

4-1949

UWOMJ Volume 19, Number 2, April 1949

Western University

Follow this and additional works at: <https://ir.lib.uwo.ca/uwomj>



Part of the [Medicine and Health Sciences Commons](#)

Recommended Citation

Western University, "UWOMJ Volume 19, Number 2, April 1949" (1949). *University of Western Ontario Medical Journal*. 150.
<https://ir.lib.uwo.ca/uwomj/150>

This Book is brought to you for free and open access by the Digitized Special Collections at Scholarship@Western. It has been accepted for inclusion in University of Western Ontario Medical Journal by an authorized administrator of Scholarship@Western. For more information, please contact tadam@uwo.ca, wlsadmin@uwo.ca.

MEDICAL JOURNAL

University of Western Ontario

Vol. 19

April, 1949

No. 2

CASE REPORT

By CHARLES F. S. FISHER, M.D.

Resident in Medicine, Victoria Hospital, London, Ontario

THIS 52-year-old lady was admitted to the Medical Service, Victoria Hospital January 8, 1949. Her complaints on admission were:

- (1) Progressive loss of strength over the last two years.
- (2) Nausea and vomiting for the past six weeks.
- (3) Recurrent headaches.
- (4) Some recent difficulty with gait because of leg weakness.

Two years ago the patient was first troubled with itching on the anterior surface of her legs. This was followed by a local erythema, and the appearance of small to medium sized raised spots. Her doctor diagnosed these as "hives," and gave her various types of local applications which seemed to relieve the itching, but which did not prevent its recurrence. This rash almost completely left about two weeks before admission, leaving only a few small residual scabs. Although the patient felt that she had progressively lost strength over this two-year period, she had been able to work in the fields and help with the harvesting last fall. Weakness, however, had become increasingly more evident in the three or four weeks previous to admission, so that on admission some loss of strength was evident. This weakness was bilateral and was associated with no sensory change with the exception of the above-noted pruritus. Nausea and vomiting had come on in the six weeks preceding admission. It had been associated with some anorexia. It followed meals. Vomitus was undigested food. There was no hematemesis. Headaches had been present many years, and were associated with emotional tension.

Past history revealed an attack of "Yellow Jaundice" when the patient was in her early twenties.

Functional inquiry revealed a weight loss of approximately ten pounds in the last two years. She had had occasional ankle edema, after being on her feet all day. Shortness of breath had occurred with unusual exercise. She had had no unusual pain, except the above-mentioned headaches. Bowel habits had been unchanged, but in the last month or two, stools had been clay colored. She had noted no unusual urinary symptoms, but stated that urine had been darker recently.

Physical examination revealed a well nourished woman, in no apparent distress. The skin was swarthy. Pupils, extra-ocular movements and fundi were negative. The sclerae had a slightly yellowish hue. Ears, mouth, nose, throat and neck were normal. The chest was symmetrical and resonant throughout. Auscultation revealed no rales or rhonchi. Blood pressure was 96/66, heart rate 72, rhythm regular, no enlargement, sounds rather fainter than usual, but no adventitious sounds were heard. The skin of the abdomen had a slightly yellowish cast. No definite masses could be made out. G.U. system appeared normal. Reflexes were physiological. No sensory change was demonstrated. A few scabs were noted on the anterior surfaces of the shins. There was no lymphadenopathy. On several occasions she had been observed scratching the skin of the forearms and the shins. No rash other than the above-noted scabs had been seen since her admission. The findings led to an investigation of liver function.

Laboratory investigation revealed the following: Urinalysis S.G. 1.019, acid, trace of sugar on one occasion, no albumin or acetone, no casts, 5-10 R.B.C.'s and 50-75 pus cells per h.p.f. Urubilinogen was negative on eight occasions and present on five occasions in dilutions of 1:2 to 1:128. Blood serology was negative, N.P.N. 30.0 mgs. %, blood sugar 87/98, blood cholesterol 176 mgs. %, blood phosphorous 3.0, and serum alkaline phosphate 8.2 Bodansky units. Haemoglobin was 64%, R.B.C.'s 3,190,000, C.I. 0.91, W.B.C.'s 7,400, 60% polys, and the smear showed slight but definite anisocytosis and poikilocytosis. E.S.R. was 30 mm. in the first hour. Prothrombin time was 25 seconds. Test for stercobilin in the feces was both positive and negative on different occasions. The Van der Bergh test was prompt, direct, from 2.0 to 3.0 units on three occasions; Cephalin-cholesterol flocculation test four plus in twelve hours; Galactose tolerance test 1.6 grams in 5 hours, Bromsulphthalein test 77% retention in 45 minutes, Plasma proteins 6.9%, Albumin 1.8%, Globulin 4.1%, and A.G. ratio 0.4:1. Gastric analysis showed no free HCl. after histamine injection. E.C.G. showed left axis deviation. X-ray of chest showed some cardiac enlargement, and an area of infiltration in the right upper lung field. G.I. X-ray with barium meal showed a small readily reducible hernia and an increase in the distance of pylorus to vertebral column. Liver biopsy showed post-necrotic cirrhosis of liver, probably post-infectious hepatitis. Diagnosis in this case was post-infectious hepatitis (atypical).

- Treatment was:
1. Bed rest.
 2. High protein, high carbohydrate diet.
 3. Ferrous sulphate.

In this connection it is interesting to note that in Copenhagen there has been an increase in the number of cases of chronic hepatitis, running a malignant course and accompanied by a high mortality. In six hospitals

there were 303 cases with a course of over three months in 1944-1945. 97% of these were women and most of them were over 40. Mortality has been 37%.*

* M. Bjorneboe, M. Jersild, K. Lundbaek, E. Hess, Thaysen, and E. Ryssing.
Lancet 1:867-868, June 5, 1948.

AUREOMYCIN

By PAUL WALDEN '49

THE discovery of the clinical effectiveness of Penicillin by Florey and others has stimulated the search for new antibiotics, with the result that many new therapeutic weapons have been discovered. Among these are Streptomycin, Bacitracin, Tyrothricin, and more recently Polymyxin, Chloromycetin, and Aureomycin, as well as many others.

The topic for discussion in this paper is Aureomycin.

Physical Properties

Aureomycin Hydrochloride is a bright, yellow, fluffy, crystalline antibiotic, obtained from the mould *Streptomyces Aureofaciens*. A 10% solution can be prepared in distilled water but the solubility is lowered by the pressure of sodium chloride. The pH of a .1% solution is approximately 4.

Sensitivity of Bacteria

Several reports of the effect of Aureomycin on cultured organisms may be found in the literature. The following is a summary of the work of Finland and his associates at Boston. 186 strains of organisms were investigated by tube dilution and streak plate methods.

Hemolytic Streptococci, Pneumococci and Meningococci were almost completely inhibited by concentration of 1 microgram of Aureomycin per cubic centimetre of solution. According to these results Aureomycin is less effective by weight than Penicillin.

Staphylococci and gram-negative-bacilli, including Typhoid and Salmonella, were inhibited by a concentration of 25 micrograms per cubic centimetre or less.

Proteus Vulgaris and *Pseudomonas Aeruginosa* (*Pyocyaneus*) are resistant to Aureomycin, requiring concentrations of 100 to 250 micrograms per cubic centimetre for complete inhibition.

There was no evidence of cross resistance with other antibiotics nor was it possible to develop Aureomycin resistant strains.

A second group of investigators has shown that 5 strains of *Brucella* were inhibited by .75 mgms. /cc.

These experiments would indicate that Aureomycin is not as effective as Penicillin by weight, against the cocci, but that it is as effective as Streptomycin against gram negative organisms. Other reports state that Aureomycin is 10-80 times less effective by weight than Penicillin against gram positive cocci and 10 times less effective than Streptomycin against gram negative organisms, with the exception of the *Brucella* group.

The action of Aureomycin is bacteriostatic, not bactericidal.

Stability

The crystalline form of Aureomycin in Ampules retains its potency for 7 months or more at room temperature. In solution potency is rapidly lost, especially in alkaline solution or blood serum. The potency is retained for longer periods in frozen solution.

Absorption

Quantitative determinations of Aureomycin in the blood serum and urine are difficult to perform because of the rapid deterioration that occurs when this antibiotic is in solution. However, certain conclusions can be drawn from the following experiments in animals and human beings.

(a) Animal Experimentation

Harned and his associates and Bryer and his associates, working with rabbits and dogs, have shown that satisfactory therapeutic blood levels of Aureomycin may be produced by intravenous and intramuscular administration.

(b) Human Experimentation

Schoenback and his co-workers have discovered serum levels of 1.2-2.4 micrograms /cc following intramuscular injection of 40 mg. in patients who have been on Aureomycin for 5 to 14 days.

Dowling has shown that the maximum concentration of Aureomycin in the serum occurs in the third hour after intramuscular injection of 100 mg. There was also a detectable amount in the serum in 12 hours.

Experiments by this same group show that the peak after 700 mg. has been administered orally occurs in 6 hours and that all sera tested contained the antibiotic in 12 hours.

Wright and his associates state that after the oral administration of 300 mg. a peak of 2 micrograms /cc was reached in 3 hours.

Excretion

The excretion of Aureomycin has been studied in Boston by Finland and his group. They could discover no Aureomycin in the spinal fluid but found it occurred rapidly in the urine and could be detected in the urine for 2-3 days after a single dose. The maximum rate of excretion occurred between the 4th and 8th hours.

Because of the very limited clinical trials of Aureomycin these experiments have suggested the proper method of administration and the dosage. They have shown that Aureomycin may be administered by the intravenous, intramuscular or oral routes, and that satisfactory serum levels are maintained for several hours after administration. In addition high concentrations are excreted in the urine.

Treatment of Disease

It is impossible at this time to give any definite statement regarding the future role of Aureomycin in the treatment of disease, but the following experimental and clinical reports of its use are an indication of what this role may be.

Rickettsia

Several of the Rickettsial organisms appear sensitive to Aureomycin.

There is good evidence that this antibiotic is effective in the protection of chick embryos and guinea pigs against the causative agent of Rocky Mountain Spotted Fever *Rickettsia Rickettsii*. Sixteen patients suffering from Rocky Mountain Spotted Fever, 13 proved serologically, were treated successfully by a group at the Johns Hopkins Hospital. The average results of the treatment were as follows:

1. Number of days for treatment: 4.5.
2. Temperature returned to normal in 2.3 days.
3. Number of days in hospital: 8.

Rickettsia Prowazeki, the causative agent in Typhus fever, also appears sensitive to Aureomycin, as shown by the protection of chick embryos and the high survival rate of guinea pigs infected with this organism.

One patient with a mild form of Typhus, Brill's Disease, has been treated successfully with Aureomycin. ;

Aureomycin is effective in the treatment of Q Fever in experimental animals and has been used successfully in several human cases. The length of treatment necessary varied directly with the time interval since the onset of the disease.

There is some experimental evidence that Aureomycin may be effective in the treatment of Rickettsial Pox, a disease of unknown origin that has recently been discovered in New York State.

Virus

Certain virus diseases appear to fall into the group sensitive to Aureomycin.

One of the most extensive trials has been carried out with Lymphogranuloma Inguinale. 39 out of 40 mice were protected after intracerebral injection. Wright and his associates have treated 25 cases of this disease with the following results:

1. Eight patients with buboes and inclusion bodies demonstrable in the buboes showed reduction of buboes and disappearance of the inclusion bodies.
2. Three patients with proctitis showed excellent results.

3. 14 patients with benign rectal stricture showed no gross pathological change after Aureomycin, but were relieved of pain and bleeding and had an increase in stool diameter.

They came to the conclusion that in the acute case, Aureomycin was the drug of choice and that Aureomycin combined with surgery was the ideal treatment in the chronic case.

There is some experimental evidence that Aureomycin protects animals against Psittacosis but as yet there have been no clinical trials.

Until now this paper has dealt with diseases that are very uncommon in this area. The treatment of Primary Atypical or Virus Pneumonia strikes closer to home. In a series of 13 patients treated with Aureomycin the temperature was normal in 24 hours in 9 patients, in 48 hours in 3 patients, and 72 hours in 1 patient. This is a marked shortening of the course of the disease, which usually runs a fever for 7-8 days.

Another small series of 20 patients with Atypical Pneumonia has been reported by Finland and his associates at Boston. The temperature was normal in all cases in 12 to 36 hours and clinical and X-ray findings followed rapidly. This series was extremely well controlled and it was cautiously concluded that although Aureomycin appeared to be responsible for the recoveries, its effectiveness in this disease could not yet be considered as proven.

It is to be hoped that further trials are as successful because none of the antibiotics in use to-day are effective in the treatment of this disease.

Bacterial Infections

Excellent results have been reported in the treatment of Acute Brucellosis in a series of 5 cases, 3 infected with *Brucella suis* and 2 infected with *Brucella abortus*. The temperature was normal in 72 hours in all cases and there was a progressive remission of all symptoms.

Spink and his associates from Mexico report the following after the treatment of 24 cases of acute and chronic infection caused by *Brucella abortus*: "The immediate therapeutic results of Aureomycin have surpassed those obtained with any other specific therapy including Streptomycin, Sulphadiazine and combinations of these two. There was clinical recovery in all 24 cases."

Five cases of Typhoid fever have been successfully treated with Aureomycin. A negative culture of blood, stools and urine was produced in 3 days from the initiation of treatment, and symptomatic relief occurred over the same period in all but one case. It would appear, however, that Aureomycin is not as effective as Chloromycetin in the treatment of Typhoid fever.

Aureomycin appears successful in the treatment of disease caused by three intestinal organisms: *Escherichia coli*, *Aerobacter aerogenes* and

Streptococcus fecalis. In a series of 8 complicated urinary infections involving these 3 organisms the results of Aureomycin therapy were good in 7 and fair in 1. Two cases of peritonitis, one caused by *Strep. Fecalis* and the other by *E. Coli*, one case of Meningitis and one case of Subacute Bacterial Endocarditis caused by *Strep. Fecalis* were successfully treated by Aureomycin.

Seven out of 8 patients suffering from chronic infection caused by penicillin- and sulfa-resistant *Staphylococcus Aureus Hemolyticus* showed prompt satisfactory responses to therapy with Aureomycin. One brain abscess caused by the same organism was successfully treated.

Sixty-six patients with Gonorrhoea have been treated with Aureomycin. Results of treatment were excellent but the length of time necessary for treatment exceeded that of Penicillin so that Aureomycin is considered inferior to Penicillin in the treatment of Gonorrhoea.

Experiments on the protection of mice after Intraperitoneal injection of 10,000 MLD of Pneumococci show that Aureomycin is 5 times less effective than Penicillin under these conditions. Four cases of Pneumonia treated with Aureomycin had final results comparable to those of Penicillin but the response is slower with Aureomycin.

Braley and Sanders have reported the effects of Aureomycin in the treatment of eye infections. 100 cases were studied and the following results obtained:

100 Case Break Down	No. of Cases and Results
1. Staphylococcal Conjunctivitis	1. 56—cured in 12-24 hrs.
2. Epidemic Kerato Conjunctivitis	2. 13—shortened course (all responded).
3. Follicular Conjunctivitis	3. 9—morbidity 48 hrs. only.
4. Pneumococcal Conjunctivitis	4. 5—cured in 16 hrs.
5. Influenzal Conjunctivitis	5. 4—cured in 24 hrs.
6. Vernal Conjunctivitis	6. 4—3: relief of symptoms during administration. 1—no change.
7. Dendritic Keratitis	7. 4—3: improved. 1—no change.
8. Mooren's Ulcer.	8. 2—controlled ulcer in both.
9. Inclusion Conjunctivitis.	9. 2—cured in one week.
10. Parinaud's Conjunctivitis	10. 1—no results.

Conclusions

1. Aureomycin borate in 0.5-1% solution is non-irritating to the inflamed conjunctiva and only slightly so to the normal conjunctiva.

2. Aureomycin borate is .5% as effective against Staphylococcal, Pneumococcal, influenza and inclusion conjunctivitis. It is more effective than Penicillin against Staphylococci in eye infections.

3. Aureomycin appears to be effective in cases of Mooren's ulcer and atypical Mooren's ulcer.

4. Aureomycin has some effect on Epidemic Kerato-conjunctivitis provided that treatment is started the 4th day of the disease.

5. Aureomycin may be of value in Dendritic Keratitis.

Toxicity

Reports to date indicate that Aureomycin is relatively non-toxic to animals and human beings.

The lethal dose in mice is 50-100 mg/kilo injected intravenously and 3000-4000 mg/kilo injected subcutaneously.

150 mg/kilo intravenously killed dogs and caused hemoglobinuria, the latter explained by the acidity of the injected material, not by the toxicity of Aureomycin.

Repeated large doses are tolerated well by dogs, rabbits and mice.

Diarrhea and nausea are the only common constitutional signs of toxicity in human beings. It has a local irritant action when dropped in the eye, and when injected it causes pain.

Spink and his associates, using Aureomycin in a small series of 24 patients, observed that with the initiation of treatment in a few cases there was an increase in body temperature accompanied by a drop in blood pressure.

Administration and Dosage

The oral route is preferable because injection causes pain at the site of injection. The drug is promptly absorbed from the gastro-intestinal tract and there are no local toxic symptoms.

Doses of 50-100 mg/kilo/day have been advocated in milder infections.

The course of treatment should last 5-14 days, depending on results.

It has been suggested that the antibiotic should be administered every 4 hours for the first 24 hours or until the temperature is normal, and every 6 hours after that.

For Ophthalmic use 25 mg. Aureomycin dissolved in 5 ccs. of distilled water or a solution of 25 mg. of Sodium Borate and 62.5 mg. of Sodium Chloride may be used. 1-2 drops should be instilled every 1-2 hours for 24-48 hours.

Summary and Conclusions

Aureomycin appears to be an active antibiotic agent against Rickettsial diseases, including Rocky Mountain Spotted Fever, Typhus, Q Fever and Rickettsial Pox; certain Virus diseases, including Lymphogranuloma Inguinale, Psittacosis, and Primary Atypical Pneumonia; certain bacterial infections, including Acute Brucellosis, Urinary and other infections caused by *E. Coli*, *Aerobacter Aerogenes*, Typhoid Fever, Staphylococcal infections, Pneumococcal infections, Gonococcal infections, and a variety of eye infections.

It is of uncertain use in Salmonella infections and is no good in Whooping Cough or infections caused by Bacillus Proteus and Pyocyaneus.

The ease of administration, the absence of toxicity, the lack of cross resistance with other antibiotics and the inability to produce Aureomycin resistant organisms give sufficient reason to believe Aureomycin may be used extensively in the future.

It does not appear to be as effective as Penicillin against the cocci nor as effective as Chloromycetin against most gram-negative organisms.

The use of Aureomycin is still experimental and it has yet to stand or fall according to its therapeutic efficiency. Its discovery indicates that the spectrum of organisms affected by antibiotics is increasing and it is interesting to contemplate what the future of antibiotic therapy may be.

BIBLIOGRAPHY

- Bliss, E. A., Chandler, M. A.; Proc. Soc. Exper. Biol. & Med.; 69:3, 1948.
Braley, M. D., Sanders, M., New York; J. A. M. A.; 138:6, 1948.
Bryer, M. S., Schoenbach, E. B., Chandler, C. A., Bliss, E. A., Long, P. H., Baltimore; J. A. M. A.; 138:2, 1948.
Finland, M., Collins, H. S., Paine, T. F., Boston; J. A. M. A.; 138:13, 1948.
Finland, M., Collins, H. C., Wills, E. B., New England J. Med.; 240:7, 1949.
Kneeland, J. Jr., Rose, H. M., Silson, C. D.; Am. J. Med.; 6:1 (Jan.) 1949.
Long, P. H., Schoenbach, E. B., Bliss, E. A., Chandler, C. A., Bryer, M. S., Report of Address before the American Pharmaceutical Manufacturers Association, Dec. 7, 1948.
Ross, S., Schoenbach, E. B., Burke, F. G., Bryer, M. S., Rice, E. C., Washington; J. A. M. A.; 138:17, 1948.
Schoenbach, E. B., Baltimore; J. A. M. A.; 139:7, 1949.
Schoenbach, E. B., Bryer, M. S.; J. A. M. A.; 139:5, 1949.
Spink, W. W., Brande, A. T., Castaneda, M. B., Goytia, R. S., Mexico; J. A. M. A.; 148:16, 1948.
Wright, L. T., Sanders, M., Logan, M. A., Prigot, A., Hill, L. M., New York; J. A. M. A.; 138:6, 1948.

THE ANXIETY NEUROSIS

By DENNIS A. J. MOREY '50

ANXIETY is a state of apprehensive uneasiness and vague dread of prospective disaster, associated with a heightened tension, which results from any situation constituting a threat to the personality. It is the response to the threat of disclosure of repressed dangerous impulses deep within the personality, or of conflicts rising in the realms of vocational, social or marital adjustment, producing a persistent feeling of apprehension and impending harm, which is not associated with its true cause by the individual, but by means of the mental self-defence mechanisms of displacement, rationalisation and projection, is attached to conditions or objects, which are covertly related to the unconscious conflicts.

The term, "anxiety neurosis," was coined by Freud, in 1895, who believed it to be the response to ungratified sexual impulses. Although the original meaning has been lost, the term is still retained, and is now applied to those states of anxiety which are felt and expressed directly, are not confined to specific situations or objects but are always ready to attach themselves to any suitable ideational subject and in which there is the development of morbid fears, as well as anxiety, together with mental and somatic symptoms, which, originally the result of his fears, later become for the patient their apparent cause.

It must be emphasised that not all cases showing anxiety should be labelled "anxiety neuroses" without due consideration, since anxiety may also be experienced in the phobias, other psychoneuroses, and the depressive and schizophrenic illnesses, in which the causes of anxiety are more specific and may be clinically differentiated from the true anxiety neurosis.

The anxiety neurosis is one of the most common of all the neurotic reactions and is most frequently encountered in adults of both sexes, between the ages of 15 and 35, during which period the individual is endeavouring to adjust to his adult responsibilities and to establish satisfying economic, social and sexual relationships. Frustrations encountered in these fields lead to conflicts, tension and anxiety; these may be resolved by neurotic reactions, which may be psychic or somatic, and often both; but the essential mechanism of this reaction is a transference of the anxiety, from its association with the disturbing emotional factors, to some apparently unrelated idea or situation, which may give rise to one of the most distressing and intolerable of mental disorders.

This neurosis shows fine gradations in its severity from the mild anxieties which merely come to be regarded as character traits, to the disabling distress of the acute anxiety paroxysm.

Aetiology:

Individuals suffering this form of psychoneurosis commonly show

evidence that the emotional conflicts playing a predominant, if not exclusive, role in the production of the anxiety neurosis, were encountered in early childhood, and have become so deeply ingrained into the individual's psychological make-up that often they appear to be almost constitutional. However, it is not thought that the psychoneurotic states are inherited according to Mendelian ratios, but that they are acquired from unstable parents creating about themselves an unhealthy psychological environment, which imparts the neurotic characteristics to their children during their most impressionable years when they are so closely associated and dependent upon the family unit.

Such children are frequently found to have had behaviour problems associated with emotional tensions, such as enuresis, speech disturbances, sleep walking, crying out during sleep, food fads, emotional excitability, temper tantrums, fear of the dark, periods of destructiveness, shyness, compulsive actions and nailbiting.

It is in these people with psychoneurotic tendencies that hostile and aggressive impulses, dissatisfaction in emotional relationships with others, and feelings of guilt may constitute anxiety-producing factors. These, if not too difficult, may be successfully solved by the development of certain psychic self-defense mechanisms, which impart to the individual a sense of security, but, actually lead to the formation of a neurotic personality. Such persons frequently are tense, timid, sensitive to the opinions of others, apprehensive, easily embarrassed, hesitant to make decisions and afraid of making mistakes. They are introverted and impose upon themselves high standards of conduct and achievement. Thus, they only suffer the moderate distress of apprehension and social uneasiness, and avoid the crippling distress of the full-blown anxiety neurosis.

All too often, however, the automatic self-defense mechanisms fail to meet the requirements of such individuals; or the conflicts may become so numerous or intense that an overt anxiety state appears, being merely the culmination and exaggeration of tendencies which have always characterized their emotional attitudes to the vicissitudes of life. The precipitating factor is some overwhelming anxiety, or unresolved conflict which threatens to endanger the individual's moral or social standards. The war neuroses have demonstrated this on a large scale, where the individual was unable to resolve the conflict between the demands of society upon him and his personal safety.

It is now believed that among the most common sources of anxiety are disturbing interpersonal attitudes and relationships, and the feelings of guilt and shame which have their sources in the sex life.

The individuals afflicted with this neurosis are not usually aware of the true nature of their conflicts, or, at least, do not openly face them, but tend to turn their attentions to the mental, and somatic symptoms, which are but the result of their anxiety, and not its cause.

Symptoms:

The anxiety neurosis manifests itself in two forms, the acute and the chronic. The former occurs in acute panic-like exacerbations lasting from a few minutes up to an hour, the first attack of which may be traced back to some specific experience. Subsequent attacks may occur as a result of events associated with the original experience, which multiply as more and more attacks occur until the acute form becomes a conditioned reflex, precipitated by some apparently completely unassociated event. In these acute attacks there is an over-stimulation of the automatic nervous system, producing a dilatation of the pupils, vasomotor flushing, marked perspiration of hands and face, tachycardia, palpitations, extra-systoles, precordial discomfort, nausea, diarrhea or constipation, dyspnea, spasm of the cardiac and pyloric phincters, hyper-chlorhydria, a desire to micturate, a feeling of suffocation, and an increased metabolic rate. The patient is restless and may assume tense postures, complain of weakness, dizziness, fainting, has a sense of impending death, inducing him to reveal his apprehension in beseeching appeals for help, in a voice which may be uneven or strained. These attacks vary in their intensity from the severe cases described above to merely mild fluctuations in the chronic form of the neurosis. Those exhibiting recurrent acute attacks are rarely free from symptoms between these attacks, but are irritable, dissatisfied, anxious and unhappy, and show many of the symptoms of the chronic form.

The latter, the chronic form, also expresses itself in mental and somatic symptoms. The mental symptoms include varying depths of anxiety and morbid fears. These cause depression, irritability, sleeplessness, restlessness, attacks of weeping and feelings of inadequacy and inferiority. The latter are sometimes accompanied by a paranoid attitude, which may lead the patient to become unsociable, shy and excessively diffident. Loss of his ability to concentrate, memory defects, absent-mindedness, worrying without knowing about what or why. All of these frequently engender in the patient's mind the fear that he is becoming or may become insane.

The physical accompaniments of anxiety have been experienced by everyone at some time or other, and can be produced artificially by injections of adrenalin, caffeine, benzadrine and other stimulants. These somatic symptoms are limited in their range and variety only by the number of bodily structures and functions possessed by the individual. They completely engage the individual's attention and in turn become the object of his anxiety, but they are not accompanied by objective evidence of organic disease. The emphasis placed by the individual upon the physical manifestations of anxiety is not only due to its displacement from its psychological basis, but also to the fact that the essential purpose of these symptoms is to disable the individual and thereby secure his release from the original conflicts.

The most constant complaint of the chronic anxiety state is that of pain or discomfort in the head, variably described as a "band around the head," lightness in the nape of the neck, a sensation of bursting, compression, burning, tingling and of weights, all of which are said to be aggravated by any mental or physical strain. Complaints of pain in the back are often made. The visceral manifestations are similar to those described in the acute attack but are usually less intense, such as tachycardia, elevated blood pressure, palpitations, morbid blushing or pallor, tremors, excessive sweating, clammy hands and feet, dryness of the mouth, sighing, restlessness, gastro-intestinal disturbances, particularly nausea, flatulence, diarrhea or constipation, and sensations of weakness, dizziness and fainting. A feeling of choking may lead to hyper-ventilation and this in turn to tingling in the extremities, muscular twitching and finally blurring of consciousness.

Sexual disturbances may also be encountered such as lessening of desire in the male. This may lead to feelings of inferiority and further aggravate and complicate the neurosis. In the female vaginismus, painful coitus or frigidity may be experienced, but these rarely have such aggravating qualities, since they are, in themselves, purposive and defensive symptoms.

The anxiety neurosis ranked amongst the major war neuroses, and became evident as insecurity, fear of injury and the enemy increased. At first the symptoms were sleeplessness, nightmares, excessive sweating, pronounced startle reactions to loud noises and a tendency to become unsociable and irritable. Later on, there were sudden acts of fury or violence over the most trivial argument or disagreement. The power to concentrate became reduced and memory defects became apparent, making the soldier afraid of what he might do or forget. As the anxiety increased the soldier developed coarse tremors and dizziness, lost weight and began to drink to excess in order to escape from the unpleasant realities. Finally he sank into a temporary stupor, or lost all emotional control and sobbed like a child. Many exhibited the symptoms of the acute anxiety attack, and showed the "adrenalin syndrome" with nightmares, in which they re-lived terrifying experiences and, in some instances, developing extra-pyramidal-like syndromes. In air-crew, blurring of vision, errors in depth perception, vertigo, deafness, pain in the ears and respiratory difficulties were commonly experienced.

Briefly, the picture is that of a physically healthy individual, subject to deep anxiety and marked fears, which he considers the result of his symptoms, rather than their cause. These symptoms are extremely uncomfortable self-inflictions, yet they enable him to avoid the resolution of his distressing emotional conflicts.

Treatment:

The majority of cases are of the relatively mild form, which is

extremely widespread and constitutes a great deal of the chronic ill-health which the general practitioner is required to treat. Fortunately the anxiety neurosis is the most readily amenable to treatment of the psycho-neuroses, and for many patients all that is required is a short time of treatment at the hands of any careful, sympathetic and patient family doctor. However, in the more severe cases, where marked symptoms develop in persons of evident instability, the aid of a psycho-therapeutic specialist is indicated.

It is essential that the initial stages of the treatment should consist of the taking of a careful history. This should concern itself not only with the present illness but with the entire background of the patient's life; and of a thorough physical examination to establish that there is no physical disorder. The patient should then be reassured that there is nothing organically wrong with him, after which no further attention should be paid to physical complaints or symptoms. The use of drugs should be carefully avoided lest the patient be led to believe that his disease is physical, except for sedatives during the anxiety attacks to tide over the period during which the patient is inaccessible to psychotherapy, or, in the chronic case, to relieve the symptoms of insomnia. But their role as purely adjuvant should be made perfectly clear to the patient. In the severe cases of terror and panic encountered in the war neuroses prolonged narcosis proved to be most efficient in preparing the patient for psychotherapy.

Great care should be taken to avoid committing the patient to bed, but hydrotherapy, physical exercise and recreation advised where possible. Disturbing sex problems, including those arising from faulty contraceptive technique, should be corrected, and other problems promptly settled and then dismissed.

At this stage the nature of his disorder should be explained to the patient. The manner in which a shifting of emphasis has taken place should be made clear, and also how emotional states, such as anger, fright and anxiety, may lead to distressing physical symptoms such as palpitations, shortness of breath and gastro-intestinal upsets. The anxiety neurosis is an illness of the personality, not of the body, and the treatment should be openly conducted upon this understanding.

The treatment of the basic neurosis consists essentially of revealing the unrecognized sources of anxiety and establishing a relationship between events in the patient's life and the onset of the anxiety, and the determination of the emotional cause of the conflict. These are revealed by careful study of the patient's personality, and of his attitudes, and the situations which produce frustration and tension in him, or where the anxiety is of long standing or is severe. It may be necessary to use psycho-analysis, narco-hypnosis or hypnosis, which require considerable experience.

It should be emphasized that any given conflict does not produce a constant reaction pattern, even in the same individual; at one time there may be submission, at another escape from the situation, while from time to time the conflict may be resolved by an escape into neurosis.

Once the original conflict has been revealed it is necessary to re-educate the patient. The sources of his anxiety is explained to him. He must be taught to recognize and accept defeat and to adjust to his emotional drives by sublimation rather than by struggling against insurmountable obstacles, through an attitude of pride or over-conscientiousness.

Many psychiatrists have reported that the period of treatment required for recovery from an anxiety neurosis may be materially shortened by electro-shock and insulin therapy.

Prognosis:

Most patients show no tendency to spontaneous cure without treatment, but respond readily to psychotherapy. With good mental hygiene they may enjoy a life relatively free from morbid anxieties, although in the acute recurrent form there is seldom a complete recovery from the attacks and the individual rarely enjoys prolonged periods of complete freedom from them. It should always be borne in mind that in the subject of a neurosis we are dealing with an individual who is emotionally unstable and there is, therefore, without the practice of a sound mental hygiene, a tendency to relapse when other emotional conflicts arise, particularly in the more severe cases. However, it is encouraging to realize that while the everyday efficiency of most people is impaired by their psychoneurotic tendencies, yet much of the outstanding artistic and humanitarian work of the world is done by those neurotics who have successfully sublimated their emotional problems through creative production.

Summary:

The anxiety neurosis is a reaction characterised by morbid fears and anxiety, accompanied by mental and somatic symptoms, which come to be regarded as the cause of the anxiety, rather than its effect.

Most anxiety neuroses are encountered in people in early adulthood, who have shown personality and behaviour difficulties in childhood, engendered by an emotionally unstable parental environment, and finally precipitated by unresolved emotional conflicts resulting from requirements which the individuals cannot or fear they cannot meet.

The most common source of anxiety-producing factors are the troublesome conflicts arising over inter-personal relationships and attitudes. The automatic psychological self-defence mechanisms designed to protect the individual from the strains of anxiety constitute the mental and somatic symptoms of the neurosis.

The anxiety neurosis is a disorder of the personality, not of the body, and as such requires psychological treatment which will reveal the emotional sources of the anxiety, adjust the individual to his problems and re-educate him in the principles of sound mental hygiene.

BIBLIOGRAPHY

- Conybeare, Sir John, Textbook of Medicine, E. & S. Livingstone Ltd., Edinburgh, 1947.
- Grinker, R. R. & Spiegel, J. P., Men under Stress, Blakeston, Philadelphia, 1945.
- Louitt, C. M., Clinical Psychology, Harper & Brothers, New York, 1936.
- McDowall, R. J. S., Sane Psychology, James Murray, London, 1944.
- Munn, N. L., Psychology, Houghton Mifflin Co., New York, 1946.
- Noyes, A. P., Modern Clinical Psychiatry, W. B. Saunders Co., Philadelphia, 1948.
- Stevenson, G. H., and Neal, L. E., Personality and Its Deviations, The Ryerson Press, Toronto, 1947.
- Teagarden, F. M., Child Psychology for Professional Workers, Prentice-Hall Inc., New York, 1940.
- Walshe, F. M. R., Diseases of the Nervous System, E. & S. Livingstone Ltd., Edinburgh, 1947.
- Wechsler, I. S., The Neuroses, W. B. Saunders Co., London, 1929.

COLD AGGLUTININS AND OTHER TESTS FOR ATYPICAL PNEUMONIA

By ROBERT ELDER '49

IN recent years clinical mention has frequently been made of certain tests which may be employed as an aid in the diagnosis of primary atypical pneumonia. With the development of Chloromycetin, Aureomycin and other new antibiotics, such tests assume a new importance. In this paper a review of the recent literature on the subject will be presented with an attempt to assess the practical value of such tests.

Cold Agglutinins

In 1917 Clough and Richter (1) noted auto-agglutination in a case of broncho-pneumonia. During the acute stage of the illness it was impossible to do an erythrocyte count unless the solution was warmed. Investigation showed that the patient's serum not only agglutinated his own cells at low temperature but also Group O cells. Agglutination was maximal at 4.0° C. and disappeared above 22.0° C. The agglutinins could be released from the cells by washing with saline at 37° C. During the acute phase of the illness the titer rose to 1:500 and after convalescence it fell to 1:16.

Clough and Richter did not believe the agglutinins were related to the patient's illness since they persisted for two months and were present in the serum of a daughter of the patient.

During the last decade the presence of cold agglutinins in cases of primary atypical pneumonia has drawn the attention of many investigators (1, 3, 8, 9, 10, 11).

The method determining the presence of cold agglutinins varies slightly with each group of workers. The procedure to be described here is that of Young (11).

Blood is collected in corked sterile tubes and the serum separated by centrifugation after the blood has stood at room temperature for a number of hours. If a specimen has been inadvertently refrigerated it should be warmed in an incubator at 37° C. for one hour before being centrifuged.

Serial two-fold dilutions are made with saline in test tubes. To 0.5 ml. of each dilution is added an equal volume of a 1% suspension of fresh Group O human red cells. The tubes are then shaken and placed in a refrigerator at 4.0° C. overnight and examined grossly the following morning immediately after removal from the refrigerator.

Each tube is held in a nearly horizontal position and gently shaken until all the cells in the bottom have been dislodged. The cell suspension

is then carefully examined over a well-illuminated white background. The last tube showing grossly detectable agglutination is taken as the end-point. Titers are recorded in terms of the final dilution of the serum after addition of the cell suspension. Thus the first tube containing 0.25 ml. serum + 0.25 ml. saline + 0.5 ml. cell suspension has a dilution of 1:4. Reversibility of the agglutination may be checked by examining the tubes after they have stood at room or incubator temperature for one or more hours.

The findings of the several groups of workers (1, 2, 3, 8, 9, 10, 11) who have studied cold agglutination in primary atypical pneumonia are summarized below.

1. Approximately 55% of the cases of primary atypical pneumonia have cold agglutinins. But only 30% have titers sufficiently high to distinguish them from other respiratory infections.

2. Titers of 1:64 or more in a patient ill with respiratory infection is strong evidence in favor of a diagnosis of atypical pneumonia. Lower titers are also of value, especially if sera taken at intervals during the course of the illness show a rise in titers in early convalescence and a drop thereafter.

3. The highest titers are obtained in the 2nd and 3rd week after the onset of the disease when the patient is well past the acute phase of his illness.

4. Generally, the more days of fever, the higher the titer, the higher the temperature, the higher the titer, the higher the leucocyte count, the higher the titer and the more lobes involved the higher the titer.

5. In a patient with primary atypical pneumonia a high titer on admission or a rapidly rising titer seem to indicate a favourable prognosis. A patient with primary atypical pneumonia in whom high titers of cold agglutinins are not observed usually has a prolonged illness in which pleural complications are frequent.

6. There is no definite correlation between the age of the patient and the height of the titer.

7. High titers are uncommon except in primary atypical pneumonia while low titers are encountered in a variety of diseases as well as in supposedly normal persons.

From this it may be concluded that, since cold agglutinins are present in only half of the cases with the clinical picture of atypical pneumonia, the test is not of diagnostic value in the individual case. Cold agglutinins are, however, of some confirmatory value in the diagnosis of atypical pneumonia since a high titer in the patient with the clinical picture of atypical pneumonia does confirm the diagnostic impression. The test would also appear to be of some prognostic value.

Streptococcus M. G.

Streptococcus M.G. is a non-haemolytic encapsulated streptococcus which is present in the upper respiratory tract of 12% of normal people, 25% of people with acute respiratory disease and in 55% of people with atypical pneumonia. It is present in the lung tissue of 75% of fatal cases of atypical pneumonia.

Antibodies against *Streptococcus M.G.* are produced in some cases of primary atypical pneumonia. The presence of such antibodies may be detected by:

1. Agglutination of either the encapsulated streptococcus or the non-encapsulated R-variant.
2. Precipitation of the capsular polysaccharide.
3. Capsular swelling of the micro-organism.
4. Positive skin reactions on intradermal injection of the capsular polysaccharide.

Streptococcal *M.G.* agglutinins of 1:20 or more develop in 50% of patients with primary atypical pneumonia. 20% of mild cases show a titer of 1:20 as do 75% of severe cases or cases of long duration.

The agglutinins usually appear during the 2nd or 3rd week of the disease, reach a maximum in the 4th or 5th week and decline during the 7th or 8th week. The more severe cases have a higher titer. A significant increase in agglutinins apparently has not been demonstrated in any condition other than primary atypical pneumonia. Some patients develop agglutinins against *Streptococcus M.G.* and do not show cold agglutinins, while in other patients the reverse condition exists. Many patients develop both types of agglutinins.

The value of tests for *Streptococcus M.G.* agglutinins appears to be similar to that for cold agglutinins. In the individual case the tests are not of diagnostic but may be of some confirmatory value. Since one type of agglutinin may be present in the absence of the other it is probably better to carry out tests for both cold-haemagglutinins and *Streptococcus M.G.* agglutinins.

Summary

The cold agglutinin and the *Streptococcus M.G.* agglutinin have been described, and their value in the diagnosis of primary atypical pneumonia discussed. At the present time they are not in themselves of any diagnostic value. But they may confirm the clinical impression of primary atypical pneumonia. These tests have a new practical value since we may now have an active treatment for primary atypical pneumonia.

BIBLIOGRAPHY

1. Clough and Richter, Johns Hopkins Hospital Bulletin 29, 86-93 (1918).
2. Commission on Acute Respiratory Diseases, Am. J. Med. Sc.; 208, 742-50 (1944).

3. Finland, M., Peterson, O. L., Allen, H. E. Samper, B.A., and Barnes, M. W., *J. Clin. Invest.*; 24, 458-73 (1945).
4. Goldstein, R., *New England J. of Med.*; 240, 180-187 (1949).
5. Horsfall, F. L. Jr., *N. Y. State J. Med.*; 46, 1910-14 (1946).
6. *Lederle Bulletin*, January (1949).
7. Long, P. H., Schoenbach, E. B., Bless, E. A., Chandler, C. A., and Bryer, M. S.; *Sep't. of Preventive Med., Johns Hopkins Univ. School of Med.*
8. Platt, W. R. and Ward, C. C. Jr., *Am. J. Clin. Path.*; 15, 202-210 (1945).
9. Spingarn, C. Z., Jones, J. R., *Arch. Int. Med.*; 76, p. 75 (1945).
10. Strutes, G. C., Farmer, T. W. and Hayes, G. C., *Johns Hopkins Hosp. Bull.*; 75, (1944).
11. Young, L. C., *Am. J. Med. Sc.*; 211, 23 (1946).

MIGRAINE SYNDROME

By D. MARSHALL '49

MIGRAINE headache is not a disorder of Modern Civilization for Hemicrania, Sick or Bilious Headache, was known to Galen, who introduced the term Hemicrania to Celsus and others of the ancients. In the 12th century the visual aura associated with the headache was considered by some to be of spiritual significance. Among the physicians suffering from migraine headache have been Wollaston, Fothergill, Parry, Wilks, Sir James MacKenzie and many others.

Definition: A definition is difficult because the syndrome varies from rudimentary forms which are hardly to be recognized, through the classical syndrome of periodic recurrence of violent and mostly unilateral pain, preceded by auras in the shape of visual malfunction, often accompanied by nausea and vomiting, to severe forms which can simulate cerebral trouble of a more serious nature.

The syndrome consists of the recurrence against a background of relative well-being, of severe, incapacitating headaches. It is frequently hemicranial, often alternating. However, it may be less typically, frontal, parietal, occipital or generalised. The pain varies in type and severity in different persons. The severity varies from time to time in the same individual. The type of pain, however, is fairly constant for each patient.

The headache is more frequently associated with nausea and vomiting, i.e. in 75%, and less frequently with visual disturbances — in about 50%. The visual phenomena are quite variable, the classical syndrome being scintillating scotomas against a hemianopic field. Frequently, however, they consist merely of blurring of vision or photophobia. Hypersensitiveness to sound is frequent. Other less characteristic concomitants are: Facial flushing or paling, localized areas of edema, chilly sensations, paraesthesias or numbness of the extremities. Occasionally motor phenomena are present. The duration of an attack ranges from an hour (rarely less) to several days.

Etiology

1. *General Incidence:* Balyeat and Rinkel state that about 7% of their American countrymen develop the syndrome some time in life. Grimes found that of 15,000 individuals examined in general practice with reference to migraine, 1200 or 8% were afflicted, but less than half of the victims ever consulted a physician for relief of their symptoms.

2. *Sex Incidence:* The composite statistics of a number of observers show a ratio of female to male of about 3 to 1. Allan, however, took 195 unselected cases (physicians and their wives) and found identical proportions in the two sexes, but concluded that more women are seen simply

because their headaches are often more severe, last longer, and more often have nausea and vomiting superadded. Gowers likewise believes that the preponderance in females of the condition has been greatly exaggerated.

3. *Age of Onset*: As a rule it starts before twenty, onset after thirty being unusual. Balyeat and Rinkel in a series of 202 adults found it developed in the first decade in almost 30% and in as many more before the end of the second. It has been described in infants as early as the second year and may appear as late as the sixth decade.

4. *Importance of Social and Intellectual Status*: It is a quite widely accepted notion, that brain workers and the more cultured classes generally are more commonly afflicted. Kinnier Wilson states that as many of his patients came from the hospital classes as from the higher social level. Harris found the majority of his to be of less than average intelligence. The disorder is widespread throughout all social and intellectual levels but is more common in urban than rural dwellers. Derbes, Engelhart and Watters believes the incidence is higher in intellectual people and explain it on the greater incidence of mental fatigue and emotional tension which accompany their everyday life.

5. *Role of Heredity*: Direct inheritance is a strong feature, the disease being transmitted possibly as a Mendelian dominant, though not definitely sex-linked. In Flateau's series the maternal line was concerned in 79% and the paternal in 21%. In a group of migrainous women, 63% received it from their mother, 30% from their father and 7% from both. Although it is conventionally believed that the sufferer is weighted by a neuropathic legacy from his forefathers, Allan found that psychoses and psychoneuroses occur as often in non-migrainous as in migrainous stock.

6. *Relation to Epilepsy*: Comparison of the relative incidence of these two conditions in the ancestry of patients suffering from either was made by Ely. "Convulsive Disorders" were noted in the families of 5.7% of 104 migrainous subjects and migraine in those of 15.2% of 171 persons suffering from "Idiopathic Convulsive States." Allan on the other hand has found epilepsy just as often in non-migrainous pedigrees as in migrainous. Cobb and Ely found from their investigations that the inherited migrainous tendency imparted a greater predisposition in the offspring to development of convulsive disorders than did the occurrence of convulsive disorders in the antecedents. Their series was too small to justify sweeping conclusions, yet the inferences drawn from them are both interesting and startling.

Dr. Mary O'Sullivan states that in only 0.8% of her series of 300 cases was there a history of epilepsy in either the offspring or the antecedents. She feels that the hereditary link between migraine and epilepsy has been strongly over-rated.

Frequency of Migrainous Attacks

Attacks of migraine may exhibit a high degree of regularity in their

periodic recurrence. In some instances menstruation seems to play a distinct role in the periodicity. The attacks may occur shortly before the onset of menstruation or alternate with it.

Some patients suffer from attacks every 2 or 3 days or almost regularly once a week. They may occur as frequently as several times a day or they may appear only once in one or two years. In the majority, however, they occur irregularly with no definite interval between the crises.

Allan has estimated that in 82% of cases they occur once a month and in 53% once in two weeks or more frequently. He noted also that in many cases there seems to be a definite immune period following the attack, during which the disorder does not recur. Occasionally the attacks may appear in a series of sufficient frequency to establish a Status Hemigranicus.

The Migrainous Personality

The following is Harold G. Wolff's clever and understanding description of the migrainous personality.

"Patients with migraine are tense, driving, perfectionistic, order-loving, rigid persons who, during periods of threat or conflict, become progressively more tense and fatigued. Personality features and reactions dominant in individuals with migraine are feelings of insecurity with tension, manifested as inflexibility, conscientiousness, meticulousness, perfectionism, and resentment. These temperamental features lead to frustration; to dissatisfactions about family, financial, or personal status; and to intolerance of periods of low energy in themselves or relaxed standards in themselves or others.

"The tension associated with repeated frustration, sustained resentment and anxiety, often followed by fatigue and prostration, becomes the setting in which the migraine attack occurs.

"In short, certain individuals have a predisposition and psychobiologic equipment which makes them prone to sustained and pernicious emotional states. During such states labile physiologic mechanisms set off the chain of events constituting the attack of migraine."

Classification of Types

Although migraine is often subdivided into Allergic, Colonic, Endocrine, Duodenal, Psychic, Migraines, et cetera, nothing but confusion follows such subdivision. Because of this, I shall not classify the types which have an obvious primary factor, but will refer to them under Treatment.

Each case usually presents factors suggestive of several of these processes, one of which appears to be predominant. Each of these etiological factors appears to be reasonable for a selected group, but none for the entire series, indicating a multiple pathogenesis for the migraine syndrome.

Diagnosis

In a syndrome presenting as many variations as migraine, diagnosis is of the utmost importance not only in handling individual cases but in evaluating the many studies concerning its etiology and therapy. As described by Von Storch, the four cardinal components of the syndrome in order of diagnostic importance are:

1. Recurrent headache, preferably but not necessarily hemicranial in type.
2. Associated visual symptoms, classically scintillating scotomas.
3. Temporary G.I. phenomena, usually nausea or vomiting.
4. Hereditary migraine diathesis, occasionally an epileptic history.

The first of these components associated with one other is necessary before the diagnosis can be considered. At least 3 components must be present for any degree of certainty. A fourth, with or without less characteristic vasomotor, motor or sensory concomitants, elevates the diagnosis to one of comparative surety. The diagnosis may be expressed in order of certainty as follows:

(1.2.3.4); (1.2.4); (1.3.4); (1.2); (1.4); and (1.3)

There are two exceptions to the invariable inclusion of recurrent headaches in the migraine syndrome. The first occurs when recurrent headaches have, over a period of time, gradually merged into a constant state of cephalgia of varying degree. In such a situation the history of previously recurrent headaches becomes essential. The second exception occurs when the patient is at the time of diagnosis, suffering from recurrent bouts of nausea and vomiting which had previously appeared in conjunction with headaches. This constitutes "Abdominal Migraine" and necessitates an hereditary factor before diagnosis can be made.

With the exception of a few classical cases the diagnosis of migraine should always be one of exclusion. Of practical importance are a careful history, a thorough general physical and neurological examination, adequate cranial roentgenography and a lumbar puncture. In spite of these features one hour of careful questioning is worth ten hours of examination.

In addition it must be kept in mind that the presence of the migraine syndrome does not exclude the presence of abdominal disease, glaucoma, cardio-vascular accidents, sinusitis, and so on. Nor does it prevent the addition of menopausal symptoms, psychogenic headaches and neurotic complaints to the underlying picture of migraine. Many patients have another less well defined cephalgia as well as typical migraine attacks. These are frequently a source of confusion to patient and physician when attempting to evaluate the results of any particular therapy.

Differential Diagnosis

1. *Epilepsy*: Careful consideration of the auras of each, the hemi-

cranial pain and vomiting hours after the discharges have ceased as in migraine, and the absence generally of motor symptoms but presence of sensory ones in migraine, readily distinguish the two conditions.

2. *Cerebral Tumor*: Family history, intermittence, reversibility, absence of papilloedema and course dispel any hesitation.

3. *Trigeminal Neuralgia*.

4. *Vertigo*: Once in a while this co-exists or alternates with hemicrania but there is no tinnitus or loss of hearing in the migraine syndrome.

5. *Histamine Headache*: Horton emphasized the paroxysmal nature of the attacks occurring several times in twenty-four hours, the unilateral pain, lacrimation, nasal engorgement and flushing of the involved side.

6. *Tension Headache*: This is generally bilateral, throbbing or pulsating and occipital. They have no aura, no visual disturbances, and usually no nausea and vomiting. They may come on daily for a few hours or last many days.

Mechanism and Site of Preheadache Phenomena

Little accurate information concerning the mechanism of the pre-headache phenomena is known. Indeed, sometimes the pre-headache phenomena are not followed by headache. In about 50% of cases pre-headache phenomena are present. Scotomas are the most readily studied. Dr. A. M. Cahan, a migraine sufferer, made accurate and rapid observation of his own visual defects.

To ascertain whether dysfunction of the cerebral vasculature is responsible for the pre-headache symptoms, amyl nitrate, which is a known cerebral vasodilator, was used. Cerebral vasodilation induced without a fall in blood pressure increases cerebral flow, whereas a sharp drop in blood pressure regardless of the state of the cerebral arteries, decreases the cerebral blood flow. Symptoms due to cerebral vasoconstriction should be overcome by cerebral dilatation if the blood pressure is not lowered, but should be made worse if the blood pressure falls.

This physician-patient between attacks practised inhaling amyl nitrate so that he took just enough to induce a head flush without lowering the blood pressure. By inhaling large amounts he caused a sharp fall in blood pressure with light-headedness.

He developed a defect in one visual quadrant, inhaled amyl nitrate to cause a flush and his vision cleared, his blood pressure remaining the same. The defect returned in a few minutes and again disappeared after amyl nitrate inhalation.

On another occasion a defect appeared. He inhaled amyl nitrate and the defect disappeared. It returned and he inhaled very deeply to the point of disorientation, the defect becoming much worse, leaving only central vision. When his blood pressure returned to normal, his vision cleared again but within 5 minutes the scotoma began to reappear.

We may infer that cerebral vasoconstriction was responsible for the visual defect in this case because:

1. During an attack there was a sparing of central vision.
2. Homonymous quadrantic defects could readily result from a single defect in the visual cerebral cortex, but a bizarre arrangement of multiple retinal defects would otherwise be necessary.

High-grade visual auras endorse the cortical theory. Vertigo, paraesthesias, aphasia and other motility defects likewise favor a cortical site.

Adie describes a series of cases with long standing periodic headaches preceded by defects in the visual fields. Such defects were of relatively short duration and left the patient free from symptoms between attacks. However, in each case, after years of short-lived attacks, the patients finally failed to recover and a permanent hemianopic defect resulted. It may be inferred from the data of these experiments that permanent tissue damage resulted either from thrombosis in a constricted cerebral artery or from too prolonged ischemia. A retinal arteriolar vasoconstriction has not been seen consistently on ophthalmoscopic examination during the pre-headache period in spite of frequent attempts.

We may conclude then that the preheadache phenomena are due to cerebral vasoconstriction, the cause of the vasoconstriction being as yet undetermined.

Pathways of Pain in the Head

The following structures in the head have been shown by Wolff to be pain sensitive.

1. Tissues covering the cranium, especially the cranial arteries.
2. Certain intra-cranial structures:
 - a. Parts of the dura mater.
 - b. The dural arteries.
 - c. The venous sinuses and some of their tributaries.
 - d. The cerebral arteries at the base of the brain.
3. Certain nerves that carry pain to consciousness: The sensory branches of the fifth, ninth and tenth cranial nerves and the first, second and third cervical nerves. Certain structures are not sensitive to pain. These are the cranium itself, the parenchyma of the brain, the pia, arachnoid and most of the dura, the ependymal lining of the ventricles and the choroid plexuses.

Stimulation of pain sensitive structures above the superior surface of the tentorium cerebelli produces pain in front of a vertical line across the ears and is carried by sensory branches of the trigeminal nerve; structures below the tentorium produce pain which is felt behind the ear and the pain is carried by branches of the glossopharyngeal, vagus and upper cervical nerves.

Physiology of Headaches

Physiologically headaches are produced in four principal ways or clinically by a combination of them.

1. Distention and dilatation of arteries inside or outside the skull (most often by branches of the internal and external carotid arteries).
2. Traction on the vessels within the skull.
3. Edema and spasm of muscles of the scalp and neck.
4. Direct irritation of pain-carrying nerves or structures by inflammation or pressure.

Mechanism and Site of the Migraine Headache

Pulsations of the temporal branch of the external carotid artery were recorded by Sutherland and Wolff by means of a tambour placed on the artery where it could be palpated under the skin. The pulsations were recorded on a bromide tracing in such a way that their length was proportional to the force of the impulse. Changes in intensity of the headache were estimated by the patient. Measuring the change in amplitude of pulsation due to various vasoconstrictor drugs like caffeine, benzedrine, ephedrine, et cetera, it was found that the decrease in intensity of the headache was directly proportional to the decrease in amplitude of pulsation of the temporal artery.

Pressure over the common carotid artery reduced the severity of the attack during the pressure, and associated with this was a decreased amplitude of pulsations of the temporal artery.

The use of amyl nitrate and histamine greatly increased the amplitude of pulsation during a headache, making the pain almost unbearable. This indicates that increasing the relaxation of the branches (scalp and dural) of the external carotid artery intensifies the migraine headache. Faradic stimulation and traction on the middle meningeal artery causes pain in the temporal region or behind the eye. Since pain is common in this region during migraine headache, it is possible and very probable that the middle meningeal contributes to the headache. Ligation of this artery has abolished migraine headache for six months.

There is some evidence that the larger arteries at the base of the brain and their immediate branches may be implicated in some patients during severe migraine headache. However, there is considerable evidence against it. Raising the intracranial pressure up to 800 mg. of water does not relieve the intensity in even the worst attacks of migraine, but it does in histamine headache where the arteries at the base are involved.

The superficial frontal and supraorbital arteries arise from the internal carotid artery and since the area supplied by these arteries is commonly involved in migraine headaches, branches of the internal carotid may contribute to the pain.

We may conclude that the initial pain of migraine headache is due to vasodilatation and distension, resulting in increased pulsations of the external carotid artery (scalp and dural), and at times to branches of the internal carotid artery.

Mechanism of Action of Ergotamine Tartrate — Gynergen

Gynergen has no analgesic action in itself like that of codeine or aspirin. Graham and Wolff in 1938 showed that relatively small amounts of Gynergen contract rather than dilate the smooth muscled arteries. Von Storch has shown that vasoconstriction occurs even in the absence of vasomotor nerves. The response of smooth muscle to sympathetic nerve stimulation was not abolished by the I.V. injection of 0.5 mg. of Gynergen.

Pool and Mason showed that ergotamine tartrate causes a constant constriction of the dural arterioles but a totally variable response in the pial vessels. Wolff reports that ergotamine in therapeutic doses in man constricts the branches of the external carotid arteries (temporal and middle meningeal) as shown at direct observation and photographs, but doesn't alter or has uncertain effect on the internal branches (i.e. the pial and cerebral).

Termination of attacks of migraine headache by Gynergen regularly paralleled the decrease in the amplitude of pulsations of the cranial arteries, especially branches of the external carotid. Reduction of the amplitude of pulsation by 50% was adequate to relieve the headache. When the amplitude was rapidly reduced, the headache rapidly disappeared, but when the pulsations were slowly decreased so was the headache.

We may conclude that the head pain of the migraine attack is produced by distention of the cranial arteries and the termination of the headache by ergotamine tartrate is due to the capacity of this agent to powerfully constrict these cranial arteries and thereby reduce the amplitude of their pulsations.

Prolongation of the Headache

As a sequence of persistent head pain and distension of cranial arteries, the skeletal muscles of the head and neck contract, and this, as previously mentioned, is a source of pain.

After several hours of migraine headache, the temporal artery appears more prominent and distended than normal and becomes more readily palpated through the skin. It becomes rigid and pipelike and less readily compressed and tender. Wolff and Torda postulated an edema or thickening of the muscular and adventitial coats. Sections taken from patients during an attack suggested this but controls were not possible.

Cats were used as experimental animals and acetyl choline bromide was used as a dilator. Sections proved that prolonged vasodilatation did

increase the thickness of the arterial walls. With edema of the walls, the pain changes from a pulsating one to a steady ache.

It has been shown that ergotamine tartrate contracts a distended artery with thickened walls less promptly and completely than a normal one.

During the attacks of migraine headache, the cranial arteries involved may undergo similar changes after prolonged vasodilatation. Such changes may explain the rigid, pipelike texture of the arteries, the steady aching pain, and the tenderness of these structures when headache has persisted for several hours. These changes may explain the decreased ability of ergotamine tartrate to reduce promptly the intensity of prolonged headache.

Course and Prognosis

Chances of recovery, never perhaps bright, are best if the case is neither severe nor chronic, but seems to depend on factors of an intangible kind as much as on the effects of persevering treatment. Symptoms may tend to self-cure; some patients respond readily to treatment to which others do not. Pregnancy frequently affords a 7 to 10 months relief. The menopause (artificial or natural) does not afford so much relief as is generally supposed. Many patients become worse thereafter and others date the onset of their attacks at the menopause.

Wolff believes that the important factor in improvement of women at the menopause and men at 45 to 50 may be that this age brings with it declining drive, resignation, or spontaneous adjustment of major conflicts. For rigid persons, however, middle life may bring with it increasing difficulty with adjustment and their migraine may become worse instead of better. When migraine begins during the age between 45 to 50, the prognosis is poor.

The prognosis of a patient with migraine should be viewed somewhat as that of a patient with peptic ulcer. Migraine headaches may be terminated, or the interval between episodes greatly prolonged, but unless the subject has discovered a suitable pattern of life and is able to adhere to it, the headache will recur.

Treatment

Because the migraine attack may be initiated by various pathological processes, and complicated by the influence of multiple secondary abnormalities, the ideal treatment must be variable and individualized.

A.—Symptomatic Therapy

1. *Ergotamine Tartrate* (Gynergen)—Von Storch reported this effective in 90% of 600 cases of migraine. It is a specific means of aborting or terminating the headache.

Parenteral injections are thoroughly effective in over 90% of cases. I.V. injections afford rapid relief but should only be used under a physician's supervision. No more than 0.25 mg. of ergotamine should be given at the first injection. A simultaneous subcutaneous injection of 0.25 mg. may be given.

Subcutaneous and I.M. injections are most practical for routine use. The average effective dose is 0.5 mg. Results should be manifest in 30 to 45 minutes. The patient may be instructed in self-administration. After ascertaining the effect of 0.5 mg. on several occasions, the drug should be progressively decreased to the minimal effective dosage.

Oral Administration: Lennox and Von Storch have found that orally it is effective in 40% to 70% of cases. Approximately 10 times the parenteral dose is necessary, i.e. 5 mg., in order to obtain sufficient absorption after ingestion.

The five 1 mg. tablets should be broken and swallowed at one time. If more ergotamine is necessary, it may be ingested at the rate of 2 mg. per hour until a total of 9 to 11 mg. has been taken. Sublingual absorption is more rapid but because of the taste many patients don't care for this form of therapy. Neither method of oral administration is of any value when vomiting is part of the syndrome. Whenever oral administration must be extended over three hours, the subcutaneous route is preferable.

No more than 0.25 mg. should be given in any single dose nor more than 2 such injections in any day. No more than 0.5 mg. should be given at a single subcutaneous injection, nor more than two such injections per day. No more than two parenteral injections of ergotamine should be given in any single week, nor more than 6 per month. No more than 11 mg. should be ingested in any one day nor more than 11 mg. three times per week.

Side Effects of Gynergen:

1. Nausea and vomiting is extremely common. Ingestion sublingually or injection of 1/100 gr. of atropine sulfate before or during the administration of ergotamine relieves this.
2. Muscle cramps along the course of the main arteries in arms and legs. Relief is obtained by massage.
3. Temporary paraesthesias of fingers and toes are frequent. Persistent paraesthesias suggest the possibility of early ergotism.
4. Substernal oppression may alarm the patient but in the absence of organic heart disease this need not distress the physician.

Contra-Indications of Gynergen:

1. Septic or infectious states.
2. Vascular diseases, especially of the extremities.
3. Coronary sclerosis and history of angina of effort.
4. Pregnancy.

2. *Ergonovine* (Ergotrate) — According to Wolff it is only about half as effective as ergotamine. It causes less nausea and vomiting, and is useful in patients who complain of severe paraesthesias following ergotamine. The dosage and administration are the same as for ergotamine.

3. *Dihydroergotamine 45* (D.H.E. 45) — D.H.E. 45 is less predictable in its effect but may reduce or abolish the headache when given in 1 mg. I.M. amounts without causing nausea and vomiting.

4. *Oxygen*: Oxygen is useful in the abortion or termination of migraine. Alvarez reports that 88% of 97 cases with "typical migraine" headaches were relieved, although only 42% were completely relieved. Oxygen may be of benefit when ergotamine fails and at times they are better together than either alone. It causes no accessory symptoms and may relieve the gastric symptoms. It may be administered by the B.L.B. mask or by the ordinary B.M.R. apparatus. 100% O₂ in a flow of from 6-8 litres per minute is desirable. Inhalation should be continued for two hours unless relief is obtained sooner.

5. *Miscellaneous Drugs*: In occasional cases I.V. injections of 25 to 50 cc. of 25 to 50% glucose; 20 cc. of 10% sodium chloride; 1 cc. of sodium thiosulfate; 10 cc. of 10% calcium gluconate have all been recommended to terminate attacks.

Subcutaneous injections of $\frac{3}{4}$ gr. of ephedrine sulfate, 1 cc. of 1:1000 adrenalin; $\frac{1}{2}$ cc. of 1:1000 histamine, or 1 cc. of antuitrin are occasionally effective.

B.—Preventive Therapy

If the patient awakes in the morning with the discomfort that is known by him to merge into intense hemicrania, it is sometimes possible to abort the attack by remaining in bed relaxed, in a darkened room for at least two hours. Further relaxation may be induced by a prolonged, warm bath and sodium amytal gr. 3 may be taken by mouth.

1. *Allergic Migraine Therapy*: In 862 cases of migraine reported by Von Storch and Follensby, ten different allergists found that 661 cases were significantly allergic. In these 661 cases relief by allergic treatment varied from 0 to 100% of the cases with an average of 73%. In the entire group of 862 cases some degree of relief was obtained in about 56% of the cases while complete relief was obtained in only 25%.

The allergic aspect of migraine warrants investigation in children with migraine or cyclic vomiting, and in patients with a strong hereditary background of allergic tendencies.

Accurate food diaries and elimination diets are usually necessary to discover the allergens. Dietary experimentation often proves that substances which give doubtful or negative skin tests are nevertheless responsible for the attacks. The inhalents are relatively unimportant in migraine.

The food diary is of most value in those cases in which the attacks occur at somewhat infrequent intervals. It consists of listing the foods eaten daily, indicating the days on which the attack occurs. Then the physician may identify the responsible foods and eliminate them from the diet by finding a period of a week or ten days during which no attacks occur; he may use the foods eaten during the period of freedom as a nucleus of the diet.

The elimination diet is most useful in those persons whose headaches are frequent. Alvarez uses one consisting of lamb, pears and rice, foods which are relatively infrequent offenders. If the headaches persist on this diet after one week, it is highly unlikely that the headaches are allergic in origin.

2. *Endocrine Therapy*: A careful analysis by Price and Von Storch of 163 unselected cases in women revealed that only 10% were definitely related to the menstrual or ovarian cycles. Another 22% were questionably associated and in the remainder the relationship was coincidental or absent.

Oestrogenic Therapy was most significant in those with a definite relationship but after three years' treatment relief became progressively less noticeable and certain cases became worse after prolonged therapy. Various female hormones such as Emmenin, Progynon B, and Stilbesterol have been found effective in special groups of cases.

Migraine ceases after the menopause in many women, but in others it commences then or becomes worse after it. Therefore, artificial induction of the menopause is to be avoided.

Carefully regulated use of thyroid extract may be beneficial in patients with B.M.R.'s below -20%, especially if their headaches are related to fatigue and strain.

3. *Vitamin B Therapy*: Palmer has reported that 65% of 60 patients were completely relieved during treatment with Vitamin B and supplemented by Vitamin B complex. However, in his series only 58% were relieved by Gynergen, thereby questioning the diagnosis. Derbes, Engelhardt and Walters feel that Vitamin B therapy is of little value.

4. *G.I. Therapy*: Weekly duodenal lavage, using magnesium sulfate, has been effective in about half of the patients in a carefully selected group reported by McClure and Huntsinger. Conservative bowel therapy is helpful but not curative. Hygienic bowel regimens, oils, fluids, stewed fruit, exercise are recommended.

5. *Metabolic and Dietary Treatments:* T. R. Brown found from clinical experience that some headaches were due to excess carbohydrates in the body of the migrainous person and almost as many headaches were due to protein dietary factors. He therefore first puts his patients on a very low carbohydrate diet and if unsuccessful, then on an animal protein-free diet. On a low carbohydrate diet, Brown claims complete relief in 37%, distinct improvement in 32% and some improvement in 25% of 328 cases.

Similar improvements have been reported in a smaller series of cases treated with a Ketogenic diet as reported by Barborika.

6. *Ocular Treatments:* Despite the frequent occurrence of ocular symptoms, evidence is lacking that the source of migraine lies in the visual apparatus. In most instances correction of ocular abnormalities is helpful but not curative.

7. *Psychotherapy*—as stated by Wolff: The long term aim of therapy should be that of helping the individual to understand the basis of his tension, the factors in his life that aggravate it, and to aid him in resolving his conflicts.

Therapy centres about the prevention of pernicious moods by enabling the subject to become aware of his tension and to recognize fatigue, the existence of dissatisfaction, feelings of frustration, and the obsessiveness of his pre-occupation with work or responsibilities. The patient must appreciate that elimination of the headache may demand more in personal adjustment than he is willing to give. The physician must bring into focus the cost to the patient of his manner of life and the subject must then decide whether he prefers to keep his headache or attempt to get rid of it.

It may be necessary to work out for the patient a pattern of life to which he should adhere closely. This pattern should include details of occupation, recreation and rest.

Much energy is wasted by the patient in his daily life, partly by anxiety and partly by the desire for excessive speed in order that he may accomplish by a given time all that he has set out to achieve. It may be suggested to the subject that he accomplish three-quarters as much work, assuring him that an attempt at three-quarters will usually result in greater productiveness because of the lessened tension. Also after periods of increased stress, more recreation is necessary and of great therapeutic value. Rest and change must be enforced for those under physical, mental or emotional pressure. The importance of regular holidays, vacations and time off during the day or the week should be stressed.

Summary

This paper has defined migraine and listed the four cardinal points

in diagnosis. The mechanism of the preheadache phenomena is likely a cerebral vascular vasoconstriction. The headache is due to increased pulsations, the result of vasodilatation of the branches of the External Carotid artery principally.

The effectiveness of Gynergen in over 90% of cases is the result of its action on the branches of the External Carotid artery. Whether its principal action is directly on the smooth muscle cells or whether its sympathomimetic action is the more important one, has not been determined.

The highly interesting but very controversial subject of Migraine Equivalents has been omitted. A review of the symptomatic and preventive therapy has also been presented.

Conclusion

As a result of the very fine experiments of Harold G. Wolff and his associates in New York, great advances have been made in understanding the vascular mechanism of migraine. As yet, however, the factors causing the vasoconstriction in the cerebrum and the vasodilatation in the External Carotid artery have not been determined. To make progress in an orderly fashion, I believe it will be necessary for researchers to completely investigate a small group of typical cases in an endeavor to find some common denominator upon which to branch out and investigate in a larger series of persons, normal and migrainous.

BIBLIOGRAPHY

1. Brown, T. R.; J. A. M. A.; 77:1921, 1936.
2. Butler, S. and Thomas, A. W.; J. A. M. A.; 135:967, 1947.
3. Derbes, Engelhardt and Walters; Southern Medical Journal; 38:533, 1945.
4. Graham and Wolff; Arch. of Neurol. and Psych.; 39:737, 1938
5. Lennox and Von Storch; J. A. M. A.; 105:169, 1935.
6. McClure and Huntainger; New Eng. Med. Ass. J.; 199:1312, 1928.
7. Morlock, C. G. and Alvarez, W. C.; J. A. M. A.; 114:1744, 1940.
8. Riley, H. A.; Bull. of Neurol. Instit. of New York; 2:429, 1932.
9. Schumacher and Wolff, H. G.; Arch. of Neur. and Psych.; 45:199, 1941.
10. Sutherland and Wolf; Arch. of Neurol. and Psych.; 44, 1940
11. Torda, C. and Wolff, H. G.; Arch. of Neur. and Psych.; 1317, 1941.
12. Von Storch, T. J. C.; Med. Prin. of N. Amer.; 1317, 1941.
13. Von Storch, T. J. C.; New Eng. Med. J.; 217:247, 1937.
14. Wilson, K.; Neurology, 1570-1594.
15. Wolff; Modern Medicine of Canada; 3:July, 1948.
16. Wolff, H. G.; Arch. of Neur. and Psych.; 37:895, 1937.



DISEASES OF THE EYE

By SIR JOHN HERBERT PARSONS AND SIR STEWART DUKE ELDER
J. & A. CHURCHILL LTD., LONDON, 1948, pp. 732; price \$7.00

This text on the Diseases of the Eye was first published in 1907. It is now in its eleventh edition, a fact which is, in itself, a recommendation of quality.

The authors have written this book to satisfy the needs of the student and the general practitioner in the essentials of ophthalmology and its clinical practice. The material has been presented in a clearly understandable and very readable manner. The sections on treatment have been revised to keep pace with the recent advances in the field of ophthalmology.

The only defect that one can find in this text is the scarcity of good illustrations. However, the quality of the descriptions of the diseases and of the treatments makes this text an extremely useful addition to the library of the student and the general practitioner.

—J. R. BUTTON, *Meds.* '49.

DEMENTIA PRAECOX

By LEOPOLD BELAK, M.D.

GRUNE AND STRATTON, INC., NEW YORK, 1948, pp. 456, price \$10.00

Dr. L. Belak has extracted from a forbidding mass of material of all degrees of scientific validity, the significant data and points of view and has presented them in a coherent and orderly manner, discussing the subject matter of each chapter and appending to each chapter a bibliography of the material discussed.

The book presents such treatments as the use of metrazol, insulin, and electric shock therapy and the problems that arise with each type of treatment. He discusses prognosis, etiology, pathogenesis and pathology of Dementia Praecox.

To sum the book up; it is a review and evaluation of the past decade's work and the present status of Dementia Praecox. It is a valuable text for those interested in studying this condition.

—JOHN B. DOBSON '51.

LAW AND THE PRACTICE OF MEDICINE

By KENNETH GEORGE GRAY, M.D., B.Sc. (MED.), K.C., E.D.

THE RYERSON PRESS, TORONTO, 1947, pp. 68, price \$1.50

This is a masterful little book for married, time-pressed medical students and doctors alike. Dr. Gray has that all-too-rare knack of brevity and accuracy, while at the same time covering adequately what he has set out to do — "to discuss those (legal) problems which seem to recur most frequently." Dr. Gray speaks with authority since he is a lecturer in the subject at the University of Toronto.

Completeness is achieved by the numerous references to standard texts, precedents, specific cases, etc., in the legal literature illustrative of his statements. An excellent index and bibliography are also included.

The price of less than two dollars is well repaid by the bird's-eye view of the application of law to medicine afforded by this book.

—J. VANCE '51.

A HISTORY OF THE HEART AND CIRCULATION

By DR. F. A. WILLIUS AND DR. F. DRY

SAUNDERS, PHILADELPHIA, 1948, pp. 456, price \$8.00

It has been said that the farther we look into the past, the farther we can look into the future. In the field of cardiology, as in all special fields of medical science, it is necessary to study the observations and the interpretations of the observations of great men who have worked in the field in the past. Dr. Willius and Dr. Dry of the Mayo Clinic, both well recognized in cardiological work, have assembled in this book the important facts accumulated by physicians and scientists from ancient times to the present. They tell us of the men who, with poor instruments and meagre facilities, have given the world the facts to which modern cardiology owes its basis.

The book is divided into three main sections. In the first section the material is presented in chronological order. The order used is as follows: (1) Antiquity, (2) Mediaeval Era, (3) Renaissance, (4) seventeenth century, (5) eighteenth century, (6) first half of nineteenth century, (7) second half of nineteenth century, (8) first quarter of twentieth century. In discussing each period the authors touch on the existing civilization, its social and political arrangements, influences on it of religion and superstition, the growth of institutions of learning, and of medical teaching.

The second section gives brief biographic sketches of a selected group of contributors to the study of the cardiovascular system. Included are such great men as Hippocrates, William Harvey, William Einthoven, Sir James MacKenzie, Sir William Osler, and Sir Thomas Lewis.

A summary presentation of the subject matter is given in the third section.

With the accent on organization, presentation of the known facts in concise form, but without the dreariness of a scientific summary, this book will be read by physicians, medical students, and those people interested in medicine and its development.

—DONALD R. SMITH '51.

THE STORY OF JOHNS HOPKINS

By BERTRAM M. BERNHEIM, M.D.

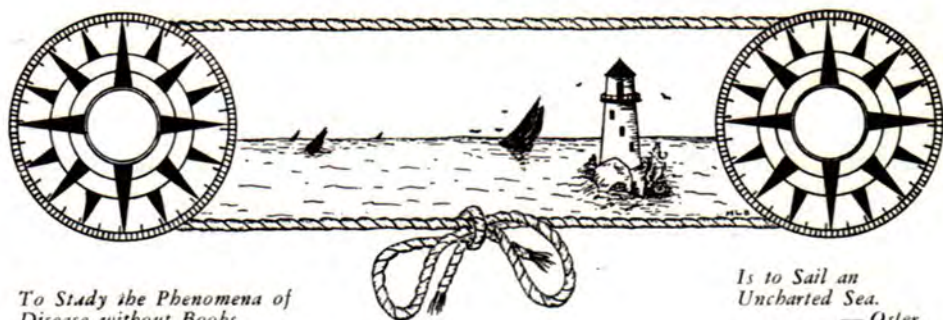
MCGRAW-HILL BOOK COMPANY, INC., New York, Toronto, pp. 235; \$3.50

This is the story of a great experiment and the men who made it possible. The Author describes the growth of the school under the guidance of "The Four Saints"—Welch, the pathologist; Osler, the physician; Halsted, the surgeon; and Kelly, the obstetrician. Rather than the usual historical approach, he uses short human interest stories to show how these men directed the growth of Johns Hopkins from the very start. As the school becomes famous many more great men are drawn to it and we hear of the contributions such men as Cushing, Walter Dandy and Hugh Young made to the Hopkins.

Dr. Bernheim is qualified to tell this story as he entered the school as a student shortly after its beginning and has since been associated with it in various staff positions. He shows a deep love for his school in this book which is more genuine than the usual over-enthusiasm of alumni.

Much has been written about these great doctors individually, but in this book we see how they combined their resources to create one of the most outstanding medical schools in the world.

—R. M. MCFARLANE '51.



*To Study the Phenomena of
Disease without Books*

*Is to Sail an
Uncharted Sea.*
— Osler.

RECENT ACCESSIONS TO THE MEDICAL SCHOOL LIBRARY

- Advances in military medicine; v. 1-2. 1948.
- American association for the advancement of science. A brief history of the association from its founding in 1848 to 1948. 1948.
- American association for the advancement of science. Section on medical sciences. Rickettsial diseases of man; a symposium. 1948.
- American public health association. Standard methods for the examination of water and sewage; 9th ed. 1946.
- Baxter. Scientists against time. 1948.
- Bell. Renal diseases. 1947.
- Bick. Source book of orthopaedics; 2nd ed. 1948.
- Bloom. Histopathology of irradiation from external and internal sources. 1948.
- Bourne and Williams. Recent advances in obstetrics and gynecology; 7th ed. 1948.
- Burn. The background of therapeutics. 1948.
- Canada. Bureau of statistics. Directory of hospitals in Canada, 1945-1946. 1947.
- Clark. Topics in physical chemistry. 1948.
- Dalcq and Fautrez. Manuel theorique et pratique de dissection. 1944.
- Daniels. Tuberculosis in the British Zone in Germany. 1948.
- East and Bain. Recent advances in cardiology; 4th ed. 1948.
- Eden and Holland. Manual of obstetrics; 9th ed. by Alan Brews. 1948.
- Edwards. Recent advances in surgery; 3rd ed. 1948.
- Engel. The child's lung. 1947.
- Ferguson and Lucas. Henderson's Materia medica. 1948.
- Gale. The chemical activities of bacteria; 2nd ed. 1948.
- Gesell. Studies in child development. 1948.
- Great Britain. Ministry of Health. Salaries of whole-time public health medical officers. 1948.
- Grulee. The child in health and disease. 1948.
- Gruneberg. Animal genetics and medicine. 1947.
- Hale-White. Great doctors of the nineteenth century. 1935.
- Heaf and Rusby. Recent advances in respiratory tuberculosis; 4th ed. 1948.
- Herbut. Surgical pathology. 1948.
- Hewer. Recent advances in anaesthesia and analgesia; 6th ed. 1948.

- Hill. Principles of medical statistics; 4th ed. 1948.
- Himsworth. Lectures on the liver and its diseases. 1948.
- Hinshelwood. The chemical kinetics of the bacterial cell. 1947.
- Hirsh. The problem drinker. 1949.
- Kleiner and Dotti. Laboratory instructions in biochemistry; 2nd ed. 1946.
- Newman. Interpreters of nature. 1927.
- Novak. Textbook of gynecology; 3rd ed. 1948.
- Nuffield foundation. Survey committee on the problems of ageing and the care of old people. Old people; report. 1947.
- Paterson. The treatment of malignant disease by radium and x-rays, being a practice of radiotherapy. 1948.
- Pawling. Dr. Samuel Guthrie, discoverer of chloroform. 1947.
- Polyak. The retina. 1941.
- Reid. The life and convictions of William Sydney Thayer, physician. 1936.
- Ryle. The changing disciplines; lectures on the history, method and motives of social pathology. 1948.
- Ryle. The natural history of disease. 1948.
- Savill. The hair and scalp; 3rd ed. 1947.
- Scotland. Medical advisory committee. Laboratory services. 1947.
- Smith. Technic of medication. 1948.
- Stockings. The metabolic brain diseases and their treatment in military and civilian practice. 1947.
- Taylor. Principles and practice of medical jurisprudence; 10th ed., edited by Sydney Smith in 2 v. 1948.
- Trueta and others. Studies of the renal circulation. 1947.
- Underwood. Textbook of sterilization. 1941.
- Van Hoosen. Petticoat surgeon. 1947.
- Victor Robinson memorial volume; essays on the history of medicine. 1948.
- Williams. Detoxication mechanisms. 1947.
- Willius and Dry. A history of the heart and the circulation. 1948.

CONTINUATION

- Annals of the New York Academy of Sciences. Aureomycin—a New Antibiotic. v. 51, art. 2. 1948.
- Annals of the New York Academy of Sciences. Newer Synthetic Analgesics. v. 51, art. 1. 1948.
- Annual Review of Microbiology. v. 2. 1948.
- Calendar of the Royal College of Surgeons of England. 1948.
- Cornell Conferences. v. 3. 1948.
- New and Non-Official Remedies. 1948.
- Proceedings of the American Diabetes Association. v. 8. 1948.
- Publicaciones del centro de investigaciones fisiológicas. v. 11. 1947.

Publications of the Institute of Neurology, North-western University Medical School. v. 19. 1947.

Recent Progress in Hormone Research. v. 3. 1948.

Report of Statistics of Criminal and Other Offences, Canada. No. 71. 1947.

Report of the Department of National Health and Welfare, Ottawa. 1948.

Report of the Division of Tuberculosis Control of the Department of Health and Welfare, Province of British Columbia. 1947.

Report of the New York State Department of Health. No. 67. 1946.

Report of the Ontario Cancer Treatment and Research Foundation. 1947.

Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association for 1947. 1948.

Studies from the Douglas Smith Foundation for Medical Research of the University of Chicago. Collected Reprints. v. 19. 1946-47.

Transactions of the Pacific Coast Obstetrical and Gynecological Society. 1947.

Transactions of the Southeastern Section of the American Urological Association. 1947.

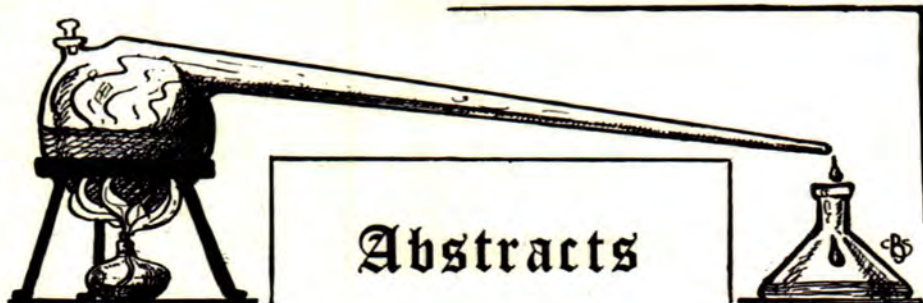
Vital Statistics of Canada. No. 25. 1945.

Yearbook of Orthopedics and Traumatic Surgery. 1948.

Yearbook of Surgery. 1948.

Yearbook of Urology. 1948.

February 15, 1949.



TREATMENT OF HEMORRHOIDS

By G. JOHNSON HAMILTON, M.D.

Am. J. Surg.; lxxvi:672-677, (Dec.) 1948

This article considers only internal hemorrhoids which are definite varices of the superior hemorrhoidal vessels. The etiology is given as follows: Some degree of stasis is prone to occur in the long column of blood extending from the rectum to the liver, especially since these veins have no valves. This leads to a local rise in venous pressure with increased carbon dioxide and decreased oxygen content. This, together with the sluggish removal of toxins tends to injure the walls of the veins. Continuation of this condition leads to the replacement of the intima and muscle cells by fibrous tissue. The occurrence of any great stress or strain or even a persistence of lesser strain causes these weakened walls to become stretched and tortuous.

Contributing factors are thought to be cardiac insufficiency, hepatic congestion, pressure from a mass in the pelvis, systemic disease and inherited weakness of the walls of the veins.

The most important symptoms were considered to be bleeding, prolapse and pruritus ani in that order.

The treatment depended upon the stage of the hemorrhoids:

1. Palpable hemorrhoids were treated by excision. The technique employed in these cases was simple ligation and excision of the involved superior hemorrhoidal vessels and then the inferior hemorrhoidal vessels if necessary.
2. Those hemorrhoids which were impalpable but visible and produced symptoms were treated by sclerosing therapy. The injection of 5% phenol in almond oil was given at the cephalad point of origin of the hemorrhoid and into the submucosal

layer. The injection should be given very slowly and continued until striae are visible on the surface of the mucosa but stopped before blanching occurs. The author advocates injecting one hemorrhoid at a time at weekly intervals. Frequently one hemorrhoid may require two or even three injections.

3. Those hemorrhoids which were not palpable and asymptomatic, even though visible, were treated palliatively.

—GORDON SKELHORST, '50.

DIAGNOSIS OF PULMONARY STENOSIS BY ANGIOCARDIOGRAPHY

By MERL J. CARSON, M.D.; THOMAS H. BURFORD, M.D.; WENDELL G. SCOTT, M.D.; JAMES GOODFRIEND, M.D.

J. Pediat., 33:525-543 (Nov.) 1948

This contrast radiographic technique has been found helpful in establishing the exact diagnosis in several types of congenital cardiac anomalies, particularly those in which cyanosis is a prominent symptom. The authors emphasize that, contrary to other diagnostic methods in this field, it can be carried out in small infants.

Essentially, the technique is one of rapid sequence exposures (ten within a period of ten seconds) and is performed on a taurograph. A specified quantity (according to age) of 70% Diodrast is injected into an antecubital vein (within a period of two seconds). The injection is begun immediately after the first exposure has been made.

It is demonstrated here that one can accurately trace the course of the circulation through the heart chambers and visualize the relative size, location and number of the

great vessels. The diagnostic points in several congenital heart conditions are shown and outlined as in these two examples:

1. *Tetralogy of Fallot.*

- (a) An interventricular septal defect as shown by Diodrast, flowing directly from right to left ventricle with progressive opacification in the latter.
- (b) An over-riding aorta as shown by simultaneous filling of aorta, pulmonary conus, and pulmonary arteries.
- (c) Enlargement of right ventricle.
- (d) Decreased caliber of the pulmonary arteries.

2. *Persistent Truncus Arteriosus with Stenotic Pulmonary Arteries.*

- (1) Large right ventricle.
- (2) Large interventricular septal defect.
- (3) A single large vessel is seen emerging from the region of the ventricles, and because rapid opacification of this vessel occurs at the same time that the ventricle begins to be visualized, the truncus likely over-rides the septal defect.
- (4) No pulmonary conus is seen but small pulmonary arteries can be visualized arising from the single large truncus.

—J. FRID, '50.

STREPTOMYCIN IN THE TREATMENT OF PERTUSSIS

By HARRY LEICHENGER, M.D., AND ALLEN SCHULTZ, M.D., CHICAGO, ILL.

J. Pediat., 33:552-555 (Nov.) 1948

The authors report on a series of 24 cases in which a diagnosis of uncomplicated pertussis had been made.

Patients were assigned in rotation to one of three groups:

Group 1 — received streptomycin one gram daily by the aerosol route.

Group 2 — received streptomycin one gram daily intra-muscularly.

Group 3 — control group received usual symptomatic whooping cough treatment.

Results:

One patient in the control group died.

The number and severity of complications were significantly greater in the control than in the other groups.

In those receiving streptomycin a more

marked diminution occurred in the average daily number of paroxysms than in the control group and a diminution in the duration of spasms.

Those receiving treatment by the aerosol route did better clinically than the other two groups, although awakening children for treatment frequently initiated a spasm.

Conclusions:

1. Streptomycin appears to be an effective therapeutic agent in the treatment of pertussis.

2. The aerosol route of administration is the method of choice.

3. No untoward results were noted after one week of therapy.

The authors feel that there is sufficient evidence to justify the more extended use of streptomycin in the treatment of pertussis. One week of treatment appears to be sufficient in the average case.

—M. P. LEITH, '51.

HYPERTENSION AS A REACTION PATTERN TO STRESS; SUMMARY OF EXPERIMENTAL DATA ON VARIATIONS IN BLOOD PRESSURE AND RENAL BLOOD FLOW

By STEWART WOLF, JOHN B. PFEIFFER, HAROLD S. RIPLEY, OLIVER S. WINTER AND HAROLD G. WOLFF, F.A.C.P.

Ann. Int. Med., 29:1056-76 (Dec.) 1948

This is a report of an investigation of the relationship between life situations, emotions, and the level of blood pressure in the normal and hypertensive subject.

Fifty-eight subjects with essential hypertension, forty-two non-hypertensive subjects, and one hundred and fifty with vasomotor rhinitis and bronchial asthma were chosen for the study. Their clinical courses, personalities, attitudes, habits and general behavior were studied in detail, over periods of one to three years.

Hypertensives and normal subjects were subjected to measurement of renal blood flow. After two or three control periods in a neutral environment, topics involving personal conflicts were introduced and discussed for two periods of 30-40 minutes. Then relaxation in a neutral environment was promoted during the final periods. Six of the hypertensive subjects were examined before and after sympathectomy.

The authors concluded that their findings supported the belief that a subject's attitudes and feelings have a good deal to do with blood pressure. The hypertensive subjects had a sharp rise in systolic and diastolic blood pressure during discussions of serious conflicts. There was also a prompt decrease in renal blood flow which outlasted the elevated blood pressure. The glomerular filtration rate varied slightly but the filtration fraction rose significantly. In nine of the normal subjects there was a slight rise in blood pressure and a slight vasoconstriction of renal vessels.

The blood pressure still rose during traumatic interviews after sympathectomy. The renal vasoconstriction, however, no longer occurred and there was no rise in filtration fraction.

The general attitudes, reaction patterns, and behaviour of the hypertensive subjects are more offensive, while subjects with bronchial asthma are more defensive in dealing with life. The authors believe that hypertension may represent an atavistic protection reaction of mobilization evoked inappropriately by these subjects to deal with environmental stresses and problems of interpersonal relations. It becomes harmful and leads to illness when this essential emergency pattern is adopted as a way of life.

—C. GORDON CAMPBELL, '49.

RESULTS OF THERAPY BY RACE, SEX, AND STAGE OF SYPHILIS

By T. J. BAUER AND E. V. PRICE

J. Ven. Dis. Inform. 30:1-6, (Jan.) 1949

This article reports an analysis made by the United States Public Health Service of the results of penicillin treatment in 6,310 cases of syphilis. These cases were selected from the records of two rapid-treatment centres on the following basis: all had been treated prior to 1947, were in the primary or secondary stage of syphilis when first seen, and had received no previous therapy.

The results of treatment, measured in terms of re-treatment rates, were calculated for each group of patients according to sex, race and stage of syphilis. The period of observation after treatment was made as long as possible, extending to twelve months in 75% of cases.

It was found that in white males, the re-

treatment rate for secondary syphilis was two to three times the rate for primary syphilis (whether sero-positive or sero-negative). In Negro males, no such difference was encountered between the two stages of the disease.

In both types of primary syphilis, the re-treatment rate of the Negro males doubled that of the white males. In secondary syphilis, however, the rates in both races and both sexes were comparable. (Female rates were not analyzed in primary syphilis because of the small number of women.)

The writers demonstrated statistically that these findings were independent of differences in treatment schedules.

Since the two racial groups did not differ in their response to the treatment of secondary syphilis, the differences encountered in primary lues were attributed to a higher incidence of re-infection among the Negroes. This interpretation is compatible with the recognized higher incidence of syphilis in the Negro population, and with our present conception of slowly developing immunity. Reasoning from this premise, the writers conclude that a truer picture of actual treatment failure can be obtained from the results of therapy in secondary lues, where relapse takes precedence over re-infection. They suggest that this principle be applied in the evaluation of any therapeutic regime.

—C. BUCK, M.D.

CONSTRICTIVE PERICARDITIS WITH OBSTRUCTION OF PULMONARY VEINS

By WALTER LAWRENCE, JR., S.B., M.D.,
W. E. ADAMS, M.D., AND DONALD
E. CASSELS, M.D.

J. Thoracic Surg., 17:832-840 (Dec.) 1948

This article starts out by reminding its readers that reports of pericardial resection did not start appearing in the literature until 1920. Typical cases of constrictive pericarditis exhibit the signs and symptoms of right-sided heart failure but the etiology is by no means so simply stated. Probably much of the variation in classification and the concepts of pathogenesis is due to the unknown etiology.

An interesting case is presented which should have responded to surgery but failed

to do so because of marked stenosis of the pulmonary veins by fibrous tissue. In this case a congenital (cavernous hemangioma) and inflammatory lesion of the mediastinum were co-existent. After the congenital lesion was removed there was temporary improvement in the patient's condition. However, progression of the inflammatory process and accumulation of pericardial fluid required further surgical interference. Drainage led to an improvement of several months duration which was followed by an increase in constriction. Surgical decortication of the compressed heart allowed the heart to increase diastolic filling but the constriction of the pulmonary vein impaired the pulmonary circulation to such an extent that improvement did not take place. A search through the literature failed to reveal any other instances of constrictive pericarditis co-existing with constriction of the pulmonary vein.

This case presented an excellent opportunity to study the development of constrictive pericarditis from the onset of the process. Decortication of the heart ordinarily yields a high percentage of cures, as was demonstrated by reference to results in seven additional cases.

—H. S. CAMERON, '50.

SURGICAL THORACIC TUMORS

By MOSES BEHREND, M.D., AND
ALBERT BEHREND, M.D.

J. Internat. Coll. Surgeons, xi:469-479
(Sept.-Oct.) 1948

The category of thoracic tumors considered in this paper are those of the mediastinum, lung and pleura. Those of the esophagus and superficial tumors of the thorax are not taken into account.

Hodgkin's Disease

Thoracotomy in Hodgkin's disease involving the mediastinal lymph glands is only to be undertaken for diagnostic purposes as surgery will not effect a cure. Diagnosis can usually be made by means of biopsy of superficial lymph glands and other clinical criteria satisfied by the symptomology of the patient.

Lymphoblastoma of the Mediastinum

This condition is extremely malignant and little can be derived from surgery other than to make or confirm the diagnosis.

Sarcoma

Sarcomas in the thorax are more prevalent in children and especially those at or near puberty. Their most common location is between the visceral and parietal pleura, and these sarcomas often affect sympathetic nerves to produce symptoms of referred pain, e.g. pain in an arm or shoulder, as well as weakness of an arm. Palliative surgery is found to be of considerable help, but no hope for a cure can be entertained by means of operative procedures.

Cysts of the Lung

Cysts of the lung often degenerate and may even undergo a malignant transformation. Single cysts or even bi-lateral cysts, if they are confined to one lobe on each side, may be removed surgically by means of pulmonary resection, while massive bilateral cysts are inoperable. It has been found that cysts of the lung may often be the cause of a spontaneous pneumothorax, and therefore should be suspected when such a condition is discovered.

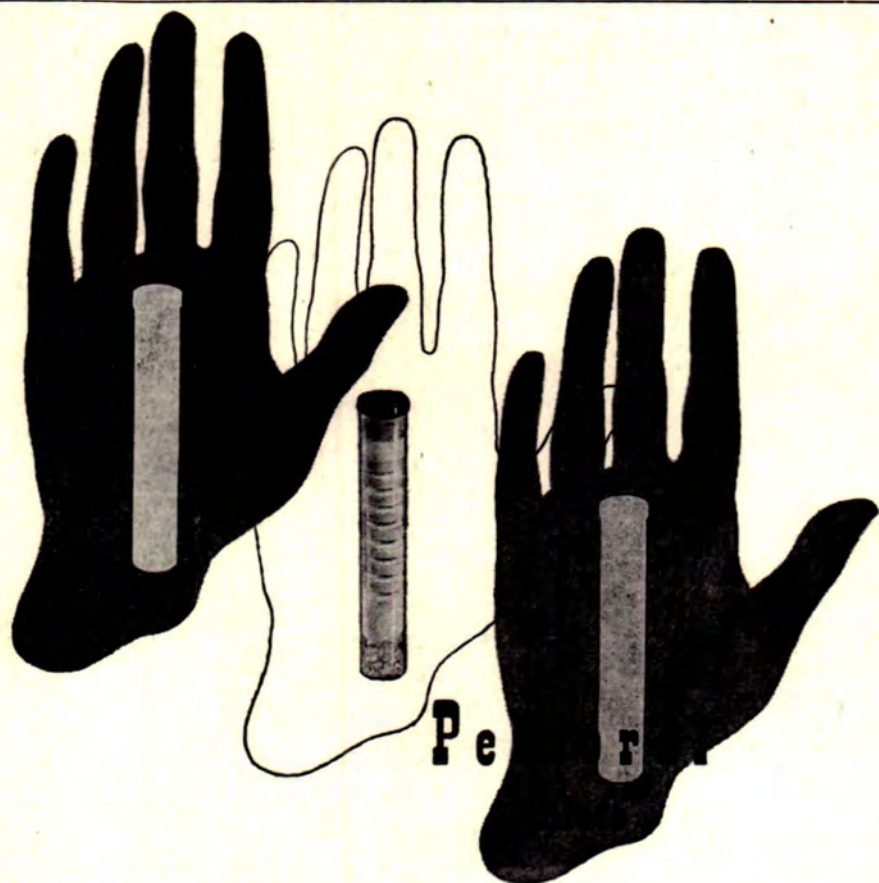
Benign Tumors

The types of benign tumors most commonly found in the thorax are: Benign Adenoma, Fibrochondroma and Cylindroma. These tumors are capable of malignant transformation. They may also be the basic factor in the production of a lung abscess or of bronchiectasis by causing obstruction in the bronchial tree. These tumors should therefore always be removed by pulmonary resection rather than by local bronchoscopic methods.

Carcinoma

The primary cause of bronchogenic carcinomas is unknown. They may occur at any age, but are probably more prevalent in the usual cancer age. They are more common in males than in females. Their general incidence seems to have increased in the last number of years and they should always be in the diagnostic foreground of the physician when confronted by a patient with persistent cough, with or without blood-streaked sputum. Early diagnosis is the only hope for surgical removal to effect a cure. Bloody effusion, much gland involvement or extensive abscess formation contraindicate the use of, as well as the benefit of surgery. Routine radiological examinations of the general population as is done in the case of tuberculosis seems the only method for an early diagnosis and surgical cure.

—W. M. GOLDBERG, '49.



CRYSTALLINE POTASSIUM PENICILLIN

Triple Protection to Assure Potency

Penioral reaches the patient laboratory-fresh because it is triply protected against moisture—arch enemy of penicillin.

- The vial has an airtight seal.
- Each vial contains a desiccant to absorb moisture after seal is broken.
- Desiccant contains a blue indicator that fades when excessive moisture threatens full potency.

Penioral Blue means Potency Protection

25,000 I.U.—vials of 12 tablets
50,000 I.U.—vials of 8 & 12 tablets
100,000 I.U.—vials of 12 tablets



JOHN WYETH & BROTHER (CANADA) LIMITED • WALKERVILLE, ONTARIO