

## Chapter 15

# Ketones and Acidosis

### CAUSES OF KETONES AND ACIDOSIS

One “emergency” in diabetes, low blood sugar (hypoglycemia), was discussed in Chapter 6. The other emergency is the build-up of ketones in the blood or urine, which can develop into acidosis. Acidosis is most common with type 1 diabetes, but it can also occur with type 2 diabetes. The measurement of urine or blood ketones is very easy and was discussed in Chapter 5.

*When people are referred to our Center, the most common knowledge deficits are:*

- ✓ the dangers/meaning of ketone build-up
- ✓ when to test for ketones
- ✓ not having the supplies in their home to test for ketones
- ✓ not knowing what to do when ketones are present

These deficits can result in a serious episode of acidosis.

“Large” urine or blood ketones are usually present for at least four hours before the total body’s acidity is increased (acidosis or DKA). Acidosis is very dangerous and people can go into a coma or die from it. It is the cause of 85 percent of hospitalizations of children with known diabetes. The good news is that it is 98 percent preventable if people follow the instructions in this chapter. **Acidosis can be prevented in a person who is known to have diabetes.**

Ketones and acidosis are due to not enough insulin being available to meet the body’s needs.

*The five main causes are:*

1. **Illnesses/infections:** extra energy may be needed by the body. This cannot be made unless extra insulin is available

### TOPIC:

## Prevent, Detect and Treat Acute Complications (Ketones and Acidosis)

### TEACHING OBJECTIVES:

1. Describe causes of ketone production.
2. Present signs and symptoms of having ketones.
3. Discuss treatment plan for preventing or eliminating ketones.

### LEARNING OBJECTIVES:

Learner (parents, child, relative or self) will be able to:

1. List two causes of ketones.
2. Describe two symptoms of having ketones.
3. Explain two methods to prevent or eliminate ketones.

## Table 1 Main Causes of Acidosis

- 🐾 Infection
- 🐾 Missed insulin injections
- 🐾 Not enough insulin
- 🐾 Traumatic stress on the body (particularly type 2 diabetes)
- 🐾 A pump insertion coming out or not functioning (Chapter 26)

to make the extra energy from sugar.

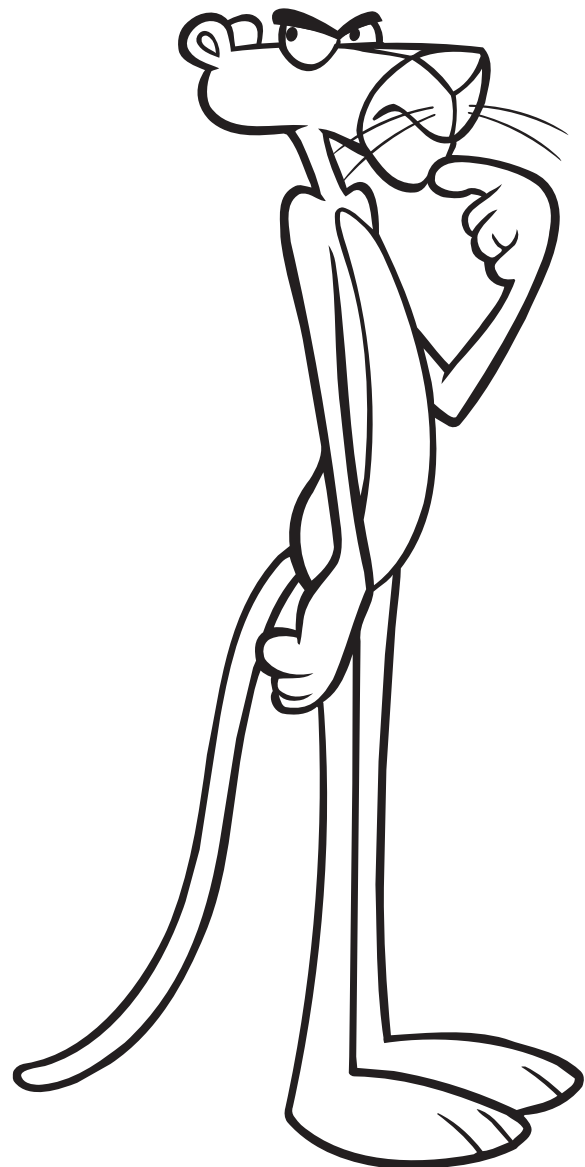
2. *Forgetting to take an insulin shot:* insulin is not available to the body.
3. *A lack of insulin (see Table 1):* this could happen in a person coming out of the “honeymoon” period who has not had insulin dosages increased.
4. *Traumatic stresses on the body (particularly with type 2 diabetes):* people with type 2 diabetes sometimes get ketones during an illness. However, other body stressors such as surgery or a heart attack may result in ketone production.
5. *A pump insertion coming out or not functioning (Chapter 26):* As pumps use rapid-acting insulins, there will be no further insulin activity 3-4 hours after an insertion malfunctions.

Remember the statement from Chapter 2:

**I MUST TAKE MY INSULIN/ORAL MEDICATION EVERY DAY FROM NOW ON. IF I FORGET MY INSULIN/ORAL MEDICATION, MY DIABETES WILL GET OUT OF CONTROL. THERE IS ABSOLUTELY NO WAY I WILL NOT NEED INSULIN/ORAL MEDICATION EVERY DAY FROM NOW ON.**

## Table 2 Main Functions of Insulin

- 🐾 To allow sugar to pass into cells where it can be used for energy
- 🐾 To turn off excess production of sugar in the liver
- 🐾 To turn off fat breakdown



*Insulin is needed to (see Table 2):*

1. allow sugar to pass into cells
2. turn off the body's machinery for making sugar
3. turn off fat breakdown in order to stop ketone production

The blood sugar is usually high with large ketones and acidosis because the second and third functions of insulin are not happening. This is because not enough insulin is available. The stress hormones are also high with illnesses/infections. These hormones act to increase blood sugar and ketone production. The high blood sugar causes sugar to pass into the urine (see Chapter 2) and the person must go to the bathroom a lot (**frequent urination**). The body may lose too much water and become too dry (**dehydration**). The tongue may feel dry and furry. Drinking lots of fluids may help prevent this. The main treatment, however, is taking extra insulin to shut off the body's machinery for making sugar and ketones.

It is not high blood sugar that causes ketones or acidosis. In fact, eating sugar does not cause acidosis. Ketones come from the breakdown of body fat (see picture at the end of this chapter). The third role of insulin (see Table 2) is to shut off fat breakdown. Fat begins to break down because not enough insulin is available and stress hormones are high. The side-product of fat breakdown is ketone production. Ketones are initially passed into the urine (ketonuria). They may start with trace or small levels and gradually build up to moderate and large levels. They also gradually build up in the blood. Once they reach the large level, they may start to build up in the body tissues. They are easier to reverse if treated early. The longer someone has large ketones, the more likely they will build up in the body resulting in acidosis (DKA). Thus, the early detection and reversal by giving extra insulin is critical.

There are several reasons why fat is broken down:

- Not enough insulin is available to help the cells burn the needed sugar.
- The body needs more energy (e.g., for illness/infections) and the fat is broken down to provide this energy.
- The stress hormones; steroids, adrenaline (epinephrine) and glucagon have been released, causing fat breakdown.
- Sugar is not available due to vomiting or not eating and fat is broken down for the energy needed. Anytime fat is broken down for energy, ketones are formed.

## SYMPTOMS OF ACIDOSIS

In any of the above cases, fat is broken down. The ketones are made from the fat. *Acidosis usually comes on slowly, over several hours, and has the following symptoms:*

- ✓ Upset stomach and/or stomach pain
- ✓ Vomiting
- ✓ Sweet (fruity) odor to the breath
- ✓ Thirst and frequent urination (if the blood sugar is high)
- ✓ Dry mouth
- ✓ Drowsiness
- ✓ Deep breathing (indicates need to go to emergency room)
- ✓ If not treated, coma (loss of consciousness)

On occasion, it may be difficult to know if a person is having difficulty with low blood sugar or with acidosis. Testing the blood sugar and ketones will help identify the correct problem. Table 3 may also be helpful in thinking about the two problems.

**Table 3**  
**The Two Emergencies of Diabetes**

Low Blood Sugar (Chapter 6) (Hypoglycemia or Insulin Reaction)	Ketoacidosis (Chapter 15) (Acidosis or DKA)
<b>Due to:</b> Low blood sugar	Presence of ketones
<b>Time of onset:</b> Fast – within seconds	Slow – in hours or days
<b>Causes:</b> Too little food Too much insulin Too much exercise without food Missing or being late for meals/snacks Excitement in young children	Too little insulin Not giving insulin Infections/Illness Traumatic body stress Pump insertions malfunctioning
<b>Blood sugar:</b> Low (below 60 mg/dl or 3.3 mmol/L)	Usually high (over 240 mg/dl or 13.3 mmol/L)
<b>Ketones:</b> Usually none in the urine or blood	Usually moderate/large in the urine or blood ketones over 0.6 mmol/L.
<b>Mild:</b> <b>SYMPTOMS</b> Hunger, shaky, sweaty, nervous	<b>SYMPTOMS</b> Thirst, frequent urination, sweet breath, small or moderate urine ketones or blood ketones less than 1.0 mmol/L.
<b>Moderate:</b> Headache, unexpected behavior changes, impaired or double vision, confusion, drowsiness, weakness or difficulty talking.	<b>TREATMENT</b> Give lots of fluids and Humalog/NovoLog/Apidra or Regular insulin every two or three hours.
<b>Severe:</b> Loss of consciousness or seizures.	Continued contact with healthcare provider. Give lots of fluids. Give Humalog/NovoLog/Apidra or Regular insulin every two or three hours. Give Phenergan medication (suppository or topical cream) if vomiting occurs.
<b>Severe:</b> Give glucagon into muscle or fat. Test blood sugar. If no response, call paramedic (911) or go to E.R.	Labored deep breathing, extreme weakness, confusion and eventually unconsciousness (coma): large urine ketones or blood ketones above 3.0 mmol/L.  <b>Go to the emergency room.</b> May need intravenous fluids and insulin.

## PREVENTION OF ACIDOSIS

Acidosis is the cause of 85 percent of re-admissions to the hospital for someone with known diabetes. Most of these admissions could be prevented if the problem were identified and treated earlier. The simple rules outlined in Table 4 will prevent most cases of acidosis. It is a good idea to review this chapter every year. Families may forget the importance of checking urine or blood ketones during any illness. Some people with diabetes who still make some of their own insulin, or who are in very good diabetes control, will have the “machinery” (enzymes) for making the ketones remain “turned off.” As a result, they may go several years and never have urine or blood ketones with an illness. As they grow older and a few more islet cells are lost, or they outgrow their remaining islets, they may suddenly find ketones present.

**The important message is always to remember to check for ketones anytime a person with diabetes is ill.** You must also check for ketones anytime the blood sugar is above 240 mg/dl (13.3 mmol/L) fasting or above 300 mg/dl (16.7 mmol/L) during the day.

The prevention of acidosis is based on being able to detect changes early. Knowing when ketones are forming in the urine or blood, but before the ketones build up in the body, is important.

*Preventing acidosis – the person with diabetes/or the family:*

- ✓ must have a method in the home to check urine or blood ketones (see Chapter 5)
- ✓ must remember to check for urine or blood ketones anytime the person is sick (even with vomiting only one time)
- ✓ needs to check ketones if the blood sugar is high
- ✓ should call the diabetes care provider immediately (night or day) if moderate or large urine ketones or blood ketones > 1.0 mmol/L are present

- ✓ needs to give extra rapid-acting insulin (Humalog/NovoLog) every two hours or Regular insulin every three hours until the urine or blood ketones have decreased
- ✓ must drink lots of fluids to wash the ketones out of the body and to prevent dehydration

**A low blood sugar can sometimes be present with acidosis, and so urine ketones must be checked with every illness, even if the blood sugar is low. A summary of the instructions is in Table 4.**

### Extra Insulin

When ketone production becomes total body acidosis, it is usually because the large amount of ketones has been present for four to 12 hours. This can happen because the urine or blood ketones have not been checked or no extra insulin has been given. Insulin shuts off ketone production. Extra insulin must be given if someone has moderate or large urine ketones or blood ketones above 0.6 mmol/L. The dose of extra insulin varies for different people, and the diabetes care provider can help decide on a safe dose.

### General Guidelines When Giving Extra Insulin

The blood sugar should be checked before each insulin injection.

- 🐾 For moderate urine ketones or blood ketones between 0.6 and 1.5 mmol/L:

The extra dose is usually in the range of 5-10 percent of the total daily dose (see Table 5). The extra dose is given as Humalog/NovoLog/ApiDra every two hours or Regular insulin every three hours.

- 🐾 For large urine ketones or blood ketones above 1.5 mmol/L:

The dose of extra insulin is usually 10-20 percent of the total daily dose. This extra insulin is given as Humalog/NovoLog/ApiDra every two hours or Regular insulin given every three hours.

Table 5 outlines a possible treatment schedule.

The extra insulin may seem like a large dose, but ketones block the normal sensitivity of the body to insulin. Although every person is different, dosages in these ranges are usually needed.

- 🐾 If the blood sugar drops below 150 mg/dl (8.3 mmol/L), it may be necessary to sip regular sugar pop, juice or other sugared drinks. This is done to bring the blood sugar back up before giving the next insulin injection.

Remember, the extra insulin and fluids are being given to clear the urine or blood ketones.

## Extra Fluids

In addition to taking extra insulin, drinking fluids (e.g., water and fruit juices) is important in the prevention of acidosis. These liquids replace the fluid lost in the urine and help prevent dehydration. The juices also replace some of the salts that are lost in the urine. Orange juice and bananas are particularly good for replacing the potassium that is lost. As discussed in the next chapter (Sick-day Management), a medication called Phenergan is sometimes used if vomiting is a problem.

When severe acidosis has been present for many hours, coma (loss of consciousness) can follow. This is dangerous. It is much better to

## Table 4 Prevention of Ketoacidosis

- 🐾 Remember to check urine or blood ketones with any illness (even an upset stomach or vomiting one time) or anytime the fasting blood sugar is above 240 mg/dl (13.3 mmol/L) or a daytime blood sugar is above 300 mg/dl (16.7 mmol/L).
- 🐾 Call the diabetes care provider immediately (night or day) if moderate or large urine ketones or blood ketones above 1.0 mmol/L are found.
- 🐾 Take extra insulin (after checking the blood sugar and urine or blood ketones). Take Humalog/NovoLog/Apidra every two hours, or Regular insulin every three hours, until the urine ketones are small or less or the blood ketones are below 0.6 mmol/L.
- 🐾 If the blood sugar falls below 150 mg/dl (8.3 mmol/L) and urine or blood ketones are still present, drink juice (preferably orange as it replaces potassium), Pedialyte® or sugared pop (soda) to keep the blood sugar up so that more insulin can be given to turn off the ketone production.
- 🐾 Drink lots of fluids to help wash out the ketones.



Table 5

## Ketone Levels\* in Blood or Urine and a Suggested Dose of Rapid-Acting or Regular Insulin

Urine	Blood (mmol/L)	Dose of H/NL/AP every 2 hours or Dose of Regular every 3 hours
Trace/Small	< 0.6	per “correction” factor for blood sugar
Moderate - Large	0.6 – 1.5	10% of total daily insulin dose**
Large - Very Large	> 1.5	20% of total daily insulin dose**

\* The blood and urine ketone results do not agree exactly and the above correlations are estimates. The blood ketone result reflects the ketone level at the exact time the test is done. If the urine has been in the bladder for some time, then the urine ketone result may not tell the current status.

\*\* The total daily insulin dose is the sum of all insulin taken in a 24-hour period (rapid-acting plus intermediate-acting plus long-acting).

prevent severe acidosis than to have to treat it with IV fluids and a hospital admission. The hospital admission is usually in an intensive care unit, which is scary for everyone. Intravenous lines are usually put in both arms (and sometimes the feet). A constant heart-monitoring machine is attached to the person. The cost is about \$10,000.

Preventing acidosis is generally possible when the rules in Table 4 are followed. Ketoacidosis in patients with known diabetes rarely occurs in people who attend clinic regularly. When it does occur, it is usually because the directions in Table 4 were not followed.

## DEFINITIONS

**Acetone:** One of the ketones which builds up in the urine, blood and body during acidosis. It is sometimes used (incorrectly) to refer to all ketones.

**Acidosis (diabetic ketoacidosis or DKA):** What happens in the body when not enough insulin is available. Blood sugar is usually high

at this time. Moderate or large ketones are present in the urine or blood and then build up in the body. The ketones make the body fluids more acidic resulting in total body acidosis.

**Beta hydroxybutyrate (β-OH butyrate):**

The most important of the three main ketones (along with acetone and acetoacetic acid). It is the ketone that is measured in the blood ketone test.

**Dehydration:** Loss of the body fluids. The tongue and skin are usually very dry and the eyes look sunken. Babies have less than half the usual number of wet diapers.

**Ketones:** Fat breakdown products that initially spill into the urine and later build up in the blood when there is not enough insulin. Many people can smell a sweet odor on the breath. The fat breakdown products cause acidosis (or ketoacidosis).

**Potassium:** One of the salts (along with sodium) lost in the urine when ketones are spilled in the urine. Orange juice and bananas contain a lot of potassium and are best to give if urine ketones are present.

## QUESTIONS AND ANSWERS FROM NEWSNOTES

**Q** Please explain what ketoacidosis (acidosis) is and how it can be prevented.

**A** Acidosis is one of the two emergency problems of diabetes (low blood sugar being the other). It is the main cause of children with known diabetes being admitted to the hospital. It is responsible for 85 percent of hospitalizations. Most of these hospitalizations can be prevented with good family education and with following instructions.

Families can check for ketones at home with urine or blood. If using urine Ketostix, use the foil-wrapped strips. The bottles of strips expire six months after they have been opened. Checking for ketones should be done **ANY TIME THE PERSON IS FEELING ILL**. Also, check ketones if the blood sugar is above 240 mg/dl (13.3 mmol/L) fasting or above 300 mg/dl (16.7 mmol/L) during the day. If moderate/large urine ketones are found or blood ketones are above 1.0 mmol/L, the healthcare provider should be called immediately. Calling the healthcare provider may be necessary every 2-3 hours for dosages of Humalog/NovoLog/Apidra or Regular insulin. After the ketones have decreased to small amounts or have gone away, the extra injections can be stopped.

On any given day, five to 10 children are being treated for ketonuria by phone by the Barbara Davis Center staff. This happens especially during the flu season. Fortunately, hospital admissions have gone down dramatically as a result of this treatment and are now infrequent.

The cause of ketone production is the body's need for energy. Sometimes, the body needs extra energy (e.g., during an illness). Because there is not enough insulin or sugar available to use sugar for energy, the fat tissue responds by releasing fats. These fats are then

broken down. Some of these fats are made into ketones by the liver. As the ketones build up following the fat breakdown, ketoacidosis eventually results. The most frequent symptoms are a stomachache and, eventually, vomiting. Deep breathing is a late sign and indicates a need to go to an emergency room.

**Q** Why does someone feel sick when the ketones are moderate or large in the urine or > 0.6 mmol/L in the blood?

**A** There are at least three parts to the answer to this question:

1. The body's acid-base (pH) balance is finely tuned (a bit on the basic side at 7.35-7.45). Acids and bases are difficult to explain. Examples of a base and an acid are: soap is an alkaline (base) material and tomatoes are acidic. Ketones (which are acids) make the body fluids more acidic as they start to build up. As the body becomes more acidic, many of the body's functions can no longer work as they should. If left untreated, death will eventually follow.
2. The second reason a person feels ill is because of a potassium and sodium imbalance. They are important body salts, and are lost with ketones going out in the urine. Potassium is important for the movement of the intestine (moving food through). If too much potassium is lost, this movement decreases or stops. When this happens, an upset stomach and vomiting can occur. We often recommend orange juice (high in potassium) and apple juice in addition to water when someone has urine or blood ketones. Drinking lots of liquids helps to keep good hydration and to flush out the ketones.
3. Poor hydration would be the third reason for feeling ill. Usually, frequent urination due to high blood and urine sugar happens together with urine ketones. This can lead to



dehydration. Our bodies are 60 percent water. If even 10 percent of body weight is lost as water, it is possible to be very sick. Fluids can also be lost in large amounts with the flu (vomiting and diarrhea). If fluid is being lost in large amounts from both the kidneys (frequent urination) **and** from vomiting and/or diarrhea, dehydration can occur even more rapidly. Children under the age of five can become dehydrated in less than four hours. They are more likely to require IV treatment sooner than older children.

or the blood ketone level is  $> 1.0$  mmol/L. Extra shots of Humalog/NovoLog/Apidra or Regular insulin are then given to reverse the ketones before DKA occurs. In one period we had only six cases of DKA among 1,200 families in 12 months! Stopping ketone formation early reduces the likelihood of a case of DKA resulting in cerebral edema. It is better to prevent DKA than to deal with its bad effects. Unfortunately, cerebral edema is more common in newly diagnosed children when the ketones have built up over a longer time period.

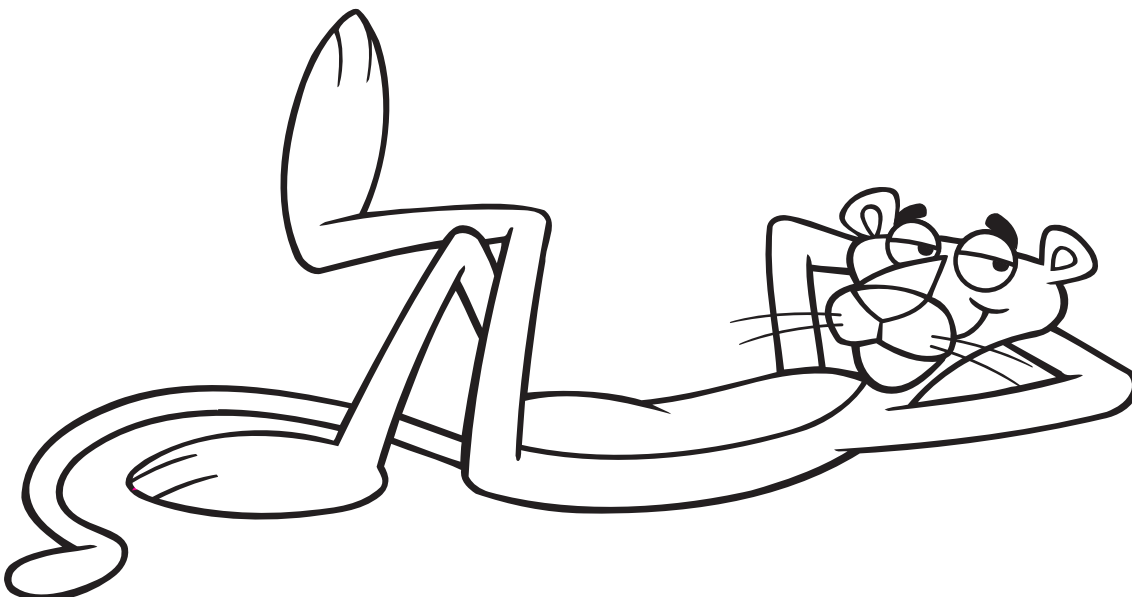
**Q** What is cerebral edema and how does it relate to diabetic ketoacidosis (DKA)?

**A** Cerebral edema refers to swelling of the brain, which is a rare complication of treating DKA. The cause is not fully understood and when it does occur, it is often fatal.

Perhaps we have been lucky. In 25 years since the Center opened, and over 30 years of working with children with diabetes, I have seen only two or three cases of cerebral edema in children who had been previously diagnosed with diabetes. Part of the reason it is so rare relates to the now relative infrequency of DKA. Our families are asked to check urine or blood ketones with every illness. They are asked to call when urine ketones are moderate or large

**Q** Our son has had diabetes for over two years. Every time he has gotten sick we have checked for urine ketones. The results have always been negative or trace. Can we stop checking now?

**A** The answer is **NO!** This is often the case for someone who still makes some of their own insulin and/or someone who is in excellent sugar control. The machinery (enzymes) for making ketones from fat are so completely turned off that they don't get turned on by the illness. Unfortunately, as your son's insulin production declines or he outgrows his remaining insulin production, he will probably suddenly have ketones with an illness. One never knows when this will occur. Thus, the only answer is to keep checking the urine ketones at least twice each day with each illness.

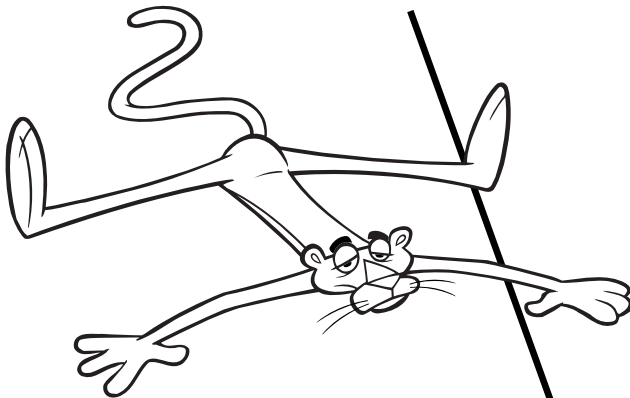


Diabetes

No Insulin

Sugar becomes high in the blood. Sugar spills into urine. Frequent urination will result in loss of body fluids or dehydration.

Sugar can't be used, resulting in fat breakdown as an energy source.



No Energy

Normal

Insulin



Energy



Fat breakdown results in:

1. Weight loss
2. Ketones, which are a breakdown product of fat and appear in the blood and urine
3. Too many ketones in the body = acidosis