

Caduceus

22 JAN 1970



MEDICAL STUDENTS' CENTRE,
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15TH JANUARY, 1970

FROM THE CHAIRMAN

Recently at the opening ceremony of the seminar organised by the H.K.F.S. Dr. Lee of the Chinese University remarked that the time when students did not care about society was gone and he credited students today of their concern for what was happening around them. This is most encouraging for it is such care and concern for one another that will make our society a better place to live in, and such a sign among students promises a bright tomorrow for Hong Kong.

It is still doubtful in the minds of some people as to what students can do for society and whether or not their time would be more profitably spent on their books instead of involving themselves with activities which in the eyes of these people have nothing to do with students. "After all," they will say, "a student's duty is to study well!"

But we must bear in mind that the real purpose of going to a school or university is the acquisition of knowledge and its rational APPLICATION so that we may be a better man. That application and acquisition of knowledge go hand in hand is plain. You just cannot preach love and charity to a person and ask him to forget about his next-door neighbour who hasn't got enough to eat. (知行合一), (知而不行, 是謂不知) has been taught in China long time ago. Thus it is not only essential that a student be fully trained in the various aspects of knowledge but also be encouraged to make use of what they have so painstakingly learned.

It is equally wrong to say that a student should wait until he graduates before involving himself actively in society for then he will be more prepared and see things better. This is the same as to say that anyone who is not a qualified surgeon must not pull at thorn out of somebody else's finger. Thus if we believe that we have taught our students sound and right principles, why should we stop them from practising it. Moreover, if one does not develop this sense of responsibility, this sense of obligation to society in his student days when he is relatively free from other responsibilities, when is he going to develop it? If one does not fulfil his obligation when he is a student, what is the magic of graduation that will change his whole attitude?

As to what students can do for society, we might as well ask what everyone can do for society. I think there is only one ideal which we all should be working for: to make our society a better place for everybody to live in. This has a special appeal to us university students for we are the future leaders of society. By a leader I do not mean a V.I.P. or the head of any establishment but rather — simply someone with a great responsibility than others because we are the few privileged to be given a chance to pursue a university course, a chance to learn a little more and a chance to think a little more. If we do not should our own responsibility, who will shoulder it for us?

If we really care for our community, if we are not thinking of leaving it at our earliest possible chance, then let us take up our obligation happily and do what we can for our society. The future of Hong Kong belongs to us and we will harvest what we sow. We will be, after all, what we deserve.

19, Sherwood Street,
Tauranga,
Bay of Plenty,
New Zealand.

22 Dec., 1969.

Mr. Ng Wing Ling,
Managing Editor,
"Caduceus."

My dear Wing Ling,

It was with very great pleasure that I received your kind letter and also a copy of "Caduceus." It was most thoughtful of you, and I have enjoyed reading your publication.

I often think of you and of the pleasant years I sent in the Department of Anatomy. It was a most enriching experience associating with my students. While I may have taught you some anatomy, I have indeed learned even more from you; and it has been great satisfaction seeing how each one of you develops his or her own special talent and make or will make your special contribution as you go through life.

It was with great sadness that I had to part from my Department, my staff, and my students. My joy in the future will be in following your careers.

I have bought a home in Tauranga in the North Island of New Zealand. Tauranga is a very pleasant small town of about 20,000 inhabitants. The people here are friendly, and the surroundings are attractive. Tauranga is 130 miles south of Auckland. There are two planes daily from Auckland, and also a bus service, and a train. The main tourist attraction of Tauranga is fishing, hunting, surfing, and the famous thermal springs only 40 miles away or about an hour by car. I hope that many of you will come this way; and if you do, we welcome you to stay with us.

Though late, we wish to send you our warmest greetings for the season. May this Christmas be truly merry; and may this New Year be especially abundant to you — abundant in health, happiness, and achievement.

Yours as ever, affectionately,

K. S. Francis Chang

Shortage of Blood

It was a warm and sunny weekend. People were off their usual duties and spending the lovely day in the most enjoyable way they could possibly think of. Lawns in the parks were occupied by families sitting placidly basking in the winter sunshine under the clear blue sky. At 3 o'clock in the afternoon Mrs. Chan was putting the last few pieces of sandwiches into the lunch box. John and Jenny were both ready. Their father could be returning at any minute to bring the family of four to a favourite country spot they frequently visit on sunny weekends like this.

The phone rang. Mrs. Chan picked up the receiver.

"Hello, it it the Chan's".

The voice was unfamiliar. She wondered who it could be.

"That's right. Mrs. Chan speaking."

"This is the nurse in charge of casualty admission. Your husband was injured in a traffic accident and admitted to our hospital half an hour ago."

Mrs. Chan felt the heart beating within her.

"How is he now?"

"How is he now?"

"We are doing our best for him. There seems to be quite a bit of internal bleeding. Could you come along at once?"

"I'll be right there."

In the operation theatre a team of doctors were all alert and busy. They knew from examination of the patient that an operation was required. They also knew from their experience that the patient will have a fair chance of survival if he could stand the surgery. As the chief surgeon was making his final check on the instruments, news arrived from the blood bank that the particular group of blood Mr. Chan required was lacking. A neighbouring hospital was ranged up, and then another. But none had any store. Then the hospital tried to track down any people whom they knew to be of the particular blood group. As the minutes dragged on, Mrs. Chan, with her two children as worried as their mother, waited at the hospital corridor.

Happening like that which occurred to the Chan family is not a rare finding. In fact the shortage of blood is a common difficulty experienced by practically all big hospitals and in many countries over the world. Over the past few decades, developments are such that a lot more of blood is required in our hospitals today than twenty or thirty years ago. Speedy travel facilities have increased the number of serious traffic accidents. The evolution of industrial processes has created new hazards and danger for workmen and paradoxically, what is worst of all, the advance of medical science has made the situation more serious than ever before. Many patients not amenable to treatment some years ago can now be saved through advances in surgical and other techniques. Disease conditions deemed incurable by standards twenty years ago are actively combated by doctors who have now mastered new knowledge and skill. Invention of the heart-lung machine succeeded in creating a cardio-pulmonary bypass in the body circulation and enabled doctors to

perform operations such as open heart surgery for the correction of defects in the septa and valves of the heart. Progress in transplant surgery has brought new hope for many patients. With all these developments, there is a real great demand in our hospitals today, of highly trained medical personnel, of various types of complicated medical equipment and above all, an unprecedented demand for that precious life-saving raw material required in the management of many patients — human blood.

This acute shortage of blood affects a great number of people. Our doctors, concerned with saving lives have spent a lot of effort to deal with the situation. They devise new methods for the shortage of blood. Some experiment while others study frac-

ment on artificial blood substitution techniques so that whole blood is separated into its various components, and only the specific component required by a patient is given to him so that a given amount of blood can be given simultaneously and effectively to patients requiring different factors. Unfortunately all these measures are inadequate as yet to relieve the condition of blood shortage. Further research are still required to find a scientific breakthrough.

However, the difficulty is not insuperable. More and more people today are beginning to realise the social obligation towards their fellow men as a contributory factor towards a better community. Some of these obligations as for example tax-paying,

(Continued on page 3)

EDITORIAL

HYPERTENSION—A NEW YEAR GREETING

Medical students apparently possess a large vocabulary distinct from many other university students judging from their word power of medical terms — this is indeed a virtue endowed to us as a natural phenomenon. Hence I apologize for using medical terms if these are used.

As 1970 walks boldly through the door into the house it sees the onset of a serious seasonal condition which propagates rapidly throughout the campus, starting an epidemic. This condition commonly known as "Hypertension" is characterised by excessive (or raised) pressure (or tension) resulting in overloading our heart (our body as a whole). Fortunately we are provided with an excellent compensatory power — compensation develops happily and readily in every generation and this is an inherited character. This process is indispensable, or decompensation means failure. Most sufferers show good tolerance. Some even develop immunity. The clinical picture as a result varies from an overt attack of variable grades of severity to a subclinical or latent condition.

To make it more evident to the most perplexed, let me venture to say more, though it is already obvious to all in the medic centre. The condition troubling medical students at the moment as 1970 steps in is a consequence of the widespread consciousness of the examinations in the near future: 1st M.B., 2nd M.B., and final M.B., all coming soon. The manifestation of "Hypertension" is most readily seen in the everyday life of a typical patient:

"Early in the morning, at 9 a.m., he arrives at the campus, immediately he fights through the entrance-turner into the library, he never looks around but aims straightly to the quietest place he found. He sits down; wasting no time, he reads at the highest possible speed, until it is noon, when his neighbours rise and he feels hungry, so he reluctantly leaves for the canteen. After a full meal, he goes for a short walk, as others do; he talks and enjoys others talking. This walking and talking period does not last long; soon he senses a tension somewhere deep in his heart, becoming so distressing that he has to set back, hoping to relieve the tension by sitting beside the book. With the book in front, the tension is momentarily suppressed; however, with a full stomach, his concentrating power is decreased, and stimulated by the neighbours, though he wishes to resist it, he yields to sleep, as deep as all his neighbours. The dream usually lasts till tea time. Caffeine has its stimulant effect on him — he depends much on a wonderful tea time to struggle till dinner moment. Then the sun is gone, the moon is up, the wind blows, the lights are on, while the poor creature stuck to his warm chair continues to creep through his black-and-white, only to emerge at the crisis when the bell rings at 11 p.m."

The above brief account does not mean to serve as an illustration of the majority or the minority of the patient's pattern of response. However, it may well manifest the serious effect of an overt attack of the condition ("Hypertension") on a newborn whose immunological mechanism is immature.

BRINGING JOY AND LAUGHTER TO SANDY BAY AND GRANTHAM HOSPITAL

It was Christmas time. As usual, the Medical Society arranged a Christmas Carolling to the sick and the handicapped. Unlike last year, however, we this year went on two different days — 19th and 23rd December, and instead of bringing along the accordion and singing on the spot, we had our Carolling performed by a recorder. Mr. William Tam, our Santa Claus, buried himself in the midst of angels,

and in a couple of minutes after our arrival, the Centre was drowned in laughter and horning from the toy-flutes we gave them. We left many a joyful heart behind.

SPORTS NEWS

In the first term, only three kinds of ball games were played and we managed to get two champions and one third place. The champions are Hockey and Badminton while Soccer, which was looked down upon by others, finished in 3RD place. Mr. Lam Chi Wai, Mr. Yeung Wah Hin, Mr. Leung Sze Kee were representatives to the Interfaculty Bridge Tournament sponsored by The Bridge Club, HKUSU. They finished in 2ND place.

The following are the tentative fixtures for the Second Term Interfaculty matches:—

Volley	7th Jan.	4.20 p.m.	Med — Arts(1)
	14th Jan.	4.20 p.m.	Sc — W-1
	21st Jan.	5.30 p.m.	FINAL
Table-tennis	19th Feb.	5.30 p.m.	Med — W-2
	23rd Feb.	5.30 p.m.	FINAL
Basketball	5th Feb.	5.30 p.m.	Med — W-2
	12th Feb.	5.30 p.m.	FINAL
Squash	10th Feb.	5.30 p.m.	Med — Arch
	17th Feb.	5.30 p.m.	Med — Sc
	20th Feb.	5.30 p.m.	Med — Eng
	27th Feb.	5.30 p.m.	Med — Arts
Lacrosse	3rd Mar.	5.30 p.m.	Med — SS
	2nd Feb.	4.30 p.m.	Med — Arch
	16th Feb.	4.30 p.m.	Med — Eng
SOFTBALL	26th Feb.	4.45 p.m.	FINAL
	17th Feb.	4.15 p.m.	Med — Eng (2)
	20th Feb.	4.15 p.m.	Art — W-2
	24th Feb.	3.15 p.m.	FINAL

News In Brief

—Union Carnival, 13th December, 1969: The Medical Society put up a stall in the Union Carnival. Thanks to the great efforts put up by the First Year, our Stall was well decorated and well earned the Runners-Up in decoration competition.

—Nuffield Scholars: Two current Final Year medical students have been awarded the Nuffield Scholarship. They are Kevin Loh and Chan Moon Cheung.

—Examination News: First M.B., B.S. (Organic Chemistry) Examination — 2nd January, 1970.

Final M.B., B.S. (Paediatrics) Examination — 6th January, 1970.

THE RING

by P.K.

It's meant for the foolish
It's foolish I know
yet I dwell

The passion
unpredictable I can't handle
Why should be her
So pure so fine
O Lord help me

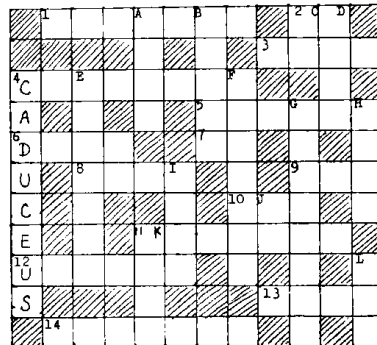
Feather-like empty heavy was I
Sudden delightment beyond compare
Creeping fear painful despair
Who is the lucky one I can't share
Don't I know so much at sea
so much in love

Not me is the answer
Why still linger
Run Be fast or you'll suffer more
(no don't blame her)
Just run away from your own Ring
(I won't if she love it too)
It's going rancid
You smell it Don't You

Please you foolish heart
Forget and forgive
It's not meant to be bitter
Believe me please though you are
Smile while you can don't sigh
Listen to me Jump out of it
But where am I.

I wrote this, what I called "modern poem", a couple of years ago for self-entertainment. Recently when I read "Ring of Bright Water" by Gavin Maxwell I was delighted to find on the first page the theme-poem which, coincidentally, was named "The Ring", but this Ring was so different from that of mine.

JUNIOR CROSSWORD B.B.



ACROSS

- an old term for the inferior and superior intrinsic longitudinal muscles of the tongue
- a short form of immunoglobulin
- the pigmented, vascular layer of the eye
- the collar bone
- the end of an alveolar duct
- the outermost membranous covering of the brain and spinal cord
- "Be silent."
- an irritating sensation in the skin
- neither fan nor fun
- the beginning three characters of "generalized weight excess due to accumulation of fat."
- a muscle in the eye used for accommodation
- a retroperitoneal structure which has three constrictions
- a belt or girdle
- a type of leukaemia characterized by the presence of polymorphonuclear leukocytes, myelocytes, promyelocytes and myeloblasts in the peripheral blood

DOWN

- the manner of walking
- a vertebra that lacks the centrum
- intravenous administration
- the knee
- any ear-shaped structure
- a bone of the base of the skull perforated for the olfactory nerves and forming the upper bony nose
- this oblique muscle is supplied by the Oculomotor nerve
- an eminence
- collectively, all the filaments covering the skin
- Bachelor of Arts
- a compartment; particularly, a hollow space in a bone
- a drug used in the treatment of tuberculosis

CORRESPONDENCE

Dear Sir,

It is with great reluctance that I force myself to bring forth to you the embarrassing fact that, for some years, the toilets (at least half of them, as far as I know) of our otherwise well-equipped Medical Centre are devoid of toilet paper.

I need hardly mention here that not only is this unhygienic, but oftentimes this can be a source of embarrassment and frustration. In their last campaign visit this matter has been brought forth by a fellow medical student to the proposed Internal Affairs Secretary of the Ex-Co, and the latter promised to contact the Faculty Authorities to solve the problem. Yet so far the toilets are still left in their gloomy state as ever. As far as we can guess, it is either that the Faculty Authorities are unwilling to install toilet paper in our toilets or that the Internal Affairs Secretary has not been keeping his promise and fulfilling his duty in informing the Faculty Authorities of the problem.

I do not believe that this is an unsolvable problem, if it has been seriously looked into. In these days when everyone seems to be so interested in student welfare, I think this is the most basic student welfare one should look into, since it concerns almost every medical student.

Yours etc,

Poor Medic.

Dear Sir,

Your letter to the Caduceus has been referred to me by the Correspondence Editor of the Caduceus. It is certainly gratifying to learn that graduates are still so concerned with the activities of the present student activities and publications.

The Elixir is still existing and we published two issues each year instead of three. Owing to the cost of publication, we regret that we cannot give every practitioner a free copy of it. However, at the beginning of every year, we send letters to all the doctors to invite their subscriptions to the journal and also donations to the Elixir Loan Fund. The subscription rate is only seven dollars per year.

I will be sending you a copy of the summer issue of Elixir. With your past experience in editing the journal, I hope you will not spare us your comments and suggestions.

As for the new address of Professor F. Chang in New Zealand, The Chief Editor of Caduceus will forward to you as soon as possible.

Yours sincerely,

Yim Chi Ming

Editor-in-Chief of Elixir

NEWS

In the recent few months, the Hong Kong University Students' Union Council has been considering the desirability of automatic membership for Faculty Societies or Associations and compulsory subscription. After much discussion and debate, the Council finally arrived at the following resolution: "For faculty societies which deem automatic membership with or without compulsory subscription necessary, the faculty society shall be empowered to hold a general meeting for ALL STUDENT MEMBERS of that faculty to resolve on the issue. The conduct of such meetings shall be in accordance with articles concerning general meetings laid down in the constitution of the respective faculty societies. The Engineering Departments and Architecture Department shall be considered separate faculties in this respect."

The Medical Society, H.K.U.S.U. will be launching a Blood Donation Campaign together with the HKFS. An exhibition is being planned. Much help will be needed and those interested are urged to join in such a worthwhile project. Please contact any Ex-Co Member.

(WONG SHOU PANG)

UNIVERSITY OF HONG KONG

Mrs. Emily Jorge Alvares Xavier Memorial Bursary

The University of Hong Kong is pleased to announce that Mr. Alfred V. Alvares has generously offered to donate to the University a sum to establish a bursary in memory of his mother. The bursary will cover tuition fees plus an allowance of \$500 for books and stationery and will be open to application from undergraduates at the end of their first academic term in the Architecture course. It will be awarded on the recommendation of a committee, on evidence of financial need and aptitude for architecture, while qualities of character, leadership and general interest in extra-curricular activities may also be taken into account. The award will be renewable annually for five years, subject to satisfactory progress.

LYMPHOCYTES AND ANTILYMPHOCYTIC SERUM

Grafting has long been used for the repair of injuries and recently it has been extended to the replacement of defective organs. A severe limiting factor, however, is that the body tends to reject any material that is considered as "not self". Lymphocytes play an important role in such rejection process, and in the body's reaction to certain types of infection and tumour.

Lymphocytes are certain cells found in the blood — making up about a quarter of the leucocytes — and in certain tissues of the body, notably the spleen, the thymus, lymph nodes and in the bowel wall. The majority are small lymphocytes; the remainder are subdivided rather arbitrarily into medium and large lymphocytes. Microscopically the small lymphocyte consists of a round or slightly oval nucleus containing dense chromatin surrounded by a narrow rim of cytoplasm. Electron microscopy reveals little more apart from a few mitochondria in the cytoplasm and one or more nucleoli. The large lymphocytes have relatively more cytoplasm, contain ribosomes and fairly numerous mitochondria.

Murphy in 1926 has shown, on the basis of morphological evidence and by the effect of depletion of lymphoid tissue by irradiation, that lymphocytes are concerned with the reaction to certain types of infection, to foreign tissues and to tumours. Recently it has further been shown that lymphocytes are more heterogenous in respect of their origin and function than would be suggested by their unremarkable appearance, and

that they play a key role in antibody production and cell-mediated immunological reaction. A major advance came with the discovery of Gowans in 1959 that there is a continuous circulation of lymphocytes from the blood to the lymphatics and back via the thoracic duct. To quote Gowans (57) "in the rat, for example, enough lymphocytes enter the blood from the thoracic duct to replace all those in the blood about 11 times daily". Cannulation of the thoracic duct demonstrated a huge output of lymphocytes in the first day or two, followed by a sharp fall. Lymphocytes in the blood stream thus have a high turnover rate. Burnet was led by this to the opinion that lymphocytes play an active part in immunity. Further progress in this field was made possible by radioactive isotope tagging technique and transplantation of various lymphoid tissues. The results of these diverse experiments point to the following general conclusion.

1. Lymphocytes circulate freely from one lymphoid organ to another via the blood stream.
2. The majority of small lymphocytes in the thoracic duct are recirculating cells of thymic origin with a life span of a few months or one year. Others are short lived with an origin from the marrow. The long lived cells respond to antigens by proliferating. They are responsible for the immunological memory. The short lived cells are precursors of cells which make antibody or are concerned in effector mechanisms of cellular immunity.
3. Immunological response often seems to depend on the antigen being taken up by macrophages. It is uncertain whether stimulation is mediated by processed antigen or macrophage RNA. How-

ever Gowans has recently suggested that the secondary response from reexposure to an antigen can occur without macrophages.

4. Lymphocytes may play a role in the transport of antigens.
- From the above, an agent which specifically damages lymphocytes would have interesting immunological properties. One such agent is heterospecific antilymphocytic serum (ALS) which is prepared by immuniz-

ing animals of one species with lymphocytes from another species.

In vivo administration of ALS or of antilymphocytic globulin derived from it, inhibits delayed-type hypersensitivity reactions; prevents or delays the rejection of homografts and heterografts of various kinds in experimental animals. The graft-versus-host reaction evoked in irradiated mice by allogenic spleen or bone marrow cells (i.e. cells from a donor of the

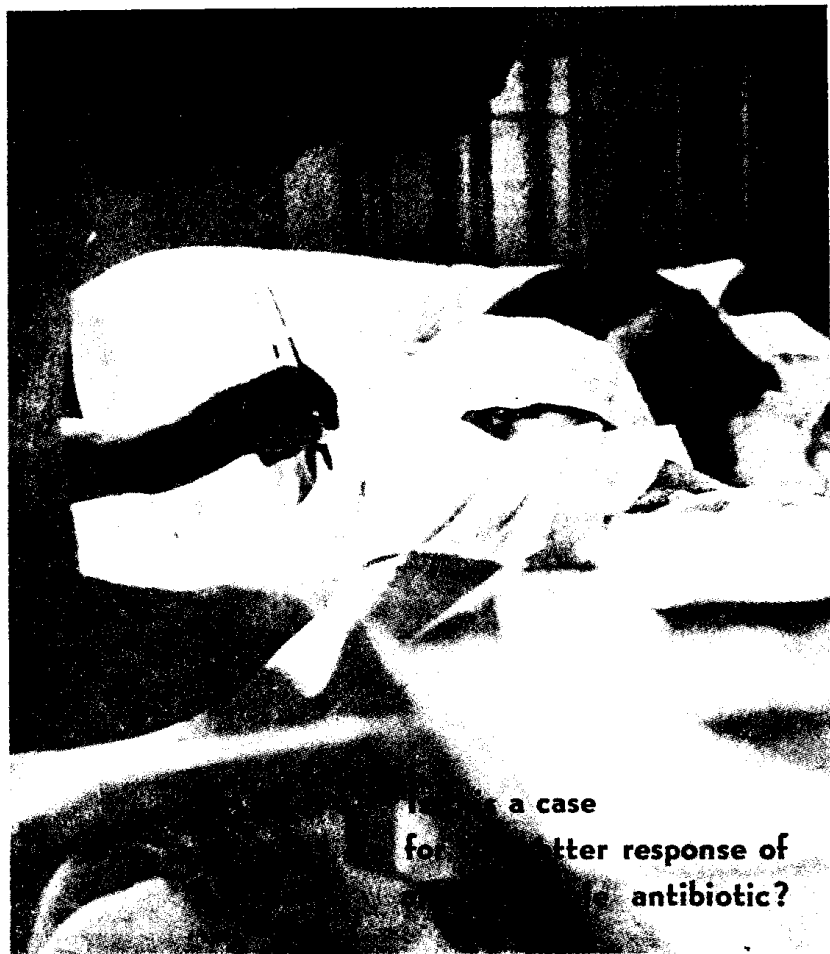
same species but different genetic constitution) may also be weakened. Pretreatment of cell donor is even more effective.

ALS has a weaker but definite inhibitory effect on antibody formation, but little effect on secondary response shown by previously immunized animals. ALS however is itself highly immunogenic, probably because lymphocytes to which it becomes attached are phagocytosed by macrophages. (To be continued on next issue)

Shortage of Blood

(Continued from Page 1)

may be enforced under law, but others are entirely voluntary. It is the recognition and practice of a voluntary social obligation which is most praise-worthy and which serves as a concrete illustration of the bright and hopeful side of man and mankind today. At a time when our society is faced with this crisis of blood shortage, at a time when the lives of thousands and the happiness of many more depend on the oversoming of the crisis, **blood donation is certainly the most honoured of such obligations.**



Is this a case for a better response of antibiotic?

To 3rd, 4th & 5th Year Students Clinico-Pathological Conferences

The programmes of the following six sessions are announced:—

January 29th	Metastatic Bone Lesions	Dept. of Orthopaedic Surgery
February 12th	Students' Session	Dept. of Medicine
February 26th	Students' Session	Dept. of Surgery
March 12th	Acute abdomen complicating Pregnancy	Dept. of Obstetrics & Gynaecology
March 26th	? Eosinophilic Granuloma	Dept. of Medicine
April 16th	? Eosinophilic Granuloma	Dept. of Surgery

N.B. The conferences will be held in the Pathology Lecture Theatre at 4.30 p.m. and all students in 4th and 5th years are required to attend.

The Department of Surgery is holding 'blind' conferences.

A 30 year old woman (18 weeks pregnant) was admitted to hospital with a urinary tract infection that presented itself as a relapse after initial oral treatment by her GP. She has pyrexia, rigors, backache and pyuria. To prevent the development of chronic pyelonephritis, treatment must be initiated as quickly as possible.

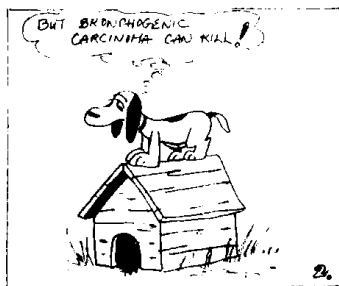
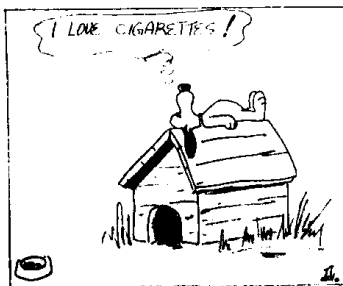
Only an injectable antibiotic penetrates quickly to the infected tissues, giving rapid, high blood levels and a better and more reliable response. Ceporan is the injectable antibiotic to use. It achieves high urine and renal tissue levels and gives a rapid kill of sensitive bacteria. It has a wide range of activity against many Gram-negative organisms—especially *E. coli* and *Proteus mirabilis*—and most Gram-positive organisms (including penicillin-resistant staphylococci).

In addition Ceporan has very low toxicity, little cross-sensitization with penicillin and is virtually painless on injection. When you need the better response of an injectable antibiotic for renal infections, you can rely on Ceporan.

Ceporan
Glaxo

Ceporan is a Glaxo trade mark

GOOD OL' SMOKY



TETRODOTOXISM

The study of poison serves three purposes. To quote Claude Bernard: "Poisons can be employed as means for the destruction of life or as agents for the treatment of the sick, but in addition to these two well recognised ones there is a third particular interest to the physiologist. For him, the poison becomes an instrument which dissociates and analyses the most delicate phenomena of living structures, and by attending carefully to their mechanism in causing death, he can learn directly much about the physiological processes of life. Such is the way in which I have long regarded the action of toxic substances."

Many sea creatures produce poisons, either for defence or to help capture food, and marine toxins include some of the most virulent known. Interest in the poison of the tetrodon fish stems partly from widespread incidence of poisoning from ingestion of the fish — for instance in Japan, puffer poisoning continued to be the greatest single cause of fatal food poisoning. The following is an extract of an original article compiled by Prof. K. K. Cheng and Dr. K.M. Li of the Physiology Dept.

CLINICAL FEATURES

The onset and symptoms vary according to the person and the amount of puffer poison ingested. Early manifestations are malaise, pallor, dizziness, circumoral paraesthesia, numbness of the tongue, and ataxia. Neurotoxic symptoms of sensory and motor disturbances are especially pronounced in mild, non-fatal cases of poisoning. In severe poisoning, hypersalivation, sweating, extreme weakness, headache, precordial pain, subnormal temperature, decreased blood pressure and a rapid weak pulse appear early, symptoms of respiratory distress, such as increased respiratory rate, shallow breathing appear and become pronounced, with central cyanosis. Finally, muscular twitchings, tremors and incoordination develop which terminate in muscular paralysis. The eyes become fixed and glossy and convulsions occur. Death results from respiratory failure and occurs within 6 hours, or within 24 hours at the latest.

OCCURRENCE AND DISTRIBUTION

All fishes containing tetrodotoxin are members of four families in the suborder Gymnodontes. They are extensively distributed throughout a broad circumglobal belt which extends approximately from latitudes 47° N to 47° S, mainly in Japan, South China, Philippines, Pacific islands, Malaysia, India and Tropical Atlantic Ocean. In Hong Kong, nine species of puffers were captured by local fishing vessels. The commonest one is *Lagocephalus lunaris* (黃肚泡) and the two most poisonous species are *Pleurananthus scleratus* (青背泡) and *Spheroides xanthopterus* (花腰泡).

Tetrodotoxin is concentrated in the fish ovary, liver, intestines and skin, while the blood and musculature generally contain relatively little poison. When tetrodon fishes enter the spawning season, the concentration of tetrodotoxin in the ovaries increases as the ovary matures and grows in size; and the concentration of toxin in the liver also increases in parallel, therefore the puffers are generally most toxic just prior to spawning. There is seasonal variation of toxicity. Moreover, different members of the same species may show different degrees of toxicity at the same season of the year.

CHEMISTRY OF TETRODOTOXIN

Tetrodotoxin is an amino perhydroquinazoline compound with a molecular formula $C_{11}H_{17}N_3O_8$ and molecular weight of 319. It is only sparingly soluble in water except in a slightly acidic condition. It is readily degraded in alkaline solution into quinazoline compounds. It has unusual groupings, viz. an abundance of OH groups, a unique hemilactal link between two

separate rings (positions 5 and 10), and a guanidinium group constituting an integral part of the molecule. Apparently, both the OH group on C₄ and the hemilactal oxygen link between C₅ and C₁₀ are essential for optimal action. (opening the latter and reducing the former, eliminates all toxicity). The guanidinium end of tetrodotoxin may be the working end of the molecule.

PHARMACOLOGICAL ACTION

Bioassay methods

1. The presence of a roughly exponential relation between the dosage and the rapidity of death of a mouse following intraperitoneal injection of tetrodotoxin.
2. The inhibitory action of tetrodotoxin on a nicotine-induced contraction of isolated guinea pig ileum.
3. The inhibitory action of tetrodotoxin on contractions of rat stomach elicited by vagal stimulation.

TOXICITY OF TETRODOTOXIN

Tetrodotoxin is one of the most potent non-protein poisons known, the intraperitoneal LD₅₀ for mice being 10 µg/Kg. Thus it is considerably more potent than Na-cyanide (LD₅₀ 10 mg/Kg), about comparable to the steroid poison batrachotoxin (LD₅₀ 2 µg/Kg), but it is much weaker than the protein poison botulinum toxin (2 pg/Kg).

Absorption of tetrodotoxin from the gastrointestinal tract is rapid. The toxin is also readily absorbed from parenteral sites. The distribution and fate of tetrodotoxin in the body is little known.

CELLULAR ACTIONS

1. Isolated nerves. Tetrodotoxin causes conduction block in nerves. (Tetrodotoxin is 160,000 times more potent than cocaine in blocking nerve conduction). Recent experiments with voltage clamp technique on giant axons from squid showed that tetrodotoxin applied to the external surface of nerve membrane abolishes action potential by causing a marked reduction or abolition of inward current through the cell membrane while the outward current remains totally unaffected. (The reduction of inward current appears to be chiefly due to a failure of Na⁺ permeability to rise, thereby inhibiting the entry of Na⁺ ions through the depolarising membrane).
2. Skeletal muscle and neuromuscular junction. The study of current-voltage relationship in the isolated frog sartorius muscle shows that treatment with tetrodotoxin considerably raises the threshold to excitation by depolarising pulse. The inhibition of spike production in the muscle indicates that tetrodotoxin has selective action on the Na⁺ permeability of muscle membrane.

At the neuromuscular junctions tetrodotoxin blocks the conduction in nerve and muscle membrane on two sides of the synapse but has no effect on the endplate receptors, viz., tetrodotoxin acts on the electrical excitable portions but not on the chemosensitive portion of the neuromuscular junction.

3. Autonomic nerves and Cardiac and smooth muscles. Tetrodotoxin has little effect on the cardiac action potentials except in high doses, and does not appear to effect the electrical activity of smooth muscle fibres of taenia coli. Tetrodotoxin blocks axonal conduction in various autonomic nerve smooth muscle preparations. However neither the capacity of the nerve to release transmitter nor the sensitivity of the muscle was impaired.

To summarise, Tetrodotoxin has specific inhibitory effect on the rise of conductance for sodium ions in excitable membranes such as nerve axon and skeletal muscle which normally follow stimulation. However it has little effect on the electrical activity of cardiac and smooth muscles.

SYSTEMIC EFFECTS

1. Neuromuscular system. Marked progressive weakening of all skeletal muscles follow tetrodotoxin administration in intact animals. This may be due to:
 1. Conduction block in motor axons and muscle membrane at the neuromuscular junction.
 2. Direct blocking action on skeletal muscle fibres. The time required for muscle block was longer than for nerve block; slow muscle is more easily blocked than fast muscles, and tonic muscles are more resistant to this blocking action.
2. Cardiovascular system. A precipitous fall of the arterial blood pressure is a striking feature in the intact animal after administration of tetrodotoxin. Peripheral vasodilatation causes this hypotension. Thus when the arterial blood pressure is falling rapidly, the heart rate and the cardiac output did not alter significantly, but the carotid and aortic blood flow decreased. In regard to the mechanism of the peripheral vasodilatation, it is most likely that tetrodotoxin blocks the sympathetic nerves supplying the blood vessels, and thereby in-

terfering with the normal vascular control.

3. Respiratory system. Clinically and experimentally, the most serious systemic effect of tetrodotoxin is respiratory depression and the cause of death in tetrodotoxin poisoning is asphyxia. However there is no general agreement as to how the respiratory failure is brought about. Some investigations showed that tetrodotoxin has a specific inhibitory action on the central respiratory centre, whilst others suggest that paralysis of respiratory nerves and muscles is important.

Recent studies show that paralysis of the respiratory muscles appear to be a dominant factor in tetrodotoxin poisoning. The respiratory muscles are apparently more vulnerable to the toxic action of tetrodotoxin than the phrenic nerve, the medullary centre, other motor nerves, or the non-respiring skeletal muscles.

4. Central nervous system. The effects on the electroencephalogram are controversial. When deposited in the cerebrospinal fluid (not intraperitoneally) the CNS visual system is depressed, vomiting, hypothermia and respiratory paralysis may occur.

TREATMENT

There is no specific antidote for puffer poisoning in man. The treatment is purely symptomatic and aimed at alleviating its pathophysiological process.

1. To remove the poison from the body as rapidly as possible. Gastric lavage and C catharsis should be instituted at the earliest possible time.
2. To counteract the respiratory depression: artificial respiration, with oxygen inhalation is the most important measure. Analeptics (Metrazol) may be used to shorten the period during which artificial respiration is required.
3. To counteract the hypotension: intravenous infusion of fluid containing adrenaline should be given.
4. If laryngeal spasm is present, tracheotomy and intubation may be necessary. The progress is good if the patient survived for more than twenty four hours.

啟思

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