to have an increased risk of an abnormal fetus because of maternal age, have had amniocentesis. Laboratory records and estimates of livebirths in Nova Scotia, New Brunswick, and Prince Edward Island in 1978 indicate that about 5% of all childbearing women ⩾ 35 years had amniocentesis. A study of factors influencing whether or not testing was done will be reported separately.[4] At present, the only Maritime laboratory providing chromosome analysis from amniotic fluid is the Cytogenetics Laboratory at the IWK Hospital for Children in Halifax.

The purpose of this report is to provide an update of prenatal testing with particular reference to Down syndrome.

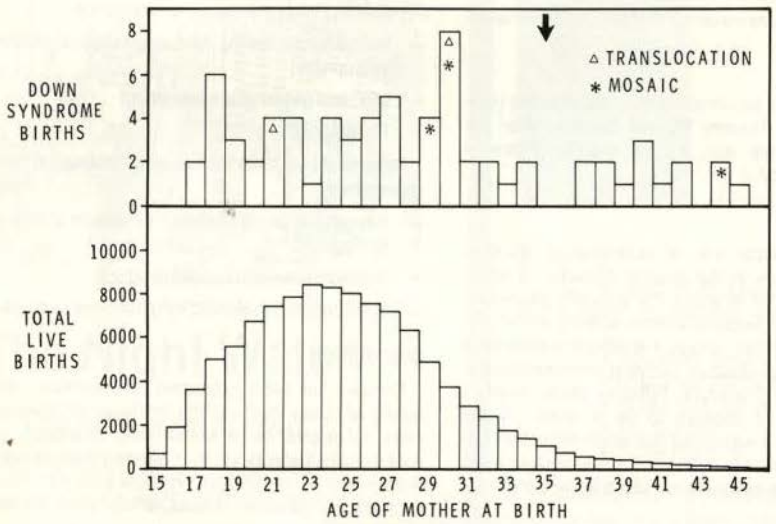
CAUSE AND FREQUENCY OF CONDITION

Down syndrome usually results from an error in cell division, either in ovum or sperm formation. The cause is not known, but the risk increases with maternal age.[5] Most instances of Down syndrome occur sporadically. In less than 5% of cases, one parent carries a translocation.

Those children with Down syndrome, born 1975-1978 in Nova Scotia, New Brunswick, Prince Edward Island, and who had cytogenetic testing, are shown in Figure 1 according to the mother's age of delivery. In this sample, 14/73 or 19% of children with Down syndrome were born to mothers 35 years or older. Estimates of the numbers of total live-births for 1975-78 are based on vital statistics for 1975 and 1976. Of all births, about 5% were born to mothers age 35 or older.[6] The number of affected children who did not have chromosome testing is not known, thus Figure 1 represents an underestimate of the true incidence. Unfortunately, there is no way of checking whether the maternal age distribution in this sample represents the distribution of mothers with Down syndrome children in the population. In British Columbia, the proportion of mothers of Down syndrome infants under 35 rose from 46% in the period 1952-55 to 80% in 1972-73.[7] The mean maternal age of Down syndrome infants in Manitoba also decreased from 1965-1974. However, in Manitoba there was an increase in absolute numbers of Down syndrome births to mothers age 35-39 years, from 19 in the five years 1965-69 to 26 in 1970-74, despite the falling numbers of live-births to mothers in the age group ($P < 0.005$).[8]

FIGURE 1

BIRTHS IN N.B., N.S. AND P.E.I.
1975 - 1978



Mailing address: Atlantic Research Centre for Mental Retardation, Rm. C-R1, Clinical Research Centre, 5849 University Avenue, Halifax, N.S., B3H 4H7.
*Lecturer, Department of Paediatrics, Dalhousie University.

INDICATIONS FOR AMNIOCENTESIS

Prenatal diagnosis may be appropriate in the following circumstances:

- Maternal age ≥ 35 years
- Previous child with a chromosome abnormality
- One parent a known carrier of a chromosomal rearrangement
- Previous child or sibling of one of the parents with a neural tube defect
- Risk of a serious X-linked disorder
- Previous child with a detectable biochemical disorder

PATIENTS TESTED AND RESULTS

Maternal age was the most common indication for testing and only those patients are presented in this report (Table I). Alpha-feto-protein measurement for detection of anencephaly and spina bifida was performed on all fluids obtained for chromosome analysis. Due to limited laboratory facilities, chromosome analysis was not always performed when the indication for testing was a neural tube defect.

TABLE I

Number of women who had amniocentesis on account of maternal age.

	35-36	37-38	39-40	<41	Total
1974	1	5	3	6	15
1975	1	1	4 (1)	8 (1)	15 (2)
1976	10	8	14 (1)	10	42 (1)
1977	8	13	9	14 (1)	44 (1)
1978	16	20 (2)	7	10	53 (2)
TOTALS	36	47(2)	37 (2)	48 (2)	168 (6)

(Numbers in brackets are the number of chromosomal abnormalities detected.)

Since 1974, a total of six chromosome abnormalities (4 — Down syndrome, 2 — Trisomy 18) was detected when the indication was maternal age. All six couples chose to terminate the pregnancy.

COMPLICATIONS

There is a theoretical risk of spontaneous abortion following amniocentesis in the second trimester of pregnancy. An increased risk of about 1% is usually quoted for counselling purposes.[9] Because women seeking amniocentesis tend to be a "high risk" group, it is difficult to determine whether a spontaneous abortion following amniocentesis is directly related to the procedure. Difficulty encountered in obtaining amniotic fluid appears to be a factor. In the Canadian MRC study, it was noted that when more than two needle insertions were made during one amniocentesis there were significantly more spontaneous abortions and stillbirths ($P < 0.001$).[10]

Of the total of 168 women tested in 1974-78 because of maternal age, twelve aborted spontaneously between the amniocentesis and twenty-eight weeks gestation. Of these, it is important to note that one fetus had a myelocele. In a second instance, the amniotic fluid obtained was brown suggesting fetal death probably occurred prior to amniocentesis.

Several culture failures occurred within a relatively short time span and a problem with laboratory glassware was identified as the most likely cause. When culture failure occurred, a repeat amniocentesis was offered. Culture failure as recorded in Table II implies that the karyotype was not known prior to delivery. If analysis from a repeat sample was successful the case was not included as a problem.

Delivery records were obtained for almost all women in this group. No errors in chomosomal diagnosis or in prediction of fetal sex were discovered. No child with Down syndrome was born to a woman for whom a result was not obtained. However, a forty-one-year-old woman who attended our clinic in 1974 and decided not to have testing, had a child with Down syndrome.

TABLE II

PROBLEMS IN PRENATAL DIAGNOSIS

	Total† Women Tested	Spontaneous Abortion <28 wk.	No Result: Failure to Obtain Fluid	No Result: Culture* Failure
1974-1977	115	10	5	5
1978	53	2	3	3
TOTAL	168	12	8	8

†Total applies only to those women tested because of maternal age.
*Each patient is recorded in the table only once. In addition, cells suitable for chromosome analysis were not obtained from five of the women who aborted spontaneously.

REFERRALS

When making referrals for prenatal diagnosis, it is helpful if physicians provide the following information:

- Indication for testing (documentation of problem when appropriate)
- LMP and gestational assessment
- Rh factor

Patients should have the following information prior to their appointment:

- Attendance at clinic does not require commitment for testing
- Husbands are encouraged to attend
- A full bladder is required for ultrasound examination

DISCUSSION

Concern has been expressed by physicians that despite testing of "older mothers" the incidence of Down syndrome does not appear to be substantially changed. Laboratory data indicate that about 80% of affected children were born to women age 34 or younger. No allowance was made in this estimate for affected fetuses which were therapeutically aborted.

In the older women, four instances of Down syndrome were detected to a total of 168 pregnancies (2.4%). In comparison, the population frequency of Down syndrome has been estimated as 1.46 per 1000 live births (0.15%).[5]

SUMMARY

1. In the period 1974-78, chromosome abnormalities were detected in 6 out of 168 or 3.6% of pregnancies to women age 35 or older.

2. About 20% of all children known to have Down syndrome were born to women age 35 and older. These women represent about 5% of the childbearing population.

3. In 1978, about 5% of childbearing women age 35 years or older had prenatal diagnosis.

4. Guidelines for referral of patients to the Genetics Prenatal Diagnosis Clinic are provided. □

For patient appointments, please contact Miss Carole Smith, Nurse Coordinator, Prenatal Diagnosis Clinic (902) 424-6491. Further information may be obtained from Dr. R. H. Lea or Dr. E. J. Winsor, Co-Directors, Prenatal Diagnosis Clinic, Grace Maternity Hospital, Halifax, N.S.

Acknowledgements

Information on the numbers of cases of Down syndrome was obtained from the Fredericton Regional Laboratory and IWK Hospital for Children. Dr. J. P. Welch and Dr. R. H. Lea reviewed the manuscript.

References

1. **Welch J P:** Genetic Screening by Amniocentesis The Current Status. *N.S. Med. Bull.* **52:**115-116, 1973.
2. **Lea R H, Welch J P and Winsor E J:** Antenatal Detection of Genetic Disorders. *N.S. Med Bull.* **53:**147-149, 1974.
3. **Welch J P and MacDonald J M:** Prenatal Diagnosis in the Maritimes. *N.S. Med. Bull.* **55:**103-106, 1976.
4. **Winsor E J T:** Patients' Attitudes toward Prenatal Diagnosis by Amniocentesis. (in preparation).
5. **Trimble B K and Baird P A:** Maternal Age and Down Syndrome: Age-Specific Incidence Rates by Single-Year Intervals. *Am. J. Med. Genet.* **2:**1-5, 1978.
6. Vital Statistics, Vol. I Births 1975 and 1976. *Statistics Canada,* November 1978.
7. **Lowry R B, Jones D C, Renwick D H G and Trinble B K:** Down Syndrome in British Columbia, 1952-73: Incidence and Mean Maternal Age. *Teratology* **14:**29-34, 1976.
8. **Evans J A, Hunter A G W and Hamerton J L:** Down syndrome and recent demographic trends in Manitoba. *J. Med. Genet.* **15:**43-47, 1978.
9. **Riccardi V M:** The Genetic Approach to Human Disease, New York, Oxford University Press, 1977, p. 165.
10. **Simpson N E, Dallaire L, Miller J R,** *et al:* Prenatal Diagnosis of Genetic Disease in Canada: Report of a Collaborative Study. *Can. Med. Assoc. J.* **115:**739-746, 1976.

There is now a Mercedes-Benz station wagon. Come. See it.

ISNOR MOTORS LTD.

2487 Maynard Street,
Halifax, N.S.
429-2300

Engineering begets performance:

The new Fiat Strada

Combined mileage rating 62 km/gal†

Standard features: front wheel drive • five-speed transmission • electronic ignition • extractable AM/FM radio • cloth upholstery • rear window washer-wiper • tinted glass all around.

Test drive before you decide!

Fiat is the only import that offers both:

- a 2 year/40,000 km power train warranty
- a 3 year/120,000 km corrosion perforation warranty

ISNOR MOTORS LTD. 2487 Maynard Street, Halifax, N.S. 429-2300

†Based on laboratory tests using Transport Canada test methods. Actual consumption may vary. Urban winter consumption will be significantly greater. 'Fiat' and 'Strada' are trademarks of Fiat S.p.A.

FIAT

® Fiat S.p.A.

Bacterial Meningitis in Children:

EXPERIENCE AT THE I. W. KILLAM HOSPITAL

R. Bortolussi,* M.D., F.R.C.P.(C), C. Camfield** M.D., F.R.C.P.(C), and M. Lee,† B.A.,

Halifax, N.S.

In spite of the availability of effective antibiotics, bacterial meningitis continues to have an unacceptably high mortality rate. Depending on the bacterial organism and the age of the patient, mortality rates range between 7 and 37%.[1] The rate of long term sequelae is equally disturbing. In the few reports in which neurological and psychological testings have been adequately evaluated, 10% of survivors had major sequelae while 20% had moderate to minor sequelae.[2,3]

In an effort to assess the quality of care of children with bacterial meningitis in Nova Scotia, we reviewed the medical charts of patients discharged from the I. W. Killam Hospital with a diagnosis of bacterial meningitis over a two-year period. This report presents the results of this retrospective study.

SUBJECTS AND METHODS

Medical charts of all children discharged from the I. W. Killam Hospital for Children from January 1, 1977 to December 30, 1978, with a diagnosis of bacterial meningitis were examined. A lumbar puncture (LP) was performed on all children suspected of having meningitis. Results of studies done at outside hospitals were included in the tabulation of our data. Patients with neonatal meningitis (less than four weeks of age), tuberculous meningitis or meningitis attributable to neurosurgical procedures, were not included in this review. All patients in our study had purulent, or culture positive cerebrospinal fluid, (CSF).

RESULTS

Thirty-nine cases of bacterial meningitis were noted during the study period. *Haemophilus influenzae (H. influenzae)* and *Neisseria meningitidis (N. meningitidis)* were the only organisms isolated from these patients. In seven patients no bacterial organism was isolated from the initial CSF but these patients were managed as if they had bacterial meningitis, because the "total picture" at the time was considered to be consistent with this diagnosis. The number of cases caused by *N. meningitidis* was greater than expected, based on the incidence of meningococcal infection across the United States over this same period.[1] The serogroup of meningococcal strains reported in 8 of the 15 isolates were as follows: serogroup A, three cases; serogroup B, three cases; and serogroup C, two cases. There were two deaths during this study period. In both patients medical attention was sought late and the children were severely ill when admitted to hospital.

Clinical information on the children included in this study is shown in Table I. Approximately $^2/_3$ of the patients in whom bacterial organisms were isolated were under 2 years of age. Between the time of onset of the first symptom and the establishment of the diagnosis of bacterial meningitis due to *N. meningitidis* or *H. influenzae*, a median interval of 2 to 3 days had elasped compared with a median of five days in the group of patients in whom no bacterial etiology was found. During this prodromal phase, $^1/_3$ of all of the patients were started on oral antibiotics but in most of these instances, the reason was not clear. Four of the patients in whom no bacteria were isolated had received oral antibiotics before a lumbar puncture was done. At the time of admission to hospital five of the patients were considered to be in coma or severely obtunded. None of the patients, however, in whom sterile CSF was obtained, were in this severe degree of debilitation.

TABLE I

CLINICAL FEATURES OF MENINGITIS AT I. W. K. HOSPITAL

	N. meningitidis	*H. influenzae*	Unknown
Number of patients	15	17	7
Age in Months* (1-130)	21 (4-140)	18 (2-17)	45
Prodrome in Days*	2 ($^1/_2$ - 14)	3 ($^1/_2$ - 7)	5 (1 - 14)
Antibiotics Prior To Diagnosis	22%	43%	57%
State of Conscience:			
Coma	13%	17%	0
Lethargy	78%	83%	57%
Mortality	$^1/_{15}$	$^1/_{17}$	0

*Median (Range).

The diagnosis of meningitis could not be established by the initial examination of CSF cells in all patients (Table II). In two patients the cell count was not elevated and no organisms were seen on gram stain; however, organisms were isolated on culture. In several patients, sufficient CSF was not available to do both cell count and gram stain and only one of these studies was performed. The ratio of CSF glucose to serum glucose was depressed in all groups, and was most severely depressed in patients with meningococcal disease. The white blood cell count (WBC) was elevated in all three groups. Surprisingly, the greatest elevation in WBC was found in patients in whom no organism was isolated from the CSF.

An attempt was made to evaluate the quality of medical management of the patients at the time of admission to hospital. The guidelines of the American Academy of Pediatrics[4], and other authorities on bacterial meningitis management,[5,6] were used for this purpose. The choice of

*Assistant Professor, Department of Paediatrics and Microbiology, I. W. Killam Hospital.

**Assistant Professor, Department of Paediatrics, I. W. Killam Hospital, Halifax, N.S. B3J 3G9.

†Fourth Year Medical Student, Dalhousie University, Halifax, N.S.

antibiotics was considered appropriate in 95% of the charts reviewed. In addition, the dose of antibiotics was consistent with standard recommendations in all but two instances; in whom an excessively high concentration of antibiotic was administered. In 80% of the patients, the rate of intravenous infusion was restricted. Intravenous antibiotics were continued for at least seven days in 94% of the patients assessed; and 70% of the patients were treated for ten days with intravenous antibiotics. In more than half of the cases where meningococcal meningitis could not be excluded, prophylactic antibiotics were not offered to the rest of the family.

TABLE II

LABORATORY FEATURES OF MENINGITIS AT I.W.K. HOSPITAL

	N. meningitidis	*H. influenzae*	Unknown
CSF cell count (median)	2,700	3,100	1,300
Gram Stain (Percent Positive)	50	83	0
CSF Glucose (Percent of Serum*)	9 (0-65)	33 (22-43)	41 (10-59)
WBC count*	16,500 (5-36,000)	16,000 (8-25,000)	22,000 (14-27,000)
Percent Neutrophils*	54 (22-82)	39 (11-68)	72 (21-84)
Bands*	27 (10-37)	17 (3-45)	9 (2-20)

*Median (Range).

Follow-up arrangements made for the patients at the time of discharge were not always recorded in the chart and, therefore, it was difficult to evaluate this aspect of treatment. Fewer than half of the patients, however, had formal audiometric studies done and arrangements for follow-up EEG's, skull x-rays or psychological testing were rarely requested.

DISCUSSION

Bacterial meningitis occurs most commonly in preschool-age children, and mainly during the first two years of life. In most medical centers *H. influenzae* type b is the predominant organism isolated from CSF. Among children under the age of five years, *H. influenzae* is isolated three times more frequently than other organisms.[1] Since the majority of children in our series were less than five years of age when diagnosed, the high frequency of isolation of *N. meningitidis* is very striking. A further review with the Department of Public Health is underway to determine if the incidence of *N. meningitidis* disease across the province is elevated.

More than half of the patients in our series had been ill for two days or longer before the diagnosis was established. This prodromal period is longer than reported in other series.[2,3] Several factors, such as difficulties in transportation or the failure of parents to recognize the significance of symptoms, may have contributed to this delay. However, one-third of the children had been seen by physicians and been given oral antibiotics before a lumbar puncture was done. In these treated patients, the diagnosis of bacterial meningitis could not be ruled out if the CSF was later found to be sterile. This consideration reinforces the need for establishing an accurate diagnosis before beginning antibiotic treatment.

Although recommendations for the treatment of bacterial meningitis vary from one centre to another, the regimen outlined in Table III is most commonly used and is followed in our centre. Chloramphenicol is included with Ampicillin in the initial antibiotic regime since Ampicillin resistant strains of *H. influenzae* have become common in the Maritimes and presently constitute 14% of isolates.[7] Antibiotics should always be given by the intravenous route in order to assure that levels in the CSF are adequate.

Unless patients are in shock or severely dehydrated, intravenous fluids should be restricted to $^2/_3$ of maintenance requirements. This is necessary because the majority of patients with bacterial meningitis have inappropriate secretion of anti-diuretic hormone.[8] In these patients excessive fluid retention can lead to cerebral edema and death. The failure to recognize this problem was the commonest error in management among patients before transportation to our hospital.

Recommendations for prophylactic antibiotics were frequently overlooked. If meningococcal meningitis cannot be ruled out, household and close contacts of the patient should be offered rifampin as chemoprophylaxis for meningococcal disease. Although secondary attack rates in families of patients with *H. influenzae* meningitis was also increased, recommendations for prophylaxis are not yet available. However, susceptible family members should be watched carefully for signs of infection and treated accordingly.[9]

It was not possible to estimate the incidence of major or minor sequelae among our patients because of the lack of consistent re-evaluation. In other centers, high-tone deafness has been found to be a common major sequelae.[2] In our review, fewer than half of the patients had audiometric examination after diagnosis. Learning disorders and disturbances in fine motor co-ordination are the most common minor sequelae of meningitis and occur in 20 to 30% of patients.[2] None of the patients in our review were followed for these disorders.

On the basis of this review the following recommendations are made to physicians across Nova Scotia:

(1) When the diagnosis of meningitis is considered, culture of the blood and CSF should be obtained immediately; if evidence of meningitis is found, the patient should be begun on intravenous antibiotics (Table III). If facilities for obtaining or examining CSF in a safe manner are not available, a blood culture should be obtained. A positive blood culture will be found in approximately 90% of patients with bacterial meningitis. The patient may then be transferred to a centre able to perform a lumbar puncture. *Treatment should not be delayed while the patient is transferred to another centre.*

(2) Once the diagnosis has been confirmed the patient should be transported to a medical centre able to treat and manage the complications of bacterial meningitis. These complications include subdural effusion, inappropriate antidiuretic hormone secretion, seizure disorders and ventriculitis.

TABLE III

RECOMMENDED TREATMENT OF BACTERIAL MENINGITIS

1) I.V. Antibiotics:
   (a) Ampicillin 400 mg/kg/day (divided to every 4 hours).

   plus

   Chloramphenicol 100 mg/kg/day (divided to every 8 hours), and given more than one hour after ampicillin.

   (b) Continue I. V. treatment for at least 10 days.

2) Initial intravenous fluid:

   Two-thirds of calculated normal maintainance fluids unless child is in shock or severely dehydrated.

3) Prophylaxis for close or household contacts:
   (a) *N. meningitidis* suspected:

   Rifampin 5 mg/kg every 12 hours for four doses (2 days), for children under 12 months. For children over 12 months 10 mg/kg every 12 hours for four doses, (maximum daily dose 600 mg).

   (b) *H. influenzae* suspected:

   — observe family members carefully for signs of infection.

(3) If meningococcal meningitis cannot be ruled out, household or close contacts should be given rifampin orally in the recommended dosage (Table III).

(4) All patients with bacterial meningitis should be followed closely and audiometric and psychological testing conducted after discharge. A clinic to follow patients in this manner has been established at the I. W. Killam Hospital. Physicians wishing to enter patients into this follow-up program should consult the author, (R.B.).

At the I. W. Killam Hospital, additional studies for assessment of CSF are available. Lactic acid concentrations in CSF are almost universally elevated in bacterial meningitis.[10] This assay has been reviewed in our hospital and the results of other centers confirmed.[11] Recently, we have added the detection of bacterial antigen in CSF to our investigative tools. This test is particularly valuable in patients who have been treated with antibiotics before CSF was obtained for culture. Both lactic acid and bacterial antigen studies may be done using one milliliter of CSF sent to the I. W. Killam Hospital Research Laboratory.

The results of our review of bacterial meningitis indicate that the treatment regimen and mortality rate in our series compare favourably with those in other medical centres. Since the bacterial agents responsible for meningitis in childhood are universally susceptible to antibiotics in current use, it seems likely that further improvement in the mortality rate will occur only if cases are diagnosed sooner and appropriate treatment started earlier in the course of disease. This will occur only if there is a heightened level of suspicion among parents, nurses and physicians. It is hoped that our review will contribute to this. □

Acknowledgements

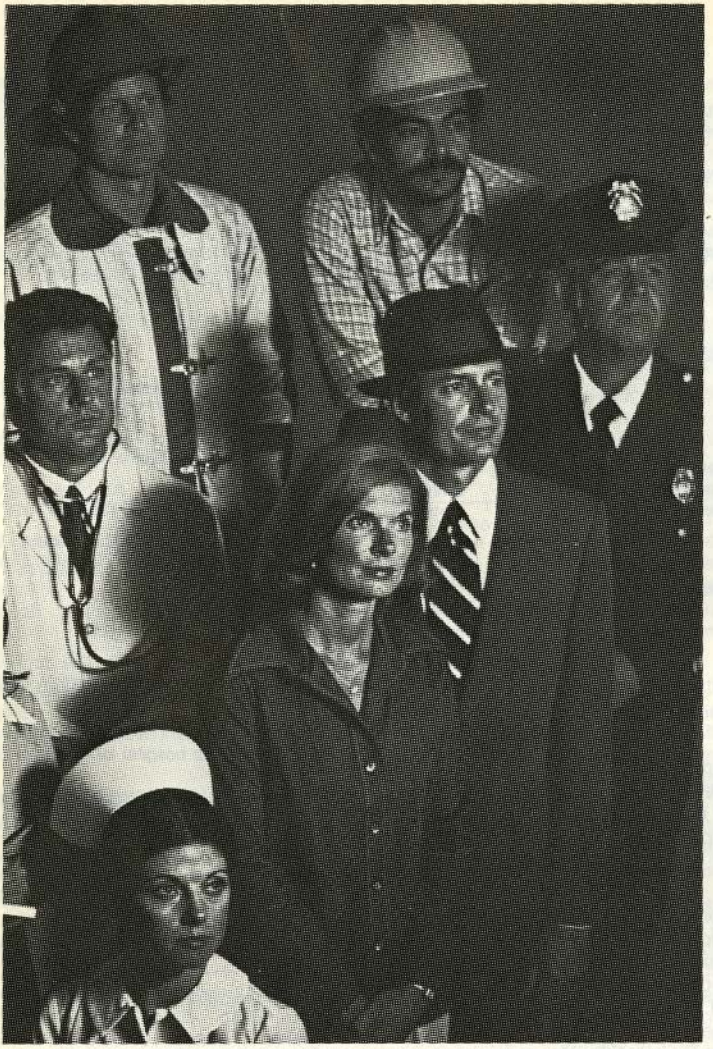
The authors wish to express their thanks to Dr. John Wort and Judie Larson, for their help in obtaining the data on which this review was based.

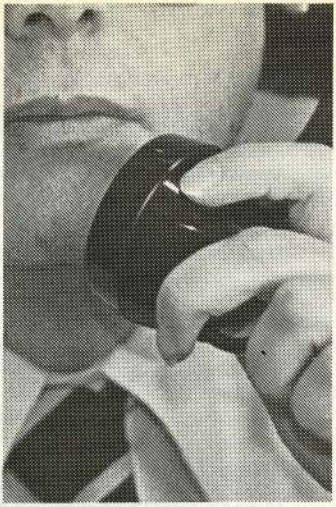
"As a result of this review, we have established a clinic to evaluate patients recovering from bacterial meningitis. At the clinic audiometric and psychological testing is done as well as a detailed neurological examination. Our goal is to see each patient at least twice; six months after discharge and at age 5 years. This is considered as the minimum follow-up that would be recommended and is frequently not obtained because of difficulties in scheduling such tests.

"For patients not treated at the I. W. Killam Hospital, arrangements for follow-up examination can be made by contacting Dr. R. Bortolussi".

References

1. Bacterial Meningitis and Meningococcemia — United States, 1978. *Morb. Mortal Wkly. Rep.* **28:** 277, 1979.
2. **Sell S H, Merrill R E, Doyne E O,** *et al:* Long-term sequelae of *Hemophilus influenzae* meningitis. *Pediat.* **49:**206, 1972.
3. **Ellsworth J, Marks M I and Vose A:** Meningococcal meningitis in children. *Can. Med. Assoc. J.* **120:**155, 1979.
4. **Report of the Committee on Infectious Diseases:** 18th edition, American Academy of Pediatrics Evanston Illinois, 1977.
5. **Smith D H, Ingram D L, Smith A L,** *et al:* Bacterial meningitis: a symposium. *Pediat.* **52:** 586, 1973.
6. **Murray J D, Fleming P, Weber J,** *et al:* The continuing problem of purulent meningitis in infants and children. *Pediat. Clin. N. Am.* **21:** 967, 1974.
7. **Scheifele D W:** Ampicillin — resistant *Hemophilus influenzae* in Canada: nationwide survey of hospital laboratories. *Can. Med. Ass. J.* **121:** 198, 1979.
8. **Kaplan S L and Feigin R P:** The syndrome of inappropriate secretion of antidiuretic hormone in children with bacterial meningitis. *J. Pediatrics.* **92:** 758, 1978.
9. **Ward J I, Fraser D W, Baroff L J,** *et al: Haemophilus influenzae* meningitis. *N. Engl. J. Med.* **301:** 122-126, 1979.
10. **Komorowski R A, Farmer S G Hanson G A,** *et al:* Cerebrospinal fluid lactic acid in diagnosis of meningitis. *J. Clin. Micro.* **8:** 89, 1978.
11. **MacDonald S:** Unpublished data, Halifax, 1979.





A lot of people depend on AIR-PAGE®

. . . to help them keep in touch.

Maritime owned and operated, AIR-PAGE understands the communication needs of local businesses and professionals. Poor communications can often result in a waste of time and money. AIR-PAGE is fully experienced in solving these problems in the most cost effective way.

With the addition of a **Direct Dial* Voice Paging** service to the already accepted operator assisted voice paging and tone only paging, AIR-PAGE is again leading the way. Only with AIR-PAGE can you choose from three different ways to page.

Direct Dial* Voice Paging allows the person receiving your message to hear it directly from you, in your own voice. Each pager has it's own number which you can give out to the people who need to reach you. All they do is dial the number and in a matter of seconds they give you their message privately. This service is available with all models of voice pagers presently in use.

Operator Assisted Voice Paging is designed for those who need a timed message holding service. If you should miss a message or inadvertantly have your pager turned off you simply call the AIR-PAGE * operator who has kept a written record of all your messages.

For those who don't require a spoken message we have a wide selection of **Tone Pagers.**

For further information on how AIR-PAGE can help you keep in touch call us at 453-2640.

*Operates via human interface

Carcinoma of Stomach

COMBINATION OF CHEMOTHERAPY AND SURGERY

J. F. Filbee,* M.B., F.R.C.P.(C), and B. K. Coady,** M.D.,

Halifax, N.S.

The stomach is a relatively uncommon site of carcinoma in Caucasians. In a population of 800,000 in Nova Scotia, 2,363 cases of cancer of all sites were recorded in 1973. Of these, 99 were in the stomach with an incidence of 12.3 per 100,000.[1] It is more common in other areas; e.g. Japan, probably for dietetic reasons.[2] The disease is a characteristically agressive carcinoma with poor differentiation and high mitosis rate. Many cases are inoperable for local or distant spread at first diagnosis, and average life from the first symptom is usually a few months. The overall five-year survival rate is about 7%.[3]

The treatment of choice is generally held to be a total gastrectomy with or without celiac node dissection, but the large majority of patients are inoperable at laparotomy. Response to radiotherapy is disappointing. Adenocarcinoma of the stomach is a relatively radio-resistant tumour arising in a radiosensitive part of the body, and the dosage required for adequate control is often in excess of the tissue tolerance. Specific organs; e.g. kidneys, may limit dosage to less than 4,000 rads while tumour control typically needs between 4,500 and 6,000 rads.

CHEMOTHERAPY

The most promising single agent has been chemotherapy with 5-Flurouracil. Dosage must be individualized, as treatment must usually be taken to a toxic level to be effective, and the mortality rate, especially in inexperienced hands, is unacceptable. The original published dosage was 15 mg/kg body weight intravenously daily for 5 days. This has proved excessive for Caucasians and the more usual dosage is 12.5 mg/kg daily, interrupted if stomatitis or diarrhea develop.[4] Intravenous treatment has been shown to be more effective than oral medications.

An intensive initial "loading" course followed by weekly maintenance is preferrable to weekly treatment only.[5] The response rate is approximately 23% and duration of the response may be as long as two years, but is more likely 9 to 12 months.

COMBINED THERAPY

Considerable success has been obtained with combination 5-FU with radiation therapy. One useful regimen is cobalt therapy 4,500 to 5,000 rads to the involved area delivered over 4 to 5 weeks, combined with 5-FU 500 mg intravenously daily for the first 3 days of treatment. Doctor Aquino has found a response rate from this course of management.[6]

The second chemotherapeutic agent, 1, 3-BIS — (2-chloroethyle)-1-nitrosourea (BCNU) is also effective in about 20% of cases, but when combined with 5-FU the response rate rises to 41%. Response can be remarkably prompt and relatively durable. One of us (J.F.F.) has embarked on a study of this agent. Patients selected are those with inoperable carcinoma of the stomach. The regimen is as follows: BCNU 40 mg/m^2 intravenously daily for 5 days combined with 5-FU 10 mg/kg daily for 5 days, subject to lack of toxicity. Response rates approaching 50% have been obtained.[7] Following is a report of one case:

This 69 year-old Caucasian man presented with a one year history of eructations and 30-pound weight loss. There was a large epigastric mass. At laparotomy "The stomach was found to be involved in an extensive cancer at approximately the mid portion and posteriorly a plaque of carcinomatous tissue was found to be extending up towards the region of the esophagus. A few nodes were palpable in the omentum. The liver appeared free". It was thought that a radical resection was not practical and a total gastrectomy unjustified. The abdomen was closed without any gastric suction. Post-operative healing was satisfactory.

November 14-18, 1975 — 5-FU 660 mg I.V. 'push', BCNU 50 mg I.V. daily for 5 days. Treatment was well tolerated. Patient was discharged in good condition.

December 1975 — a repeat course of same treatment was well tolerated.

February 1976 — Upper G.I.: considerable reduction of tumour mass. Gastroscopy: A remarkable response with no tumour ulceration. BCNU 75 mg, 5-FU 750 mg given I.V.

April 1976 — two further treatments of chemotherapy.

May 27, 1976 — Laparotomy: Carcinoma of the lesser curvature of the stomach markedly decreased in size. High subtotal gastrectomy performed with Bilroth II gastrojejunum anastomosis.

Pathologist Report: Moderately well differentiated adenocarcinoma of stomach January 1977 — patient is well. Weight is steady. Physical examination is negative. No palpable nodes. No abdominal masses.

SUMMARY

Many attempts have been made in the last 70 years to render tumours of borderline resectability operable. This has been attempted for the breast, but with doubtful success. Current attempts are being made to assess this technique with carcinoma of the prostate.

This report concerns an apparently successful gastrectomy for a patient with an originally inoperable carcinoma of the stomach following treatment with a combination chemotherapy using 5-FU and BCNU. □

Acknowledgements:

My thanks to Dr. A. Laycock, Librarian, Halifax Infirmary for her advice and help with references.

The BCNU was supplied by the National Institute of Health, Bethesda, Maryland under licence No: NCS-409962.

*Radiation Oncologist, Halifax Infirmary, Halifax, N.S.

**Deceased, lately Chief of Surgery, Halifax Infirmary, Halifax, N.S.

References

1. Cancer Incidence in Nova Scotia, 1973, Cancer Registry Province of Nova Scotia.
2. **Merliss RR:** Talc-Treated Rice and Japanese Stomach Cancer, *Science,* **173:** 1141-1142, 1971.
3. **del Regato Juan A, Spjut Harlan J:** *Ackerman & del Regatto's Cancer* pgs. 486-488, C.V. Mosby Company, St. Louis, 1977.
4. **Carter Stephen K, Bakowski Marie T, Kurt Hellman:** *Chemotherapy of Cancer.* A Wiley Medical Publication, John Wiley & Sons 1977, Pg 55.
5. *ibid,* pg. 125.
6. **Aquino Jose A:** Presented as a Paper — Royal College of Surgeons, Montreal, 1977.
7. **Kovach JS, Moertal CG, Schmitt AJ et al:** A controlled study of combined 1, 3-bis (2-Chlorethyl) — 1 — Nitrosourea and 5-Fluorouracil therapy for advanced gastric and pancreatic cancer. *Cancer* **33:** 563-567, 1974.

Baclofen (Lioresal[R]) for Spasticity

C. B. Tuttle,* M.Sc. Phm., and T. J. Murray,** M.D., F.R.C.P.(C),
Halifax, N.S.

Baclofen (Lioresal[R]-Geigy) is a recently introduced oral muscle relaxant, indicated for the alleviation of signs and symptoms of spasticity in patients with multiple sclerosis (MS) or with other disorders of the spinal cord. It may be of particular value for the relief of flexor spasms and concomitant pain, clonus and muscular rigidity.[1,2] It may also be of some value in patients with spinal cord injuries and other spinal cord diseases. Baclofen appears to be of less benefit in patients with spasticity resulting from cerebral lesions such as stroke and cerebral palsy. This drug is of particular value in the treatment of MS, a disorder in which spasticity constitutes the most important factor in disability.

BACKGROUND

Baclofen is an analogue of the naturally occurring CNS inhibitory transmitter, gamma-aminobutyric acid, which has been modified by the addition of a lipophilic group to enable penetration across the blood-brain barrier.[2,3] Most opinions hold that baclofen acts on the spinal cord to reduce the excitability of monosynaptic reflex arc spindles, so reducing gamma motor activity.[2,4-6] Prior to its introduction, the most effective drug for the long-term management of spasticity was diazepam 15 to 60 mg/day in divided dosage.[7,8] It acts centrally as well as on the interneurons of the spinal cord to depress tonic reflex activity. However, patients often experience drowsiness before adequate control of spasticity is achieved.[8-10] Baclofen's action appears to be mediated predominantly through a spinal cord mechanism, and hence, is able to provide a more selective muscle relaxation without the excessive sedation or decrease of residual voluntary muscle power which characterizes the use of diazepam.

Another drug, dantrolene sodium (Dantrium[R]), given in doses up to 300 mg/day, acts by interfering directly with the role of calcium in the muscle itself.[11-13] Its usefulness is restricted by the muscle weakness it causes.[14] Its use has also been associated with the development of abnormal hepatic function and fatal hepatotoxicity.[11,15,16]

PHARMACOKINETICS

Baclofen is absorbed relatively rapidly and almost completely following oral administration. Peak blood levels occur after 1-2 hours and serum half-life is 3-4 hours. The drug is metabolized to a limited extent only, and is excreted largely unchanged in the urine. About 80 per cent of an oral dose appears unchanged in the urine within 24 hours. At peak plasma levels, effective concentrations of baclofen are reached in the brain and spinal cord.[17]

CLINICAL TRIALS IN MULTIPLE SCLEROSIS

Since 1966, evidence has been accumulating that baclofen is an effective and well tolerated antispastic drug for patients with MS. These data are reviewed by Brogden *et al.*[18] and Sachais *et al.*[1] Baclofen has been shown to be effective in reducing flexor and extensor spasms, stretch reflex, clonus and pain associated with spasm. This effect has been noted in placebo controlled trials, where doses of 15 to 100 mg per day of baclofen have been used.

There are limited data on the comparative effects of baclofen and other antispasticity agents when studied in a controlled, crossover fashion. Cartlidge *et al.*[19] in England and From and Heltberg[6] in Denmark, independently, found baclofen to be significantly more effective than diazepam in reducing spasticity due to MS. Baclofen was associated with considerably fewer intolerable reactions. Ketelaer and workers' experience with baclofen and diazepam in 200 patients reveals that baclofen 30 mg daily is more effective than diazepam 15 mg daily and is well tolerated even after treatment periods of over two years' duration.[20] In some unpublished work, Hattab[21] found no significant difference between baclofen and diazepam in the improvement in spasticity, flexor spasm, clonus and bladder function. The dosage of baclofen varied between 30 and 75 mg/day. Other workers report a satisfactory response to baclofen 60 mg in five out of six cases "resistant" to diazepam 30 to 60 mg/day.[3]

Much of the necessary therapeutic information and evidence of efficacy has been obtained from open trials with baclofen. Generally, about 60 to 86 per cent of patients with MS or spasticity of purely spinal or cerebral origin, have obtained some degree of improvement in spasticity and other symptoms.[18]

The pharmacology of baclofen suggests trials might be worthwhile in the management of pain syndromes such as trigeminal neuralgia, tardive dyskinesia and in dementia, but trials have not been carried out as yet. It may also be of benefit in myotonia.

SIDE EFFECTS

The most common side effects include drowsiness, nausea, dizziness and weakness, although the drowsiness is usually less than that caused by diazepam. Gradual introduction of baclofen and slow increases to maintenance dosage levels can often minimize these side effects. Less commonly, nausea and vomiting, asymptomatic hypotension, insomnia, mental confusion, hallucinations, euphoria, depression, depersonalization, headache and allergic skin reactions may occur. These effects may prove dose-limiting in specific patients and occasionally may necessitate withdrawal of therapy. Some patients with convulsive disorders have experienced deterioration in seizure control while receiving baclofen.[18] The most troublesome side effect has been the development of increased weakness of the limbs. A dose-related effect, this muscular weakness is often the main cause for withdrawal of therapy[1,18,22], but it can be reduced by lowering the dosage over 7 to 21 days.

*Supervisor, Drug Information Centre Camp Hill Hospital, Halifax, N.S.
**Professor of Medicine, Dalhousie University and Chief of Medicine, Camp Hill Hospital, Halifax, N.S.

There have been reports of auditory and visual hallucinations, anxiety, sweating, insomnia and tachycardia, following within 12 to 30 hours of the abrupt withdrawal of baclofen.[22-25] Unless the side effects or complications are serious, the drug should be reduced gradually over days to weeks when therapy is discontinued.

DOSAGE

Gradual titration of dosage is critical for achieving an optimal antispastic response with minimal side effects. The recommended schedule is to start with 5 mg three times daily for at least 3 days and increase by 5 mg three times daily every fourth day, to 20 mg three times daily. Thereafter, additional increases may be necessary but the total daily dose usually should not exceed 100 mg. Occasionally, under careful supervision, the dosage can be increased to 150 mg daily with improved results. Most patients require between 40 to 60 mg of baclofen per day.[22,26]

LIMITATIONS TO THE TREATMENT OF SPASTICITY

In the nonambulant population with spinal cord lesions, substantial benefits in terms of the reduction of pain associated with flexor spasms and in facilitating nursing care, are derived from the relief of spasticity. On the other hand, spasticity itself may help some patients stand or walk, and the reduction in tone of a spastic lower limb in an ambulant patient may uncover greater incoordination and underlying weakness. Hence, antispasticity therapy may be more handicapping than the spasticity it relieves. In such cases the dosage should be low to achieve only a minimal but potentially helpful antispasticity effect, or not continued at all.

SUMMARY

Baclofen is an effective and well tolerated drug for relieving many of the troublesome symptoms of spasticity in patients with MS. It may increase independence in activities of daily living and improve nursing care and physical therapy. Patients who receive baclofen in the early stages of disease, before major disabilities become permanent, are more likely to gain significant benefits with activities of daily living. The more disabled patients with advanced disease may not experience significant functional improvement, but may obtain symptomatic relief of painful spasms and better tolerate their immobility. Physiotherapy and nursing care may also be easier and more successful with baclofen therapy in the severe cases. Like any muscle relaxant, it is unlikely to make nonambulatory patients ambulatory; and in some cases, the gait of the ambulatory patient may worsen. Baclofen is probably of greatest value in the management of nonambulant patients who do not require their spasticity for support. Even those who do improve seldom obtain much improvement in gait.

Baclofen must be introduced gradually and titrated to meet the requirements and tolerances of individual patients. Many patients will experience weakness, somnolence and vertigo as a matter of course during therapy. These reactions are generally transient; however, 15-20 per cent of patients cannot tolerate the medication because of these side effects. Muscle weakness will be dose-limiting in some patients. Baclofen should not be discontinued abruptly, but should be withdrawn slowly over 7 to 21 days depending on the dosage reached. Despite its limitations, baclofen is the best antispasticity agent presently available. □

References

1. **Sachais BA, Logue JN and Carey MS:** Baclofen, a new antispastic drug; A controlled multicenter trial in patients with multiple sclerosis, *Arch Neurol* **34:** 422-428, 1977.
2. **Hedley DW, Maroun JA and Espir MLE:** Evaluation of baclofen (Lioresal) for spasticity in multiple sclerosis, *Postgrad Med J* **51:** 615-618, 1975.
3. **Jones RF, Burke D et al:** A new agent for the control of spasticity, *J Neurol Neurosurg Psychiat* **33:** 464-468, 1970.
4. **McLellan DL:** Effect of baclofen upon monosynaptic and tonic vibration reflexes in patients with spasticity, *J Neurol Neurosurg Psychiat* **36:** 555, 1973 (From ref 2).
5. **Knuttson E, Lindbloom U and Martensson A:** Differences in effects in gamma and alpha spasticity induced by the GABA derivative baclofen (Lioresal), *Brain* **96:**29, 1973 (From ref 2).
6. **From A and Heltberg A:** Double-blind trial with baclofen (Lioresal) and diazepam in spasticity due to multiple sclerosis, *Acta Neurol Scand* **51:** 158-166, 1975.
7. **Cook JB and Nathan PW:** On the site of action of diazepam in spasticity in man, *J Neurol Sci* **5:** 33-37, 1967 (From ref 1).
8. **Anon:** Drug treatment of spasticity (Ed), *Lancet* **2:** 918-919, 1970.
9. **Anon:** Baclofen in spasticity, *Lancet* **2:** 594, 1977.
10. **Burke DJ:** An approach to the treatment of spasticity, *Drugs* **10:** 112-120, 1975.
11. **Pinder RM, Brogden RN et al:** Dantrolene sodium; a review of its pharmacological properties and therapeutic efficacy in spasticity, *Drugs* **13:** 3-23, 1977.
12. **Dykes MHM:** Evaluation of a muscle relaxant; dantrolene sodium (Dantrium), *J Am Med Assoc* **231:** 862-864, 1975.
13. **Barto MH:** Dantrolene sodium evaluation, *Drug Intel Clin Pharm* **9:** 42-44, 1975.
14. **Gelenberg AJ and Poskanzer DC:** The effects of dantrolene sodium on spasticity in multiple sclerosis, *Neurol* **23:** 1313-1315, 1973.
15. **FDA:** Dantrolene hepatotoxicity, *FDA Drug Bull* **5:** 12, 1975.
16. **Utili R. Boitnott JK and Zimmerman HJ:** Dantrolene-associated hepatic injury; incidence and character, *Gastroenterol* **72:** 610, 1977.
17. **Faigle JW and Keberle H:** The metabolism and pharmacokinetics of Lioresal, *In* Birkmayer W (ed): Spasticity, a topical survey, International Symposium, Hans Huber, Vienna, 1972. pp 94-100 (From ref 1 and 18).
18. **Brogden RN, Speight TM and Avery GS:** Baclofen; a preliminary report of its pharmacological properties and therapeutic efficacy in spasticity, *Drugs* **8:** 1-14, 1974.
19. **Cartlidge NEF, Hudgson and Weightman D:** A comparison of baclofen and diazepam in the treatment of spasticity, *J Neurol Sci* **23:** 17-24, 1974 (From ref 1).
20. **Ketelaer CJ and Ketelaer P:** The use of Lioresal in the treatment of muscular hypertonia due to multiple sclerosis, *In* Birkmayer W (ed): Spasticity, a topical survey, International Symposium, Hans Huber, Vienna 1972 pp 128-131 (From ref 1 and 18).
21. **Hattab JR:** Overview of European clinical experience with baclofen (Lioresal), *In* Spasticity — A disorder of motor control, Lioresal International Symposium, Scottsdale, Arizona, 1972, pp 25-26.
22. **Anon:** Baclofen (Lioresal); A new muscle relaxant for multiple sclerosis, *Med Lett Drugs Therap* **20:** 43-44, 1978.

Continued on page 27.

L-Dopa Therapy and Parkinson's Disease
A 10-YEAR REAPPRAISAL

S. Phillips,*B.Sc.,
London, England,
and T. J. Murray,**M.D., F.R.C.P.(C),
Halifax, N.S.

INTRODUCTION

The first 22 cases of Parkinson's disease to be treated with L-Dopa at the Victoria General Hospital Parkinson's Clinic were reviewed in 1972.[1] Results after two years of therapy were excellent in 9 cases (40%), good in 3 (14%), fair in 5 (23%) and poor in 5 (23%). They were sufficiently impressive that the possibility of the medication arresting the disease in some instances was considered. Today, worldwide experience with L-Dopa is extensive and its impact on long-term results, progression of the disease and mortality in patients with Parkinson's disease is becoming clear, as are its side effects. This paper examines the current status of L-Dopa therapy.

THE DEVELOPMENT OF L-DOPA THERAPY

In 1960, Ehringer and Hornykiewicz reported that the normally high concentration of dopamine in the human corpus striatum was severely reduced in patients with idiopathic and postencephalitic Parkinson's disease.[2] The depleting of striatal dopamine was considered a causal factor in producing Parkinson's disease and the depletion itself was seen as a consequence of viral infection (postencephalitic), drugs or idiopathic degeneration.

This hypothesis had clear therapeutic implications — if the reduction of brain dopamine contributed to the clinical features of Parkinson's disease, correction of the depletion should alleviate the syndrome. The initial investigations, undertaken independently in Vienna and Montreal, reached the same conclusion — L-Dopa, a precursor of dopamine which could pass the blood-brain barrier, was beneficial in Parkinson's disease. Nevertheless, the clinical improvement was limited because small doses were used and side effects, such as nausea, were troublesome. In 1967, Cotzias *et al* found that very much larger doses of L-Dopa could be tolerated if the intake was increased slowly and that clinical results were often dramatic.[3]

The combination of L-Dopa with a peripheral decarboxylase inhibitor resulted in a marked decrease in the amount of L-Dopa required to achieve similar results, with less nausea, vomiting and hypotension. Now that experience with dopa decarboxylase inhibitors has been extensive, L-Dopa is seldom used alone. With the addition of inhibitors, patients can tolerate the dopa well and larger brain concentrations are achieved; however, the incidence of central nervous system toxicity has increased.

*University of London, London, England.
**Professor of Medicine, Dalhousie University and Chief of Medicine, Camp Hill Hospital, Halifax, N.S.
Mailing Address: Dr. T. J. Murray, Department of Medicine, Dalhousie University, Halifax, N.S. B3H 4H7.

THE OUTLOOK BEFORE L-DOPA

To assess the impact of L-Dopa therapy, it is necessary to understand the natural history of Parkinson's disease before this drug was used. Hoehn and Yahr[4] compiled statistics from 802 patients with Parkinson's disease who were seen between 1949 and 1962. They noted 340 deaths (42.8%). The mean age of onset of idiopathic Parkinson's disease in these patients was 55.3 and the mean duration of illness 9.7 years. Among 241 patients seen within two years of onset of the disease and followed up, there were 91 deaths or 3 times the number predicted from life expectancy tables. Death was usually due to pneumonia, urinary tract infection or other consequences of being bed-ridden in the late stages of the disorder.

With the advent of L-Dopa therapy one must now ask:

1. Does L-Dopa therapy improve the quality of life?
2. Does L-Dopa therapy alter the progression of the disease?
3. Does L-Dopa therapy prolong life?

LONG TERM THERAPY: PROBLEMS AND RESULTS

About 15% of patients fail to respond to L-Dopa therapy. The remaining 85% divide into three roughly equal groups — those who obtain dramatic relief, those with moderate relief and those with only modest benefit. The greatest improvement is reduced hypokinesia and most patients experience significantly less rigidity; a smaller number have reduced tremor.

Significant complications and side effects arise in 5% of patients in the initial period of therapy. Nausea, vomiting and hypotension have been reduced significantly by the dopa decarboxylase inhibitors. However, involuntary movements appear in a reasonably large number of patients as early as two months after the start of therapy and become an increasing problem as therapy is continued. It is felt that the loss of nigrostriatal neurons results in denervation supersensitivity of dopamine receptors in the striatum.

Usually the first manifestation of dyskinesia is an orofacial dyskinesia involving tongue movement, lip smacking, facial twitching, gnawing and chewing movements.

Abnormal involuntary movements in the limbs appear later, particularly in the hands and eventually the legs. When the legs are involved the patient may be able to predict the onset because of a strange feeling of warmth or tingling in the part of the body that is affected. This initial orofacial dyskinesia can be reversed by decreasing the dose of L-Dopa, although the abnormal movements may recur at lower doses later on. Patients seldom complain or seem to notice the orofacial

dyskinesia, although it may be a concern to the family and may be quite noticeable. The orofacial dyskinesia resembles tardive dyskinesia in patients on long-term phenothiazines. Phenothiazine may reduce the dyskinesia, but usually at the expense of worsening the parkinsonian features. It is of interest that dyskinesia is not seen in non-parkinsonian patients taking L-Dopa.

Other side effects include insomnia, agitation, irritability, anxiety, hallucinations and paranoia. An acute confusional state may occur, often with hallucinations; organic brain syndrome or dementia predating the onset of Parkinson's disease may be aggravated by L-Dopa therapy.

End-of-dose akinesia is the complete re-emergence of tremor, rigidity and akinesia occurring 3 to $3^1/_2$ hours after each dose. It often follows a period of dyskinesia, but abnormal involuntary movements are not present during this phase.

The **"on-off" phenomenon** is a period of extremely rapid change alternating between dyskinesia and akinesia, often appearing within minutes of a dose. It usually occurs in patients who have previously suffered from abnormal involuntary movements for several months. The patient may be quite mobile, usually with orofacial dyskinesia, but then may suddenly switch to a rigid akinetic state without dyskinesia that lasts from a few minutes to an hour. Occasionally the "on-off" phenomenon merges slowly into end-of-dose akinesia. In both the "on-off" phenomenon and end-of-dose akinesia the plasma dopa levels are low.

Akinesia paradoxica or hypotonic freezing occurs when encountering obstacles or certain constrictions in visual input, especially when there is an element of psychological stress. This problem also occurs in patients with Parkinson's disease who are not on L-Dopa, but it is often more marked in those on L-Dopa. It can occur at any time during therapy. The patient will appear to have decreased tone in the leg muscles and decreased postural stability, to the point of easy and frequent falling. The freezing often clears rapidly and is frequently of only short duration. There does not appear to be an associated change in dopa levels. Barbeau considers this problem to be a noradrenalin-related phenomenon caused by the involvement of the locus coeruleus in the degenerative process.[5] L-Dopa probably does not stop the progression of this process.

Dementia occurs in about 30% of patients with Parkinson's disease; it becomes more severe as age increases and the disease progresses. The incidence of dementia and the finding that typical Alzheimer's changes may be present in the cortex indicate that neuronal degeneration in Parkinson's disease extends beyond the substantia nigra, and undoubtedly involves diffuse cortical and subcortical areas in some patients. This becomes an important limiting factor in treatment since L-Dopa may worsen the dementia.

In his six-year follow-up of 80 severely akinetic patients, Barbeau[6] reported that the post L-Dopa course of illness seems to follow four phases: (1) notable improvement in 80% of patients; (2) plateau period of 3-4 years; (3) slow, gradual decrease in function over 2-3 years; (4) rapid downhill course in which renal and cardiac insufficiency develop and death occurs in a state of refractoriness to L-Dopa.

Barbeau found no evidence that L-Dopa prolonged life. The ratio of observed to expected deaths was 2.4, a finding not dissimilar to that seen before L-Dopa therapy (2.9). Others have reported ratios of observed to expected deaths as follows: 1.94,[7] 1.46,[8] 1.0,[9] and 1.85.[10] In a multicentre study of 1,625 patients, the ratio was 1.33. Taken altogether, these studies suggest some improvement in life expectancy with L-Dopa therapy.

It appears that L-Dopa significantly improves the quality of life in most patients, despite its many side effects with long-term treatment. It also reduces the number of deaths due to Parkinson's disease, but it does not halt the progression of the disease. In combination with a peripheral dopa decarboxylase inhibitor, however, L-Dopa remains the treatment of choice. Other drugs of importance in treating patients with Parkinson's disease are bromocriptine and amantadine; these can be used with L-Dopa to increase the benefit to the patient or to overcome some of the complications of long-term therapy. But the problem is by no means solved.

New drugs are needed that more significantly affect the degenerative process in Parkinson's disease. Furthermore, we must find the underlying cause of idiopathic Parkinson's disease and develop techniques for prevention as well as more effective treatment. □

References

1. **Murray T J:** L-Dopa Therapy in Parkinson's Disease. *N.S. Med. Bull.* **51**:67-70, 1972.
2. **Ehringer H and Hornykiewicz O:** Verteilung von Noradrenalin und Dopamin (3-Hydroxytyramin) im Gehirn des Menschen und ihr Verhalten bei Erkrankungen des extrapyramidalen Systems. Klin. Wochenschr. **38**:1236-1239, 1960.
3. **Cotzias G C, Van Woert M H and Schiffer L M:** Aromatic Amino Acids and Modification of Parkinsonism. *N. Engl. J. Med.* **276:** 374-379, 1967.
4. **Hoehn M M and Yahr M D:** Parkinsonism: Onset, Progression, and Mortality. *Neurology* (Minneap.) **17:** 427-442, 1967.
5. **Barbeau A:** Long-term Assessment of Levodopa Therapy in Parkinson's Disease. *Can. Med. Assoc. J.* **112:** 1379-1380, 1975.
6. **Barbeau A:** Six Years of High Level Levodopa Therapy in Severely Akinetic Parkinsonian Patients. *Arch. Neurol.* **33:** 333-338, 1976.
7. **Sweet R D and McDowell F H:** Five Years' Treatment of Parkinson's Disease with Levodopa. Therapeutic Results and Survival of 100 Patients. *Ann. Intern. Med.* **83:**456-463, 1975.
8. **Yahr M D:** Evaluation of Long-term Therapy in Parkinson's Disease: Mortality and Therapeutic Efficacy. In: Advances in Parkinsonism, ed. by W. Birkmayer and O. Hornykiewicz. Basle, Roche, 1976, p. 435.
9. **Zumstein H and Siegfried J:** Mortality among Parkinson Patients Treated with L-Dopa Combined with a Decarboxylase Inhibitor. *Eur. Neurol.* **14:** 321-327, 1976.
10. **Rinne U K:** Recent Advances in Research on Parkinsonism. *Acta Neurol. Scan.* (Suppl.) **67:** 77-113, 1978.
11. **Joseph C. Chassan J B and Koch M L:** Levodopa in Parkinson Disease. A Long-term Appraisal of Mortality. *Ann. Neurol.* **3:**116-118, 1978.

Principles of Planning, Funding and Evaluation of Short Courses at Dalhousie*

Lynn Curry,** Ph.D., and Ian E. Purkis,† M.B., B.S., F.F.A.R.C.S., F.R.C.P.(C),
Halifax, N.S.

The close of a decade seems an appropriate time to take stock, and to plan for the future. The Division of Continuing Medical Education at Dalhousie is currently reviewing programme offerings, and planning our direction for the 1980's. As a part of this examination we have distilled three points of philosophy (Table I) that frame our short course programming. We feel it is important to present these points of philosophy for discussion. If they are supported by all the participants, in short courses, by target audience members, and by teachers and planners, we will continue to use them in producing short courses, concentrating on their educational effectiveness.

TABLE I

PRINCIPLES OF SHORT COURSE PLANNING AT DALHOUSIE

1. Target audience involvement
2. Courses "globally" self sustaining
3. Planning for evaluation

The first principle, and probably the most important, is our target audience input, which occurs in two ways. Most topics are generated from audience suggestions, solicited during the previous years: at the end of every short course, and during any informal contacts the professional staff has with the community of practising physicians. Secondly, target audience members are involved in committees planning each short course — generally two or three audience planners to one or two faculty planners. The audience planners are usually selected from volunteers outside the Halifax/Dartmouth metropolitan area but within 500 kilometres. At the end of every short course, future volunteers are asked to identify themselves for assignment during the planning phases for the following year's programmes. A total of 36 target audience members served on 14 planning committees during the 1978/79 short course year. We feel this involvement provides a more accurate reading of target audience knowledge and skill needs making the short course content more relevant and applicable to practice.

We have evolved a three-hour blitz meeting that accomplishes the basic decision-making necessary to plan a short course. It was developed due to pressure for time economies: ours, the faculty planning committee members, and particularly the target audience planning committee members. The meetings are chaired by a C.M.E. Division planner and follows a specific protocol (See Table II).

The second planning principle is that over all courses in a year, the short course programme must be self-sustaining because the Division receives no money from the University for programme production. With a zero-based budgeting system, projections about funding sources, attendance and costs, we can predict with some accuracy which courses will produce a surplus and which will incur losses. Excesses of income are applied to support the courses with smaller revenues.

By budgeting in this way, tuition fees are set which vary little from course to course. A further benefit is that specific cost estimates for expenditure items within a course can be offered to outside funding sources (drug companies for example) with a very high degree of confidence in the accuracy of the figures. We maintain strict regulation regarding crediting such outside funding sources. The participation of drug companies is limited to a one-line mention on the final programme. We feel any higher profile would distract from the main intent of the short course, which is to provide individual participants with an opportunity to remediate deficient knowledge or skills.

A third principle, one that we are working to emphasise this year, is to make planning for evaluation a part of the general planning process, and even a planned part of the instructional process. We believe that individuals attending a short course must be aware of the specific areas in which they need skill practice or knowledge, in order to keep up to date. This individual focusing allows for efficiency in learning and enhances retention, but, our problem is that most short courses deliver the same information and the same skill

TABLE II
SHORT COURSE PLANNING PROTOCOL

AT BLITZ MEETING

General Discussion

1. Introduction
2. Discussion — Role of Planning Committee, C.M.E. Confirmation of Agenda

Specific Discussion

1. Reasons for the Course
2. Listing audience needs in the topic area
3. Prioritize needs
4. Set objectives
5. Choose educational method
6. Plan evaluation strategy
7. Statement of overall goal

AFTER BLITZ

8. Finalize course content
9. Prepare draft programme: times, speakers, chairmen
10. Clarify role and tasks for new teachers
11. Set date for local housekeeping meeting prior to session

*This article has been adapted from the text of a presentation at the Association of Canadian Medical Colleges, October, 1979.

**Assistant Director for Research, Division of Continuing Medical Education, Dalhousie University, Halifax.
†Assistant Director, Division of Continuing Medical Education, Dalhousie University.

practice to all individuals at the same time. Even this similarity in delivery can be made more effective for individual learning if each participant could be cued by an individualized pre-evaluation to look for or practise some things more than others.

Most of these ideas are not innovative in themselves but what is innovative is their application in C.M.E. short course programming. We feel that these principles form a system that is both efficient and effective in producing short courses to satisfy the educational needs of large numbers of practising physicians every year. However, we continue to make improvements. We have begun to consider the educational value to the participant of assessing his learning during the short course. This makes evaluation more than a mechanism to determine the effectiveness of the short course at its conclusion. We are also working towards more audience participation in short courses, felling that passive participants learn and retain less information than those actively involved in practising and utilising the new information.

A third area of further investigation is the effectiveness of various short courses in changing physician behaviour. The question is: what is the effect of the information garnered during a short course session? Does it reinforce current practice patterns, does it contribute to changing practice patterns, or is it entirely irrelevant to practice patterns?

The issues and principles outlined in this article are forming the bases of our discussions about short course programming in the next decade. We would be most interested in your thoughts and feelings about our directions, our principles, and the issues we see as facing short courses in the 1980's. If you would like to participate in short course planning, let us know. Please call or write to us at the above address. □

Correspondence

To the Editor:

Your unrepentant correspondent, whose letter was published in the December 1979 Bulletin, is unfortunately anonymous. Would you kindly transmit to him or her my comments as follows:

"Dear Unrepentant:

Lift up thine eyes unto Ottawa from whence cometh all metrication. Blame not the local pathologists for they are sorely afflicted.

Sincerely,
Peter Handforth".

This may be published with my name if you wish. I believe there is a Federal/Provincial agreement that hospital laboratories will report their results in SI units.

Yours sincerely,

Dr. Peter Handforth
Pathologist
Colchester Hospital
Truro, N.S.

To the Editor:

I am sorry that "Unrepentant" (N.S. Medical Bulletin 58, 1979) was apparently not on my mailing list for information about the S.I. We tried to reach all practising physicians in the Halifax-Dartmouth-Bedford Area and used the list of users of our Victoria General Hospital Outpatient Blood Taking Service supplemented by the list of physicians in the Yellow Pages and all V.G. Active Medical and House Staff. The proposed introduction of the S.I. was reported to the Medical Society of Nova Scotia by the Section for Pathology at their 1977 and 1978 Annual Meetings; the reports were accepted with little comment and, I believe, summarized in the Nova Scotia by the Section for Pathology at their 1977 and 1978 Annual Meetings; the reports were accepted with little comment and, I believe, summarized in the Nova Scotia Medical Bulletin. In the Spring of 1979, we mailed a notice of the implementation date with an explanation of the system and conversion data to the above list of physicians. This was followed by the yellow conversion booklet, to the same list, about two weeks before implementation (September 1979). A further printing of the book had to be made just after implementation because some physicians' clerks had discarded the first copy without passing it on. I received no comment whatsoever after this literature was distributed. Nevertheless, I still sought the advice of the Executive Director and the Head of Medicine at the V.G. before proceeding with the conversion.

It would indeed have been presumptuous for a "group of Pathologists and Clinical Chemists" to "impose this switch" upon our physician colleagues. That decision was made early in the 70's by the Federal Government Metrication Committee after consultation with the Canadian Medical Association and other professional bodies — a member of the CMA continues to advise that committee. It would also have been presumptuous of us to attempt to "educate all those who are affected by the changeover". That task is a function of our professional society (the CMA) which was my source of information — one purpose of Dr. McQueen's article was to alert our Society to that need.

"Unrepentant" and I may not worship at the same altar but we certainly support the same religion (the Federal Government) and faced with an "encyclic" (or Bull?) containing an instruction to change to the S.I. by the Fall of 1979 and no adverse reaction to our prior notices, I complied. It seems to us that if physiological substances and drugs react with cell receptors and one another on a molar basis as they almost certainly do, it is logical to measure and report them as such. Most major Canadian and U.S. Journals report in both units and the implementation date for the rest of Canada is the Fall of 1981. That all Halifax Hospitals did not change simultaneously was a problem of organization soon to be resolved.

I sympathize with those who are having problems interpreting the new values, I am learning slower than you as I see fewer patients. We Pathologists and Clinical Chemists are trying to make the changeover as painless as possible but we cannot be blamed for a decision made by others. I suggest that we all work together to make the best of a difficult situation.

Yours sincerely,

J. T. Hindmarsh, M.D., F.R.C.P.(C)
Chairman
S.I. Committee, Section for Pathology

To the Editor:

The Antigonish-Guysborough Branch of The Medical Society of Nova Scotia has decided at a meeting in September 1979 to hold a course in Antigonish in:

(1) Business-Practice Management
(2) Investment & Financial Retirement Planning

Mr. M. Landry from the M.D. Management Ltd. has been invited as lecturer together with an associate specialist in financial matters.

The incentive for such a course came from a similar course held in Halifax in June 1979, which proved to be of great value to all those who attended, particularly to the wives of doctors.

We therefore stress this point in particular, and hope to see the wives of the attending doctors at this outstandingly important course.

The date is set for the 1½ day event for Friday, May 2, 1980 (starting in the afternoon) and for Saturday, May 3, 1980 from morning until late afternoon. Details of time, location and program will be announced when plans are completed.

For the evening of Friday, May 2, 1980 a banquet and dance are planned.

The success of the course will depend on participation.

The fee for the whole course is $125.00 per couple and $75.00 single.

We invite members of other Branch-Societies to attend with their wives.

This announcement is sent to other Branch-Societies and Hospital Staffs, and we hope to get a reply by March 15/80 indicating the interest of their members in such a course and the possible number of attending couples or single members.

Cost of the Banquet and Dance is depending on attendance and may possibly be included in the fee for the course.

Hotel accomodation can easily be arranged for any attending couple or single person.

Yours truly,

Rolf Sers, M.D.
Antigonish, N.S.

To the Editor:

Dr. T. J. Murray's very interesting article on the diseases of famous people (N.S. Med. Bull. **58:**169 1979) states that George III had porphyria — it is far from proven: the argument against the diagnosis has been summarized by Dean (who first described Porphyria Variegata) and by Watson (Dean, G., *The Porphyrias* 2nd ed, Pitman, 1971, p138) who, unlike McAlpine and Hunter, are undoubted experts in Porphyric diseases. McAlpine and Hunter first proposed that George III had Acute Intermittent Porphyria (which his mental condition somewhat resembled) but later claimed that the condition was Porphyria Variegata. They claimed that he inherited the condition from James I of England (VI of Scotland) who was somewhat eccentric (he published a book on Witchcraft) and had episodes when he passed red coloured urine, but these were frequently accompanied by typical renal colic and followed horse riding — James I was found to have renal calculi at autopsy. In support of their theory, McAlpine and Hunter described two codescendants of George III who they claimed had porphyria — they described two codescendants of George III who they claimed had porphyria — they presented biochemical evidence only in one case:

Stool Coproporphyrin 13.5 μg/g dry weight (normal <20)
Protoprophyrin 74 μg/g dry weight (normal <60)
X Porphyrin 15.6 μg/g dry weight (normal <8)

Urine Coproporphyrin 98.4 μg/liter
Normal for V.G. lab <160 μg/24 hours
Porphobilinogen 2.1 mg/liter
Normal for V.G. lab <2.0 mg/24 hours

Although I have little experience with Porphyrin X (it is one of a group of intermediates between Uroporphyrin and Coproporphyrin which are elevated in Porphyria Variegata and Porphyria Cutanea Tarda), I have found that the remainder of the above marginal elevations can be seen in patients as a response to a variety of toxins including alcohol and the contraceptive pill. As Dean records, 8,000 cases of Porphyria Variegata have resulted in South Africa from one ancestor who settled in the Cape in 1688 (the inheritance is autosomal dominant with a variable degree of penetrance) yet McAlpine and Hunter can only find two doubtful cases among the descendants of James I. Also Porphyria Variegata is almost asymptomatic unless the patient takes barbiturates or sulphonamides when it may be rapidly fatal; the disease went unrecognized until these drugs were introduced to clinical practice some 40 years ago. Madness is not a prominent feature of Porphyria Variegata. In summary, George III was undoubtedly mad, he could perhaps have had Acute Intermittent Porphyria although one would have expected frequent cases among the Royal Families of Europe — he almost certainly did not have Porphyria Variegata.

With my tongue in my cheek, I quote Allister Cook who commented that perhaps the 13 Colonies broke away more because they had "grown of age" rather than because they were mismanaged — it seems entirely reasonable that they were taxed to support an army whose main function was to protect them from their hostile neighbours.

Yours sincerely,

J. T. Hindmarsh, M.D., F.R.C.P.(C), Director,
Department of Pathology. Victoria General Hospital. □

JOINT CANADIAN MEDICAL ASSOCIATION
AUSTRALIAN MEDICAL ASSOCIATION
ANNUAL MEETING

Hosted by the British Columbia Medical Association

September 13-19, 1980 — Hyatt Regency Vancouver

CMA General Council: September 14-15

SCIENTIFIC PROGRAM

September 16-19
"Medicine in the 1980's"

- Health Care Evaluation
- Sexual Counselling — Dr.'s Family At Risk **(The Chernicks)**
- Malignancies
  - — Epidemiology; Environmental Carcinogenesis
  - — Regulator Genes; CAT in Diagnosis/ Treatment; TRIUMF Facility of Cancer Registry Use
- Diabetes
- Computer-Medical Applications in the 80's
- Computer Demonstrations
- Sports Medicine

SOCIAL EVENTS

September 13-19

- **Welcome Reception . . .** get acquainted with your Australian colleagues
- **CMA Dinner . . .** featuring ethnic entertainment
- **Atlantic Provinces Reception . . .** at Robson Square — a fine example of Arthur Erickson's design work
- **Presidential Installation and Dinner Dance**
- **Chinese Gourmet Meal . . .** in Vancouver's renowned Chinatown **. . . and much much more!**

For information on registration, hotel reservation spouses' program, post-convention tours, please write to or telephone — **The Canadian Medical Association**
Annual Meeting Coordinator
P.O. Box 8650
Ottawa, Ontario K1G 0G8
(613) 731-9331

The Vial of Life Programme to Start in Halifax County

The Quota Club of Halifax and Radio Station CHNS are jointly launching, with the assistance of many other organizations in the County, a life-saving project which has been established in other areas of Canada and the U.S.A. This new service Club was established by Quota International Inc. on November 3, 1979 and it will work with a second one being formed in Dartmouth by spring.

The first programme to be launched is the **VIAL OF LIFE SERVICE.** This project has been backed by Dr. Nigel Merchant, Emergency Services, Victoria General Hospital, and the Police and Fire Departments of Bedford/Sackville, Dartmouth, Halifax, and the County, together with ambulance services will be involved.

The Service will begin early in March with support from the media. There is the intention that the service will be province-wide, but it is necessary to begin with one particular area. It is hoped that doctors will inform their patients about the service. A sample cover-sheet is provided which will accompany the form to be completed. Information can be obtained by writing to Professor M. D. E. Fraser, Convener, Service Committee, 830 McLean Street, Apt. 24, Halifax, N.S. B3H 2T8.

VIAL OF LIFE — SAVE A LIFE PROGRAMME

Sponsored by the Quota Club of Halifax and CHNS Radio, Halifax

HOW? **VIAL OF LIFE** urges you to put life-saving information into your home, cottage, in case of crisis or emergency.

WHO? **Everyone** but particularly those who live alone or are handicapped, elderly, working parents or those with current medical problems.

WHY? to provide **Your Rescuers** with key information should you be the victim of fire, accident, sudden illness or other emergency — so that you can be cared for properly.

WHAT? **Necessary Information** about you and your family — doctors, blood types, medical needs, are stored in a plastic vial which can be easily located by ambulance drivers, police, fireman, etc.

WHERE? In the upper right-hand shelf of your **Refrigerator.** A vial is taped in.

WHEN? March 1980 distribution of vials and forms begin. Information should be updated every year, or when vital information changes. Check with your doctor if you wish to do so.

THE VIAL OF LIFE PROGRAMME is sponsored in eight countries around the world by the women of Quota International, Inc. Quota service clubs have the co-operation of ambulance, fire, police and community service personnel, as well as other voluntary organizations.

USE a moisture-proof pill bottle — your bathroom cabinet may have one. If not one can be supplied. You may need a large one if there are several family members.

INSTRUCTIONS

— Fill in this form
— Put form in your vial
— Tape vial to upper right corner of refrigerator
— Place identification sticker on front door to alert rescue personnel

A SPECIAL DECAL WILL BE AVAILABLE FOR CARS AT A LATER DATE

NEW MEMBERS

The Physicians listed below have joined The Medical Society of Nova Scotia between Oct. 1, 1979 and Dec. 31, 1979. A most cordial welcome is extended by the Society.

Dr. John M. Archibald	Sydney, N.S.	Dr. Edwin R. Luther	Halifax, N.S.
Dr. John C. Baker*	U.S.A.	Dr. Kaushika Marfatia	Bridgewater, N.S.
Dr. Helen F. Bell	Truro, N.S.	Dr. Neville L. Mason-Brown	Sydney, N.S.
Dr. Lorna J. Carter*	Alberta	Dr. Flora Mehrmanesh*	Alberta
Dr. Rachel D. Carver*	British Columbia	Dr. Martha A. McCarthy*	British Columbia
Dr. Prabhat K. Chaturvedi	Glace Bay, N.S.	Dr. L. Joan McCraken	Hantsport, N.S.
Dr. Donald F. Craswell	Middleton, N.S.	Dr. John R. MacEachern	Glace Bay, N.S.
Dr. Rand Forgie*	Alberta	Dr. Attilio G. Negro*	U.S.A.
Dr. Karamchand J. Gandhi	Bridgewater, N.S.	Dr. Mihkel A. Oja*	Ontario
Dr. Charles F. P. George*	British Columbia	Dr. Robert A. Oliver	Dartmouth, N.S.
Dr. Deborah E. Godsoe	Halifax, N.S.	Dr. Stephen M. Owen	Halifax, N.S.
Dr. Robert D. Graham	Parrsboro, N.S.	Dr. David A. E. Shephard	Sydney, N.S.
Dr. Umesh C. Jha	Dartmouth, N.S.	Dr. Shashi P. Shukla	Halifax, N.S.
Dr. B. Lynn Johnston*	Alberta	Dr. E. Alexander Wadden	Donkin, N.S.
Dr. Jeffrey C. Kirby	Halifax, N.S.	Dr. A. Crawford Walker	Kentville, N.S.

*Recent Dalhousie Graduates.

Personal Interest Notes

Dr. Ian Macdonald, Department of Medicine, Dalhousie University, was invited to The University of Texas System Cancer Center, Houston, Texas, to take part in its 1980 workshop, "Bile Acids and Large Bowel Carcinogenesis". A biochemist, Dr. Macdonald is an investigator into the causes of bowel cancer and is involved in an international research program with colleagues in the U.K. and other parts of North America. He took part in the final session, summarizing and discussing the scientific papers offered during the three-day workshop by speakers from Japan, Scotland, Sweden, England, Canada and the U.S.A.

Dr. Robert O. Jones, Professor of Psychiatry at Dalhousie University, is a member of the Executive Committee of the World Psychiatric Association. As Canadian representative his travels included visits to Vancouver, Charlottetown, Baltimore and London, England. The World Psychiatric Association is particularly concerned about the use of Psychiatry for political purposes in some of the "Iron Curtain" countries.

Dr. Daniel S. Matheson recently retired as Mayor of New Waterford. His accomplishments include restructuring New Waterford's Educational System, and the establishment of the Cape Breton Educational Centre. Successful projects completed include a Sports Facility Community Centre, Recreation and Rehabilitation programs and many community improvements. He was presented with a Paul Harris fellowship, the highest award of the New Waterford Rotary Club.

Dr. N. Barrie Coward, a founder of Easter Seal clinics in Nova Scotia, was honoured on his retirement recently. Dr. Coward has been involved with the clinics since he helped found them 25 years ago. The Canadian Rehabilitation Council for the Disabled now operates the clinics in 20 areas in the province.

Dr. E. A. Moffitt has resigned as head of the department of anaesthesia and will be on sabbatical leave until July, 1980. On his return he will understudy Dr. Lea Steeves and assume the post of associate dean of post-graduate education and clinical-hospital affairs when Dr. Steeves retires in 1981. **Dr. C. E. Hope** has been appointed acting head of anaesthesia.

An annual prize of $500 awarded by the research committee of the Faculty of Medicine was divided between three young researchers this year.

The winners of the Summer Medical Student Competition of 1979 were **Joanne Embree,** a third year student from Truro, N.S., for her summer research with **Dr. Juan Embil** into infections which cross the placenta; **Robert Hamilton,** a second year medical student from Halifax, for his work with **Dr. Harold W. Cook** and cystic fibrosis patients; and **Laurie MacNeil,** a second year medical student from Glace Bay, for his work with **Dr. J. Holland** doing spirometric testing of the lung function of Cape Breton coal miners.

In all, 29 Dalhousie medical students were involved in research programs during the summer recess.

The three competition winners presented papers on their summer research during the Friday-at-Four series of lectures: "The Scientific Basis of Medicine."

Dr. J. T. R. Clarke, chairman of the research committee, said overall quality of the scientific papers submitted by the students entering the competition was extraordinarily good. It was difficult to decide on a clear winner, so committee members recommended the three finalists be tied for the first prize.

OBITUARIES

Dr. Gerald D. Belliveau, (50) of Yarmouth, N.S., died at the Regional Hospital on December 22, 1979. Born at Meteghan, he graduated from St. Anne's College in 1949 and received his M.D. degree at Laval University, Quebec in 1954. He was an active member of the Yarmouth Regional Hospital medical staff. He is survived by his wife, three daughters and three sons to whom we extend our sympathy.

Dr. Lachman S. Gursahani, (46) of Sydney, N.S., died on January 4, 1980. Born in Karachi, Pakistan, he received his medical training and degree in Bombay and did postgraduate studies in London (England), Ottawa, McGill University and Montreal Children's Hospital. He had practised as a Paediatrician in Sydney for the past nine years. Our sympathy is offered to his family.

Dr. Lyle A. Skinner, (59) of North Sydney, died on January 11, 1980. Born in Louisbourg, he graduated as a registered nurse and served during the Second World War with the Royal Canadian Navy. In 1952, he graduated from Dalhousie Medical School and practised in North Sydney until his retirement in March 1979. Surviving are his wife, one son and two daughters. The *Bulletin* extends deepest sympathy to his wife and family.

PLEASE SEE THE INSIDE BACK COVER
FOR **NOTICE** REGARDING THE
MEDICAL SOCIETY INSURANCE PROGRAM.

The Medical Society of Nova Scotia

APPLICATION FOR MEMBERSHIP

NAME .....
Surname Given names

ADDRESS .....

.....POSTAL CODE .....

TELEPHONE NUMBER: Home ..... Office ..... SOCIAL SECURITY NUMBER .....

PLACE OF BIRTH ..... DATE OF BIRTH .....

MEDICAL SCHOOL ..... DATE OF GRADUATION .....

ARE YOU LICENSED IN N.S.? ..... DATE ISSUED ..... NUMBER .....

OTHER DEGREES .....

POST GRADUATE TRAINING .....

.....

PRESENT TYPE OF PRACTICE .....

SECTIONS: Membership in the Society entitles you to make application for membership in the Section(s) of your choice. Please mark (Section(s) you may be interested in.

- ☐ Anaesthesia
- ☐ General Practice
- ☐ Internal Medicine
- ☐ Internes and Residents
- ☐ Obstetrics and Gynecology
- ☐ Ophthalmology
- ☐ Orthopaedic Surgery
- ☐ Otolaryngology
- ☐ Paediatrics
- ☐ Pathology
- ☐ Psychiatry
- ☐ Radiology
- ☐ Surgery
- ☐ Urology

ARE YOU A MEMBER OF
A BRANCH SOCIETY? ..... WHICH BRANCH SOCIETY? .....

REMITTANCE ENCLOSED $ .....

DATE .....SIGNATURE .....

INTERNIST required, certified or eligible for certification, to associate with two internists in a regional hospital with a well equipped intensive care unit.

Please direct inquiries, accompanied by curriculum vitae to:

Mr. J. G. McEachern, Executive Director
Yarmouth Regional Hospital
Yarmouth, Nova Scotia, B5A 2P5

PROVINCE OF NOVA SCOTIA
CAREER OPPORTUNITIES

HEALTH UNIT DIRECTOR IN TRAINING

The Nova Scotia Department of Health is seeking applications from physicians interested in training for positions of Health Unit Director.

The Director is responsible for the delivery of a full range of public health services within a defined geographical area. These services include community nursing, public health inspection, dental, nutrition, epidemiology and child and maternal health. The duties entail program management, liaison with local physicians, hospitals, voluntary health agencies, municipal authorities and health related departments.

The successful applicants will be physicians, eligible for licensure in Nova Scotia and preferably with experience in private practice and who are prepared to complete post graduate training in Community Health/Medicine of at least one academic year under the sponsorship of the Department.

SALARY:

Commensurate with qualifications and experience.

Full Civil Service Benefits.
Competition is open to both men and women.
Please quote Competition Number: 80-304.

Applications and inquiries may be submitted to:

Dr. W. H. Sullivan
Administrator, Community Health Services
N.S. Department of Health
P.O. Box 488
Halifax, Nova Scotia
B3J 2R8
Telephone: (902) 424-4434

Application forms may be obtained from the Nova Scotia Civil Service Commission, P.O. Box 943, Halifax, Nova Scotia, B3J 2V9, and from the Provincial Building, Sydney, Nova Scotia, B1P 5L1.

GENERAL PRACTITIONER/ANESTHETIST

Required for Community Hospital in O'Leary, Prince Edward Island, an accredited 33 bed active treatment general hospital. The hospital serves a surgical population of approximately 14,000. The present medical staff includes two general practitioners, one general surgeon, one obstetrician/Gynecologist and one E.N.T. surgeon. Excellent arrangements for night and weekend coverage. For further information please apply to administrator Mr. Lester A. Brennan at the hospital or phone 902-859-3110.

LOCUMS WANTED — DIAGNOSTIC RADIOLOGIST
for a 100-Bed General Hospital in Nova Scotia Town. Salary negotiable.

Reply: The Nova Scotia Medical Bulletin
Box 100
Sir Charles Tupper Medical Building
Halifax, N.S. B3H 4H7

DOCTOR'S OFFICE PREMISES
SINGLE PRACTITIONER

5750 SPRING GARDEN ROAD
APPROX. 600 S.F. TOTAL, GROUND FLOOR
WAITING ROOM/RECEPTION, LARGE 240 S.F.
EXAMINATION ROOM/OFFICE, LAB, PRIVATE ENTRANCE

6 PARKING SPACES

RENOVATED VICTORIAN HOUSE ACROSS FROM THE PUBLIC GARDENS. MINUTES WALK TO ALL HOSPITALS, DALHOUSIE AND DOWNTOWN.

LEASE TERMS NEGOTIABLE
CALL 422-9339 MSSRS ROBINSON OR MITCHELL

HRDoane and Company
Chartered Accountants

Halifax	Amherst	Fredericton	Port Hawkesbury
St. John's	Antigonish	Grand Falls	St. Stephen
Saint John	Bathurst	Hamilton	Summerside
Charlottetown	Bridgewater	Kentville	Sydney
Montreal	Campbellton	Marystown	Truro
Toronto	Corner Brook	Moncton	Windsor
Vancouver	Dartmouth	Newcastle	Woodstock
	Digby	New Glasgow	Yarmouth

NEW SOCIETY SERVICE FOR MEMBERS

JAMES R. JONES, M.D.
Orthopedic Surgeon
1440 Swampside St. Phone 999-4230
Gottingen, N.S.

For Age (if under 16)

Address Date 19

Label as to contents YES ☐ NO ☐
Safety closure YES ☐ NO ☐
No Repeat ☐ Repeat ☐ X at intervals

Signature .....

Physician's License No _____
This form endorsed by The Medical, Pharmaceutical and Dental Societies of Nova Scotia

_____
_____
_____ _____
_____

For Age (if under 16)

Address Date 19

Label as to contents YES ☐ NO ☐
Safety closure YES ☐ NO ☐
No Repeat ☐ Repeat ☐ X at intervals

Signature .....

Physician's License No _____
This form endorsed by The Medical, Pharmaceutical and Dental Societies of Nova Scotia

NEW LOW COST PRESCRIPTION FORMS STAND BY YOU AND YOUR PATIENTS

Please allow not less than 28 days for delivery of order.

UNIFORM PRESCRIPTION FORMS have been endorsed by The Nova Scotia Medical Society and the Nova Scotia Pharmaceutical Society. These forms provide space for all pertinent information **and** include safety features which inhibit alteration and even counterfeiting.

AVAILABLE NOW to Society members and Nova Scotia hospitals, the forms will be custom printed to include the required individual, group or hospital name(s), address and phone number(s).

TO ORDER carefully fill in the blank form in the top right hand corner with the necessary information as per the accompanying sample copy. Your name, quantity ordered and billing address should go on the form in the bottom right hand corner.

NOTE — Actual prescription forms are printed black on yellow background.

***LOW COST FORMS** in pads of 100 each:

2,500 @ $10.50 per thousand	— $26.25
5,000 @ $ 8.77 per thousand	— $43.85
10,000 @ $ 7.07 per thousand	— $70.70

*Prices include all taxes, shipping and associated charges

QUANTITY ORDERED
2,500 ☐ 5,000 ☐ 10,000 ☐
OVER 10,000 _____forms. (Please advise me of costs)

NAME .....

ADDRESS .....

.....

PHONE .....

CHEQUE/MONEY ORDER ENCLOSED ☐
PLEASE BILL ME ☐
HAVE YOU FILLED IN THE BLANK FORM CORRECTLY?

MAIL TO: **THE MEDICAL SOCIETY OF NOVA SCOTIA**
SIR CHARLES TUPPER MEDICAL BUILDING, HALIFAX, N.S.

SCIENTIFIC FORTUNE TELLING
Continued from page 2.

References

1. **Leakey R E and Lewin R:** Origins E. P. Dulton, New York p. 84.
2. **Darwin Charles:** Origin of the Species by Means of Natural Selection, 1859.
3. **Scrimgeour J B and Cockburn F:** Congenital Abnormalities, *Lancet* **ii:** 1439-1352, 1979
4. **Globus M S *et al:*** Prenatal Genetic Diagnosis in 3,000 Amniocentesis, *New Engl. J. Med.* **300:**157-163, 1979
5. **Simpson M E *et al:*** Prenatal Diagnosis of Genetic Disease in Canada, *Can. Med. Assoc. J.* **115:**739-748, 1976.
6. **Young Phillip *et al:*** Amniocentesis for Antenatal Diagnosis, *Am. J. Obs. and Gyn.* **125:** 495-501, 1976.
7. **Harlap S *et al:*** Chromosome Abnormalities in Oral Contraceptive Brakthrough Pregnancies, *Lancet* **i:** 1342-1343, 1979.
8. **Mibashan R S *et al:*** Plasma Assay of Foetal Factors VIIIC and IX for Prenatal Diagnosis of Hamophilia, *Lancet* **i:** 1309-1311, 1979.

BACLOFEN (LIORESAL®) FOR SPASTICITY
Continued from page 14.

23. **Skausig OB and Korsgaard S:** Hallucinations and baclofen, *Lancet* **1:** 1258, 1978.
24. **Lees AJ, Clark CRA and Harrison MJ:** Hallucinations after withdrawal of baclofen, *Lancet* **1:** 858, 1977.
25. **Stien, R:** Hallucinations after sudden withdrawal of baclofen, *Lancet* **2:** 44, 1977.
26. Product Monograph, Lioresal Tablets (baclofen), Ciba-Geigy Canada Limited, Dorval Que, Oct. 6, 1978.

ADVERTISERS' INDEX