DiabetesWatch

A publication of the PHILIPPINE DIABETES ASSOCIATION, INC. for the Filipino diabetic patient

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PDA Chapters Organized

Three chapters of the Philippine Diabetes Association have been organized in Davao City, Cagayan de Oro City and Zamboanga City. As initial project of the chapters, Diabetes Clinics have been set up for patient education. Physicians, nurses and dieticians underwent intensive training by members of the Diabetes Clinic of the Makati Medical Center, with the help of MedAsia, Inc.

Officers of the Chapters are:

Davao Chapter – Dr. Crisostomo Serrano, president; Dr. Pacita San Vicente, vice-president; Dr. Luisa P. Llanes-Bisnar, secretary; Dr. Portia Pantoja-Ang, treasurer. The board of directors is composed of the officers with Atty. Galileo Cabahug, Dr. Benny Te, Dr. Felix Victorio and Ms. P. Serrano.

Cagayan de Oro Chapter – Dr. Leticia Maniego-Bautista, president; Dr. Hernando Mejia, vice-president; Dr. Wilhelmina Galupo, secretary; Dr. Bernardita Dy, treasurer. The Board of directors include Dr. Amado Piit, Dr. Chen Saranglao, Ms. Beverly Beja, and Mr. Rory Rodriguez.

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HUMAN INSULINS .....

.... are they really human?

To a diabetic, insulin is almost synonymous to survival. Since its discovery, insulin has dramatically increased the life expectancy of the diabetic patient.

The earliest preparations of insulin used in the treatment of Diabetes Mellitus were obtained from pancreases of cows (bovine insulin) and pigs (porcine insulin). Human insulin and its therapeutic use became available for extensive testing only in the last few years.

Several methods have now been developed for producing human insulin. Truly, human insulin is only produced by the human pancreas. This could be insulin secreted by the pancreas endogenously or it could be insulin extracted from cadaveric pancreases or from cultured beta cells of the islets of the human pancreas. Other "human" insulins are only human in the sense of having the amino acid sequence and tertiary structure of the natural human insulin.

In order to understand how "human" insulins are produced, let us first look at the amino acid composition of the natural human insulin and then compare this with the amino acid composition of pork and beef insulins. (Figure 1).

Human insulin has *threonine* as the terminal or last amino acid of the B chain (B 30). Pork insulin differs from human insulin in that it has *alanine* as the terminal amino acid of the B chain.

Beef insulin differs from human insulin by 3 amino acids: *Alanine* at the B30 position of the B chain, *alanine* at the A8 and *valine* at A10 positions of the A chain. Of the two animal insulins therefore, pork insulin is the closest to the naturally occuring human insulin.

The question was then asked: If threonine can be substituted for alanine in the B chain of porcine insulin, would the resulting insulin then be identical to human insulin?

Dr. Markussen and his group at the Novo Research Institute reported on a single-step enzyme mediated reaction (called transpeptidation) that successfully replaced the alanine amino acid of pork insulin with threonine, thus converting porcine insulin to human insulin (Figure 2). This process permitted the production of large quantities of human insulin which were subjected to the same purification procedures as the monocomponent insulins. Further characterization showed that this insulin was identical to the natural human

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	A-chain		B-chain
	A8	A10	B30
Bovine	Alanine	Valine	Alanine
Porcine	Threonine	Isoleucine	Alanine
Human	Threonine	Isoleucine	Threonine

Figure 1. Differences between insulins from three species

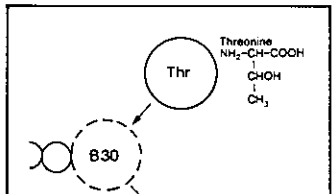

Fig. 2 Conversion of porcine insulin to human insulin.

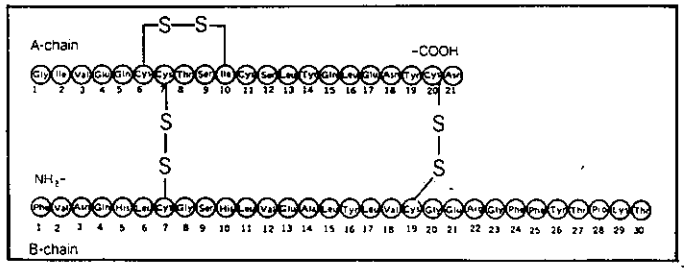

Figure 3. The molecular structure of insulin

DIABETES & HYPERTENSION
— another devastating duo

Diabetes Mellitus and high blood pressure (hypertension) are currently recognized as the two leading risk factors in predicting possible deaths from diseases of the heart and big blood vessels. If we find them in the same patient, the risk is compounded. Diabetes Mellitus results in processes that destroy big blood vessels leading to heart attacks, strokes, leg gangrene and heart failure. It also affects the smallest blood vessels resulting in kidney failure and blindness. All the processes leading to these deadly complications are accelerated if hypertension is present in a diabetic patient. Therefore, the coexistence of hypertension in a diabetic is an alarm that cannot be taken for granted, because it affects the overall longevity and the health status of the patient.

What is Hypertension?

The definition of hypertension is an arbitrary one. For most purposes a blood pressure level of 140/90 mm Hg or higher represents a point above which risk begins at a significant rate. However there are causes of "false" hypertension which must be known by physicians and patients in order not to make a wrong diagnosis. Some of them are faulty instruments, narrow cuff for obese patients, pain, acute pyschologic stress and ingestion of drugs that can elevate blood pressure like cold medicines. There are 3 main types of hypertension found in diabetic patients:

1. Diabetes with nerve disturbance (neuropathy)
2. Diabetes without kidney disease
3. Diabetes with kidney disease (nephropathy)

The hypertension of the first type usually occurs when the patient is in the supine or lying position. Characteristically, upon assumption of upright position, the blood pressure goes down to low levels causing dizziness. This hypertension is the most difficult to treat. Elastic support stockings during the day and 8-10 inch blocks under the head of the bed at night may minimize the drop in blood prssure in the morning. Some drugs can be prescribed which may only alleviate the problem. Hypertension of the second type results from factors similar to those in non-diabetics. It is a result of hardening of the arteries. It usually occurs in non-insulin dependent diabetics who are over 50 years old. Since the mechanisms involved are the same as in non-diabetics the guidelines for treatment are also similar. However, because of the additional harmful effects of hypertension on the blood vessels super-imposed upon the diabetes, hypertension in the diabetic should be treated earlier and more aggressively. Hypertensive diabetics should be treated with the goal of reducing the standard blood pressure to as close to 120/80 mm Hg as possible. It is advisable to have the blood pressure recorded at home by the patient's family and the record to be brought to the physician during consultations for evaluation. It should be known that high blood pressure is a disease for which there is no cure except in a very small percentage of cases, that once therapy is begun, even if blood pressure is controlled, therapy must be continued; that hypertension wrecks havoc on the heart, blood vessels and kidneys but these complications can be generally prevented or delayed by adequate therapy, and that a long and useful life can be led if a specific treatment program is followed. Hypertension of the 3rd type occurs eventually in more than 50% of persons with onset of diabetes early in life. However it remains a major problem even in diabetics with the onset of their disease following the age of 40. This type of hypertension universally accompanies diabetes with kidney disease (diabetic nephropathy) and is related to diabetes as to origin, and therefore is called a true "diabetic hypertension." Spillage of protein in the urine (proteinuria) is the classic early sign of impaired kidney function in diabetic kidney disease. This is why a urine test for protein should be undertaken regularly. With the development of kidney disease, the blood pressure rises to abnormal levels. Severity of the hypertension appears to parallel the severity of the underlying diabetic kidney disease. A vicious cycle ensues in which the kidney vessel lesion worsens as hypertension develops and then blood pressure rises further as vessel lesions worsen. In the earliest stage of diabetic kidney disease, control of high blood pressure is one of the primary considerations. Studies have shown that a previously inevitable decline in renal function tests with time can be slowed down by reducing blood pressure to below 140/90 mm Hg. Further benefits of normalizing blood pressure include retarding progression of eye lesions which cause blindness and delaying deterioration of heart function. As the urinary protein wasting increases, closer follow-up with modification of treatment modality should be instituted. Measurement of 24 hours urinary protein and clearance of creatinine in the blood should be done periodically. An increase in urinary protein to more than 0.5 to 2 g/24 hours and a decrease in clearance of creatinine to 30-90 ml/min signals progression of the disease. This time more

assidious control of blood pressure is desired, and dietary salt intake should be restricted especially if the patient shows signs of swelling. If there is too much swelling, a medicine to promote water and salt excretion might be needed. Protein in the diet should compensate for losses in the kidney. The ultimate effect of diabetic kidney disease is impedance of the excretion of products of protein metabolism. This is reflected by the rise in serum creatinine and blood urea nitrogen. There is progression of proteinuria with a marked diminution in creatinine clearance to less than 5 ml/minute. At this point, signs and symptoms of kidney insufficiency, are flagrant and vision can be affected. The diabetic who faces an inexorable disease should have a good relationship with his physician based on truthful interpretation of facts. A thorough understanding of the stage of illness and long term plan should be sought. A reaction of shock, anger and disbelief and panic may occur, but only if the patient hasn't been told beforehand of these possible consequences. Because of the recent progress in diabetes education, patients are now more prepared and are able to accept a difficult turn in a complicated illness. In this setting, the need for dialysis is presented to the patient and also the possibility of a renal transplant. This stage which is called uremia is not synonymous with the last stage of the disease. Survival for 5 years or longer is not uncommon. Vision can be preserved by laser therapy. Control of hypertension and high blood sugar will further extend useful life for many of today's patients. But hopefully now, armed with this knowledge about hypertension in diabetics, we maybe able to reduce the incidence of kidney failure in the next generation of diabetics. **(M.O.-S.)** ■

Fact or fantasy?

DIABETIC PATIENTS CAN EAT FRUITS IN ANY QUANTITY

"I am a diabetic so I avoid rice. I eat plenty of fruits instead." This is a very common remark from diabetic individuals. How correct is this practice?

When diabetes was first discovered, diets prescribed then were severely restricted if not totally devoid of carbohydrate foods. As more information about the disease was known, the low carbohydrate diet was found to be inappropriate. Severely decreasing carbohydrates increased the total fat content of the diet, and consequently, increasing incidences of cardiovascular complications were noted. Researches were done and it was proven that increasing the carbohydrate content of the diet has no adverse effect on diabetes control provided it is given in "complex form".

What is a "complex form" of carbohydrate? When a food is made up of many simple units of sugar linked together by bonds, this is considered as "complex." Because there are many linkages for the digestive enzymes to act upon in order to yield the end-product which is glucose, therefore glucose is not as quickly released into the circulation. Examples of this form of carbohydrate are corn, rice, tubers, cereals, and others. If the food item is only made up of two sugar units linked together by a single bond, then it is easily digested to yield glucose. Fruits are examples of the type of carbohydrate with only two simple units of sugar. Hence, fruits are also called "simple carbohydrates." A simple blood sugar test thirty minutes after eating fruits will show the effect it has on the individual. Of course, certain types of fruits will cause higher blood sugar rises in an individual; this is due to the person's glycemic response to the said items. Contrary to common belief, therefore, it definitely is not "safe" for the diabetic invididual to indulge in fruits.

Note that fruits, however, should not exceed about 15% of the total carbohydrate content of the diet (approximately about 3 measures of fruit daily based on the average Filipino diet). The total carbohydrate content of the more common fruits are shown in the table.

As shown in the table, just one serving of fruit already gives a substantial amount of carbohydrate. If

FRUIT	WEIGHT (gms)	APPROXIMATE SERVING SIZE	CARBOHY-DRATES (gms)	FIBER CONTENT
atis	50	1 small	12	0.65
guava, red	35	1 medium	8	1.7
kalmito, green	60	1medium	9	0.4
dalanghita, ladu	70	1 medium	6	0.07
durian	30	1/8 of a medium pc	11	0.6
guayabano	70	1 halfmoon slice	11	0.4
lanzones	75	7-10 pieces	11	0.6
mangga, ripe, kalabaw	60	1 medium slice	10	0.2
pakwan	155	1 cup cubed	11	0.8
papaya, ripe	90	3/4 cup balls	11	0.6
lakatan banana	40	1 small	12	0.3
chico	55	1 medium	14	1.6
suha	60	2 segments	7	0.3
pineapple	75	1/2 cup cubed	10	0.3
tiesa	30	1/2 medium	12	2.25

This is not to say that rice can be eaten without control and fruits are to be avoided totally. Everything has to be taken within the prescribed diet. after reading this article you still believe you should give up your rice intake and indulge in fruits instead, please THINK AGAIN! **(M.I.Q.-C.)** ■

Human insulins . . .
(From page 1)

insulin in terms of amino acid sequencing, conformation and state of aggregation. Thus the birth of Novo's "Semi-synthetic Human Insulins." Examples of human insulins produced by this process are: Monotard HM, Actrapid HM, Protaphane HM, Actraphane HM, and Ultratard HM.

Another method of producing human insulin is the so called bio-synthetic method using recombinant DNA techniques. Again looking at the structure of human insulin, we see that it is composed of two chains, the A and the B chains, joined to each other by disulfide bridges at some point in the molecular structure (Figure 3.)

Synthetic genes which code for the amino acid sequence of the A chain and B chain of human insulin are inserted into bacteria *(E coli).* The resultant but separate peptide chains are subsequently combined in the laboratory to form human insulins. (Figure 4.) Examples of human insulin obtained using recombinant DNA techniques are: Humulin N and Humulin R.

There are advantages in using human insulin among selected diabetic patients at particular times. These are:

1. Patients experiencing generalized or localized allergic reactions at injection sites (swelling, redness or itching).
2. Patients who are prone to developing lumps or depressed areas at injection sites (lipodystrophy).
3. Pregnant diabetic patients. (To decrease antibody formation and to lower circulating immune complexes which can affect the pancreas of the fetus).
4. Diabetic patients who need short term or temporary insulin therapy while under stress (surgery, illness, pregnancy).
5. Brittle diabetics who will benefit from appropriate insulin dosage as a result of accurate measurement of insulin levels (without interference of insulin antibodies or immune complexes).
6. Recently diagnosed insulin requiring diabetics with the aim of minimizing long term complications associated with the disease. — L.L.-A. ■

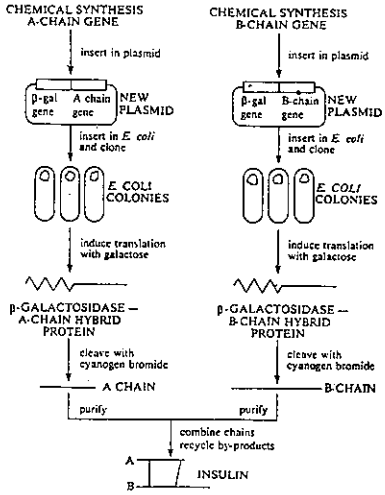

Fig. 4. The preparation of biosynthetic human insulin via separate A and B chains.

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A publication of the PHILIPPINE DIABETES ASSOCIATION, INC. with offices at Room SA 301, Lung Center of the Philippines Elliptical Road, Quezon City

President:
Dr. Augusto D. Litonjua
Vice-President:
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contributors to this issue:
Ms. Ma. Imelda Q. Cardino
Dr. Lina Lantion-Ang
Dr. May Ortiz-Sison

circulation:
Ms. Sue Ambrosio