

**College of Pharmacy/University of Baghdad .Clinical Pharmacy Dept.
Fourth year. Pharmacy Practice Workshop. 2014-2015.
(Endocrine System: Drugs used in Diabetes)**

Rx1

Mr. A. was recently diagnosed as having **type 1 diabetes mellitus** and entered the hospital in which he was stabilized on 30 unit insulin daily.

Q1-What are the available **types of insulins**? See supplement A

What are the **advantages of the human insulin analogues** (insulin **aspart**, insulin **glulisine**, and insulin **lispro**) over soluble insulin (with respect to **risk of hypoglycemia**, and **time of administration** relative to meal?)

Q2-How can this insulin dose (i.e. the 30 unit daily) be **administered** in a way to mimic the physiologic release of insulin from pancreas? And what is the **idea behind each method**?
See supplement **B**

Q3-What are the usual **body sites for S.C injection of insulin**? And how we can minimize the fat **hypertrophy** that may occurs at the injection's sites?

Q4-How should the patient be instructed about?

A-**Agitation** of insulin that present as suspension? See supplement C

B-**Withdrawal** of insulin dose from the vial? See supplement C

C-**Mixing** of short acting insulin (S.I.A) and other types of insulin in the same syringe? See supplement C and D.

D-**Storage** and stability of insulin? See supplement E

Q5- You noticed that the patient use the insulin syringe for one injection only and then discarding it!!! Is this true practice? See supplement F

Q6- If the patient has a problem in withdrawing the correct no. of unit of insulin due to limited vision!!!! What option available for such problem? See supplement G?

<p style="text-align: center;">2</p> <p style="text-align: center;">الدكتور ليث باقر اسم المريض: فاتن علي العمر: ٣٣ سنة</p> <p>Rx Glibenclamide(Daonil®)5mg tab. 1 tab. Daily. Pioglitazone (Actos®) 15mg tab. 1 tab. daily</p> <p>Q7-To which type of oral antidiabetic drug glibenclamide belong? At what time of day it is usually given? And how it may be taken with regard to food? []</p> <p>Q8-What is the max. dose of Glibenclamide? [] Does hypoglycemia occurs with it? []</p> <p>Q9-Can we use glibenclamide during Pregnancy? []</p> <p>Q10-If the patient develops mild renal impairment, would the switching to tolbutamide (or gliclazide) represent a right option? []</p> <p>Q11- To which type of oral antidiabetic drug Pioglitazone belong? How it may be taken with regard to food? (See supp.H) What are the main side effects of it ?</p>	<p style="text-align: center;">3</p> <p style="text-align: center;">الدكتور فاهم احمد اسم المريض: قيس جعفر العمر: ٤٤ سنة</p> <p>Rx Metformin (Glucophage®) 500mg tab. 1 tab daily. Carbamazepine 200mg tab. 1 tab at night Domperidone 10 mg tab. 1 tab t.i.d before meal. Fludrocortisone 100 mcg tablet 1 tab. daily</p> <p>NOTE: the patient is overweight</p> <p>Q12-Is metformin preferred in Overweight patient? []How we can increase the dose until we reach 500mg T.i.d.? [] how it is usually taken with regard to food? []</p> <p>Q13-what are the initial common Side effects of it? []does Hypoglycemia Occurs with it? []</p> <p>Q14-What do you recommend if the patient develop significant renal impairment? Why? [] can we use iodine-containing X-ray contrast media safely in patient taking metformin?(see the C/I) []</p> <p>Q15-what is the idea behind the use of Carbamazepine, Fludrocortisone and Domperidone for diabetic patients? Hint: see section 6.1.5 under diabetic neuropathy?</p> <p>Q16-What are the benefits obtained from metformin's use in the management of polycystic ovary syndrome (PCOS)? []</p>	<p style="text-align: center;">٤</p> <p style="text-align: center;">الدكتور نوفل ياسين اسم المريض: رشيد جمعة العمر: ٦٦ سنة</p> <p>Rx Gliclazide (Diamicon®) 80mg tab. 1 tab daily Acarbose (Glucobay®) 50mg tab. 1 tab. T.i.d</p> <p>Q17-whay Gliclazide is preferred over Glibenclamide in elderly patient? [] At what time of day this dose is given? And how it is usually taken with regard to food? []</p> <p>Q18-- To which type of oral antidiabetic drug Acarbose Belong? And how it may be Taken with regard to food? []</p> <p>Q19- what are the common Side effects of Acarbose? []Can we use Antacid to Treat it? []</p> <p>Q20-how should hypoglycemia be treated in patient taking insulin or Sulphonylureas as well as Acarbose? []</p>
<p style="text-align: center;">٥</p> <p style="text-align: center;">الدكتور ياسر حامد اسم المريض: سوسن طه العمر: ٤٠ سنة</p> <p>Rx Repaglinide(Novonorm®): 0. 5 mg tab. 1 tab within 30 minutes before main meals.</p>	<p>Q21-What is the onset and duration of Repaglinide(and Nateglinide (Starlix®))?and how it is usually taken with regard to meal? []</p> <p>Q22-what instruction should be given to the patient if she skip a meal (or add an extra meal)? (supp.I)</p>	

<p>الدكتور سعد احمد اسم المريض: قيس هاشم العمر: ٤٤ سنة</p> <p>Rx Glucophage® 500mg tab.: 1 tab t.i.d Exenatide(Byetta®) prefilled pen 5 Mcg/dose: : one S.c inj. B.i.d</p>	<p>Q28-What is Exenatide (and liraglutide)? what are the Indications for it and how it is given with regard to meal? Is it beneficial in overweight patients? []</p> <p>Q29-What should we told the Patients or their carers about recognition of signs and symptoms of pancreatitis? []</p>
<p>الدكتور حمدان باسم اسم المريض تماضر علي العمر: ٥٠ سنة</p> <p>Rx Glucophage® 500mg tab.: 1 tab t.i.d Sitagliptin (Januvia®) 100 mg tab : 1 tab daily</p>	<p>Q30-What is sitagliptin (and vildagliptin or Saxagliptan)? What are the indications for it? []</p> <p>Q31-What other agents approved for diabetes?) (supp.J)</p>

(Supplement)

A-Types of insulins (الأرقام ليست للحفظ)

Note: the onset, peak, and duration of insulin may vary considerably between patient and in the same patient from time to time (e.g. by exercise ..._)

(كما ان الارقام قد تختلف من مصدر الى اخر لذلك فان هذه الارقام تعطي فكرة عامة عن كل نوع)

TABLE 19-3 Pharmacokinetics of Various Insulins Administered Subcutaneously					
Type of Insulin	Onset	Peak (hours)	Duration (hours)	Maximum Duration (hours)	Appearance
Rapid-acting					
Aspart	15–30 min	1–2	3–5	5–6	Clear
Lispro	15–30 min	1–2	3–4	4–6	Clear
Glulisine	15–30 min	1–2	3–4	5–6	Clear
Short-acting					
Regular	30–60 min	2–3	3–6	6–8	Clear
Intermediate-acting					
NPH	2–4 hours	4–6	8–12	14–18	Cloudy
Long-acting					
Detemir	2 hours	6–9	14–24	24	Clear
Glargine	4–5 hours	–	22–24	24	Clear

NPH, neutral protamine Hagedorn.

Note: there is also **Premixed Insulin mixture** (Biphasic insulin):

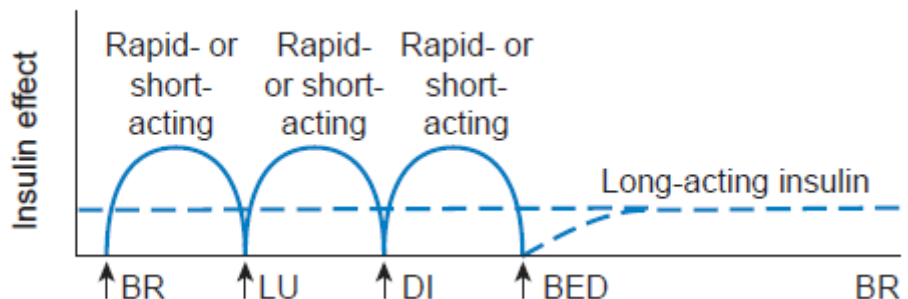
e.g.: (soluble/ NPH) -----the trade name is Mixtard®----- this formulation provides the rapid onset of regular with the longer duration of NPH⁽³⁾ e.g.:

Mixtard® 10: contain (10%soluble/ 90%NPH) and so on Mixtard® 20, Mixtard® 30, Mixtard® 50,and so on

B -Examples of insulin dosing regimen:

1-Basal-bolus insulin regimens: The regimen that most closely mimics physiological insulin release besides the use of an insulin pump, is the use of a once-daily basal insulin such as insulin glargine or insulin detemir to provide basal insulin levels throughout the day, along with doses of a rapid-acting insulin (preferred) or regular insulin before meals ⁽¹⁾. (The long-acting insulin given at bedtime, but it can be given alternatively in the morning) ⁽¹⁾.

Approximately 50% of the total daily insulin dose should be basal insulin and 50% bolus insulin, divided into doses before meals ⁽²⁾



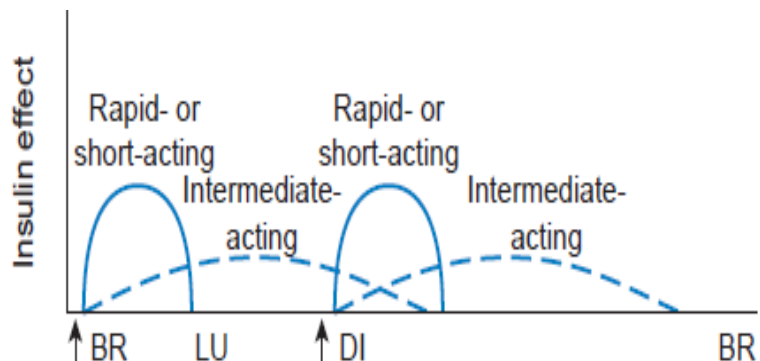
2-Twice-daily regimens.

Two thirds of the dose is given in the morning and one third in the evening. Intermediate-acting insulin (eg, NPH) should comprise two thirds of the morning dose and one half of the evening dose ⁽²⁾.

Before breakfast	Before lunch	Before dinner	bedtime
2/3 of the total daily dose (2/3 as I .A.I And 1/3 as rapid or S.A.I)		1/3 of the total daily dose (1/2 as I .A.I And 1/2 as rapid or S.A.I)	

S.A.I: short acting insulin I .A.I: intermediate acting insulin

This assumes that the morning I .A.I provides basal insulin for the day and covers the midday meal, the morning regular insulin covers breakfast, the evening intermediate I .A.I gives basal insulin for the rest of the day, and the evening regular insulin covers the evening meal ⁽²⁾.



NPH is an I .A.I and has a peak effect. When NPH is injected in the morning, the patient must eat lunch on time because of this peak effect; otherwise he or she will experience hypoglycemia ⁽⁷⁾.

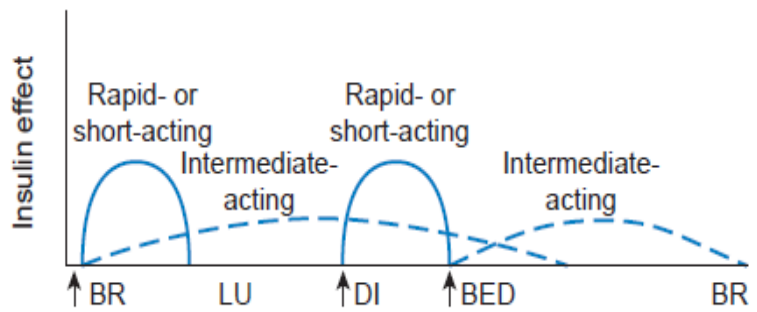
أي إن المريض ملزم بتناول وجبة الغداء لان جرعة الإنسولين الخاصة بها مأخوذة سلفا في الصباح...وبخلافه يحصل هبوط في السكر...أي إن هذا النظام Less flexible than **Basal/Bolus** regimen

Also, when NPH is taken with mealtime insulin before dinner, the patient is at risk for nocturnal hypoglycemia from the peak effect of the evening dose of NPH ⁽⁷⁾.

If the fasting glucose in the morning is too high or hypoglycemia occurs in the early hours of sleep, the evening NPH dose may be moved to bedtime (now three total injections per day)⁽²⁾.

Before breakfast	Before lunch	Before dinner	bedtime
2/3 of the total daily dose (2/3 as I .A.I And 1/3 as rapid or S.A.I)		1/6 of the total daily dose given as rapid or S.A.I	1/6 of the total daily dose given as I . A . I

This shifts the time of peak effect from approximately 2 to 3 am to approximately 7 am. By administering NPH at bedtime, nocturnal hypoglycemia is reduced, and peak insulin activity occurs when the patient is more likely to be awake and ingesting food⁽¹⁾.



C-

طريقة سحب الانسولين وطريقة رج الخابيط وطريقة خبط الانسولين الصافي (soluble) مع الخابيط (suspension):

- 1- يمسح غطاء الـ vial بقطعة من القطن المحتوية على الكحول.
- 2- قبل الاستعمال قم بتدوير الانسولين الخابيط بين راحتي اليدين (مع تجنب الرج).
- 3- اسحب بسرنجة الانسولين كمية من الهواء تساوي في حجمها حجم جرعة الانسولين الخابيط واحقنها في vial الخابيط ثم اسحب بسرنجة الانسولين كمية من الهواء تساوي في حجمها حجم جرعة الانسولين الصافي واحقنها في vial الصافي (Soluble).
- 4- اقلب vial الصافي واسحب الجرعة المقررة منه اولا ثم اقلب vial الخابيط واسحب الجرعة المقررة منه (حتى لا يختلط الصافي بالخابيط).

The vial should be **rolled between the palms of the hands** to minimize foaming. Agitation is only required for insulin suspensions.

D-Mixing of insulins: للاطلاع

Regular Insulin may be mixed with NPH in any proportion and the resultant mixture is stable for at least 1 month at room temperature without change in the kinetic property of the regular⁽³⁾.

Mixture	Proportion	Stability
Lispro + NPH	Any	Prepare mixture and inject immediately
Aspart + NPH	Any	Prepare mixture and inject immediately
Glulisine + NPH	Any	Prepare mixture and inject immediately
Regular + NPH	Any	May be premixed into syringe, to be stored under refrigeration up to 7 days

E -Storage of insulin:

The pharmacists can advice the patient that:

A-Any unopened insulins are stored refrigerated (2-8 C⁰) (**But not in the freezer**) and the expiration date printed on the vials is used for **unopened, refrigerated insulins** ⁽²⁾

B-Insulin's vial that are **currently in use** is kept **at room temperature** (injection of cold insulin is uncomfortable) and can be used for **1 month** ^(1, 3)

وهذا بخلاف المفهوم الخاطئ والشائع عند الناس من ان الانسولين يتلف بمجرد وجوده خارج الثلاجة ولو ليوم او يومين اولبضع ساعات احيانا وهو خلاف المنصوص عليه كما في المصادر اعلاه بل وحتى في نشرة الانسولين .

F-The American Diabetes Association (ADA): does not encourage syringe reuse.

patients who do reuse syringes should discard syringes if they are dull, bent, or have come in contact with surfaces other than the skin.

They do not recommend refrigerating the syringe or wiping the needle with alcohol between uses but only recapping ⁽¹⁾.

G-many Insulin dosage may be prefilled in glass or plastic syringe and remain stable for 1 week refrigerated and this is safe way of ensuring proper dosage for patients with limited vision or who have problem with withdrawing up insulin⁽⁶⁾.

H-Pioglitazone may be taken **without regard** to meals.

I-instruct the patient who **skip a meal** (or **add an extra meal**) to skip (or add) a dose for that meal ⁽⁴⁾

J-

1-Bromocriptine mesylate, an ergot derivative, is a dopamine-2 receptor agonist. It was FDA approved in May 2009 for use in type 2 diabetes. The mechanism by which bromocriptine improves glycemic control is not known. GI side effects such as nausea.

2-Sodium glucose cotransporter 2(SGLT-2) Inhibitors. e.g are canagliflozin, and dapagliflozin. They act as inhibitors of sodium glucose transporters, which lead reduces resorption of glucose in the kidney , resulting in increased urinary glucose excretion, a unique mechanism of action ⁽⁸⁾.

3-Colesevelam: In January 2008, the FDA approved a new indication for colesevelam , a bile acid sequestrant, to be used as add-on therapy in type 2 diabetes.The mechanism by which colesevelam reduces glucose is not known.

References

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