

NOAH

North Dublin Orthopaedic Animal Hospital

Our Pets and Cancer

Contents

.....	1
Introduction	2
The Vocabulary	2
Cancer Language	2
Starting With Molecular.....	2
Growth	3
Tumours.....	3
The Big Three Tumours	3
Still Hearing 'Cancer'?	4
Cancer Causing Agents.....	4
Prevention Aids.....	5
Diagnosis.....	6
Is it a Tumour?	6
Images.....	7
Samples.....	8
Grading.....	8
Clinical Staging	8
Haematological Paraneoplastic Syndromes (HPS).....	9
Treatment	9
Compassionate Care	9
Support	10
Surgery	11
Chemotherapy	12
Radiation Therapy.....	12
Nutrition.....	13
Pain Management.....	13

Introduction

There's always a sense of panic when the word Cancer is mentioned at the end of a list of possibilities of why you're in to see the doctor. When Cancer is diagnosed in our beloved dogs or cats, we're inclined already mourn our stricken friends. We're inclined to instantly assume that the outcome will be the word that hasn't entered the conversation yet, "Euthanasia".

This is most certainly not the goal, nor is it the appropriate reaction to Cancer. Let's get things straight, as your pet ages check-ups are important. As we all know spotting the big 'C' can be part of that but most definitely discovery does not mean euthanasia.

When Cancer strikes our companions it is an emotive moment. You are faced with a series of problems, and it is now the job of the Veterinarian, possibly an Oncologist, and you as the owner to create a plan to start solving these problems. With medical advancements in the last twenty years regarding Cancer treatments, many problems have been solved.

The Vocabulary

Cancer Language

As is the case with all medicine, treatment of Cancer, or its medical title, Oncology, is filled with key words that when strung together in a monologue of sorts can sound as if it is a language from the farthest of lands. As pet owner it becomes your responsibility on you to learn this new language.

Oncology is a massive area of study. It's filled with its own dictionary of words that might at first appearance render you incapacitated with fear at its enormity. Don't be scared. Step-by-step we can get through the language that is specific to your pet's Cancer. This will narrow the terms and language involved and the task will become more manageable.

Should those dreaded words of "Your pet has Cancer" be spoken, it is then that we've begun our language classes.

Starting With Molecular

Molecular is perhaps a word you've heard before? How about Molecules? First we must recognise the atom. The atom is smallest part an element can be divided into while still retaining all its original properties.

A great example is water. Water has two hydrogen atoms and one oxygen atom to make one molecule of water. So when we say molecular, we are reducing Cancer to its smallest components to discover the cause. In our pets, just like in humans, we are investigating the components in cells to establish the correct treatment plan.

Growth

We all grow. Our pets grow. This growth is all initiated by cells. Cells are of all different kinds. They exist in our bodies and in our pets like a small enclosed fully functional network with different cells responsible for regeneration, immunity or hormone production for example. A quick representation of this growth can be seen in our own skin; always growing, dying, hardening, drying, flaking off, and for most of us we never even notice this is happening. Skin cells are just examples of what are just some of the many kinds of growth and regeneration of cells in your pet. As you can imagine, there are all types of cell activity occurring in your pet's body all at once allowing them to jump, run and play.

Unfortunately the growth of bad cells can also occur. There isn't always just one reason as to why a cell goes bad. There can be many reasons and many of these are not yet fully understood in Oncology or other areas of medical study.

What you need to know is that bad growth will begin with a single cell.

Tumours

This is an aspect of Oncology associated with the growth of bad cells. Good cells, or cells reacting as they should know when it's time to die; they recognise this and in simple terms, self-destruct. One bad cell will lead to two bad cells, then four, then eight, and so on because now the self-destruct switch is off. As you might have guessed, this is the beginning of a tumour.

Molecular changes occur in our cells, and amongst whatever changes occur within a cell, one particular change can be when the self-destruct button is deactivated, or when what is formally called the genes responsible for Apoptosis are deactivated. When this occurs cells continue to grow, and do so in an uncontrolled manner.

The Big Three Tumours

Tumours can be broadly typecast for us to understand them.

Benign Tumours - This can happen anywhere in your pet's body. It can happen in skin cells or any other cell for that matter. There is often a positive clinical significance regarding these types of

tumours. For one, these tumours tend to grow locally so they don't spread to other areas. That spreading is called metastasis. Benign as a phrase is associated with tumours that do not metastasize. However, this type of tumour can also cause harm. It can create pressure, block something, and cause damage. They can also arise in very compromising inoperable areas in the body.

In-situ Tumours – This refers to a tumour that remains within its own layer of cells as pre-invasive tumours.

Cancer – This is a malignant tumour whose bad cells can jump between the body's systems establishing themselves elsewhere in the body where they invade, do damage and continue to spread and grow.

Still Hearing 'Cancer'?

Veterinarians will always look to previous studies and experience to establish why cancer occurs and this information can play an important role in deciding on a treatment plan. Your Veterinary team is there to help you understand and to be understanding of this confusing and perhaps emotionally challenging moment you're experiencing with a diagnosis of Cancer. It is vital that you utilise and work alongside your team of Veterinary personnel when deciding on treatment options. During the development of a treatment plan your Veterinary team may be able to help you with the questions as to why this occurred and/or what caused Cancer in your pet.

Cancer Causing Agents

These are things that are called oncogenic viruses or viruses that cause Cancer. Each virus has insertion abilities allowing it to place its genetic material, causing a cell to change for the worse. Feline Leukaemia Virus commonly causes leukaemia and lymphoma tumours.

Chemicals that cause Cancer exist. It is important to recognise and acknowledge this. There is a great importance placed on the care and use of Cancer causing chemicals (carcinogens). Our pets are just as susceptible as we are to the damaging effects from the use of these chemicals and they can have far worse reactions. The most notable and common carcinogen is cigarette smoke. Smoking deposits carcinogens into the air where they settle onto your pet's coat to be ingested by your pet at grooming. Studies have shown smoking households to be a high cause of Squamous cell carcinoma in our pets.

Physical agents can also cause Cancer. For example, a burn victim may experience tumour growth at the injured site. Broken bones that have a slow healing time and during the process have lots of cells grow, divide, and die might cause a cellular growth overload where just by accident the malignancy button got turned on in single or multiple cells. This has been surmised as the cause behind primary bone neoplasia.

'Parasites as a cause of Cancer' is one area of study, and it's long been known that irradiation such as direct sunlight can cause Cancer. Hormones can be behind the development of cellular replication. Some tissues need a trigger when a hormone is sent their way to stimulate growth. Inherited Cancers are genetically effected information within those tissues that when passed onto offspring can have influence and result in Cancer.

There are a great many chemicals we forget that we use in our lives. It is important to understand that many of these can have carcinogenic abilities. Pets are susceptible in many cases to all sorts of chemicals on the ground, and it's important that as an owner you are aware of this.

In our cow farmer's life, it's important to that farmer that he be sure Bracken fern isn't within the abilities of his herd to get at and eat. Bracken fern when eaten has a unique reaction with other combinations of variables involved to cause Cancer.

These possibilities to exposure are present in your pet's life, and as such the surrounding environment needs to be scrutinized and these elements eliminated so safety of the pet is ensured. It's good if everyone at home gets involved in watching for these unsafe elements.

When we use products found in our pet supply shops it's very important that we research these items. Many of these items can be damaging and cause Cancer in our pets. Take for example, one study on flea collars. These collars when worn have shown to cause a dramatic increase in Squamous cell carcinoma in cats. This type of Cancer is very aggressive so why use the collar? Spot-on treatments recommended by your Veterinary hospital are currently the most successful solution and Cancer odds are decreased.

Smoking households have shown to produce quite a significant increase in the occurrence of Cancer. It's probably of no surprise to anyone to read that. But some interesting things we forget about smoke, it is comprised of solid molecules of a kind. Chemicals, and more specifically carcinogens, can be floating looking to eventually settle. A lot of times we forget things stirred up in the air drop to the ground where our pets sleep innocently. A great many chemicals can be deposited on the coat of a pet only to later be ingested upon grooming. These residues can be deposited elsewhere on the smoker's hands or even on furniture. All these residues can be wiped off on to your pet's coat and later ingested.

Prevention Aids

It is ultimately impossible to predict Cancer. It is an ugly disease process where so many various forms have been studied in great length. Yet for all our knowledge we can't necessarily predict its occurrence. However, we are informed and getting better information every day.

Technological advancement alongside medicine and the study of a disease such as Cancer is constantly in motion. It is important that we educate ourselves. It can start with a practice of implicating some preventative measures in what we already know are potential problem areas.

In one study it was shown that cats were more susceptible to a type of tumour of the mouth from eating tinned foods or tinned tuna. It has been surmised that one possible reason could be that the foods get deposited in the rear of the mouth where can remain for some time. This time allows for bacterial growth, cell death, and the possibility of cell change. It is an important point to note that it is good practice to be aware of your pet's oral health.

Brushing is the first step to combat this. It can take some time before you and your pet find a middle ground in making this ritual happen. Stick with it. You can acquire special pet toothpastes and brushes from your local pet shop. Once a year your pet should be receiving a professional teeth cleaning, and this is something your Veterinary team can arrange at your convenience.

In many cases the spaying or neutering of a pet early on in life is theoretically based on a series of positive statements about the long-term lifespan of the pet. This elective surgery in some studies shows that it can have a positive side-effect of limiting the occurrence of Cancer.

Don't smoke! Can't be stressed enough that this has a very big effect on your pet not only based on breathing but there are residues deposited from smoke itself, hands, and other objects your pet and smoke might come in contact. Smoke free is above all the best way to be.

Harmful chemicals and carcinogens are out there. Pollution and environmental hazards are very much in existence and it's important to know that these can affect our pet's safety and health.

Vaccines are an integral part of the health and longevity of your pet. It is important to note that there are a number of viruses that can cause Cancer. Your Veterinary team can advise you on what vaccines for your pet are best and at what time intervals these should be administered.

Animals can be genetically at risk for a type of Cancer. Breed evaluations are important to establish any risk that may exist from a genetic history. This will allow for a goal plan to be established quite possibly before there is an evident problem or diagnosis.

Diagnosis

Is it a Tumour?

It is our initial goal to determine if we are dealing with tumour. To do this, your Veterinary team needs to get obtain a sample of those bad cells. The more cells available for testing, the more successful the pathologist working in the lab can be in delivering a successful and definitive diagnosis.

Understanding tumours starts with understanding the cell of origin. Then your Veterinary team will know the correct specialists to contact to determine this information. These select Veterinary scientists will be able to name the cells and the tumour for you.

When we speak about Cancer words ending in '-oma' are often mentioned. Three letters to the end of a word and you may have no clue what it means, but we presume '-oma' is bad. So it will help you to know the beginning of the '-oma' word is actually the name for the cellular type of tissue involved. So 'Lipoma' translates to 'Fat Tumour'. Lipoma is a benign tumour, which could mean we're on the road to a quick recovery. The words ending with '-oma' aren't as scary if you can quickly understand the biological references. Osteoma is simply a benign bone tumour.

Malignant tumours (the bad cells) they end in '-sarcoma', '-noma', leukaemia, and other less common phrases that are all prefaced with the tissue of origin. Understanding these names allows you a far better understanding of the complexity of your pet's problem.

Images

Radiography, what is commonly referenced as X-Rays, are imaging techniques that are used to gain a clearer picture of what is happening for the Veterinary team. Your team might want to cut or puncture the tumour to take away part or the entire tumour as a sample for the lab to discover the cell type effected. Contrast dyes can be used to study internal architecture of organs.

Ultrasound is a useful tool in identification. It's a safe scanning method in visualizing growths. It can offer guidance to the Veterinary professional gathering information through sampling. Usually ultrasound is a diagnostic tool that is effective without having to sedate the animal. Ultrasound-guided fine needle aspiration or biopsy allows for accuracy especially when dealing with small focal lesions.

Magnetic Resonance Imaging (MRI) is a diagnostic tool that is excellent for soft tissues imaging and can be quite effective for bone analysis. Your pet will have to be sedated and the study can take a longer period of time. The financial costs associated with MRI can be an off putting aspect for owners when MRI is suggested as a diagnostic tool. Although an MRI study is expensive, costs have significantly reduced in the last ten years making it much more affordable and currently many insurance companies cover this form of diagnostic testing.

Computed Tomography (CT) is another diagnostic imaging tool that utilizes radiation to determine structure. It is an excellent tool for visualization of bone related lesions, and does quite well with soft tissue imaging. It is not generally an accepted imaging technique used in Veterinary medicine, but has useful applications for specific instances.

Diagnostic nuclear medicine also serves purpose in small animal tumour recognition. Scintigraphy can be utilised for determination of metastases, and is used mostly for the discovery of lesions. In these types of studies your animal will be sedated, a radioactive isotope will be safely injected at the start of study and as it travels through the pet's body images are taken.

Samples

As we move into talking about various tests that could occur during diagnosis it's important to know that your pet will have to have its coat shaved down to skin for many different procedures. This can be a shock sometimes depending on the procedure. Bloods will have to be drawn, and possibly fluids and medicines administered.

A needle and syringe can be used to suck up cells to make a microscopic slide of representative cells taken from within the tumour. Core, incisional and excisional biopsies can be attempted to achieve a higher level of cellular content. These are punctures with a tool that creates and extracts a small cored sample.

Immunohistochemistry adds man-made antibodies designed to attach to a certain type of Cancer cell to a sample which can label and dye specific abnormal cells. Electron microscopy and the use of molecular markers can also be utilised in diagnosis following the discovery of Cancer cells.

With the aid of laboratories, the Veterinary surgeon can make a determination on what is called 'Margins'. This allows the surgeon to understand how much needs to be cut to remove the entire tumour. The lab will also give the tumour what is referred to as a grade to assist in the understanding of the progression of this particular Cancer and where else in the body there might also be subsequent issues occurring.

Grading

This is the laboratory's interpretation of degree of malignancy by interpreting a number of criteria to discover the grade such as 1, 2 or 3. Such a grade is determined by the level of invasiveness of the cancerous cells. This knowledge allows for a better understanding of how aggressive the Cancer cells are in each case.

Clinical Staging

After grading there is a determination as to classify the tumour to be the primary, or a metastasis to local, regional, or lymph node tissue. Distant metastasis is the unfortunate spread of Cancer cells to other areas of the body. This stage of tumour growth is problematic because when a tumour is large enough to be seen it's already of size to potentially continue seeding Cancer cells elsewhere in the body.

Clinical Staging takes these factors into an account and labels the results accordingly. Defining the clinical stage of the tumour helps your Veterinary surgeon create a treatment plan and a prognosis.

Haematological Paraneoplastic Syndromes (HPS)

Blood tests reveal these indicators of Cancer. Anaemia is a commonly encountered result of Cancer in dogs and cats. This has an effect on the quality of your pet's life. It also can effect potential treatments and survival time when combined with Cancer. Other symptoms can also cause similar problems such as Mast Cell Tumours having a chemical effect and producing gastrointestinal ulcerations that get so severe Anaemia is the resulting problem to contend with.

This can be describes simple as a burning hole through the stomach lining, cutting vessels as it goes like arteries and veins. This can cause bleeding and anaemia caused by the loss of blood.

Another example is the invasion of a tumour into the bone marrow. This can affect the production of blood but it should be said that other haemostatic blood symptoms might also occur such as the abnormal building of small clots inside the vessels of the body. This is usually the beginnings of a chain reaction where abnormal bleeding can now occur elsewhere in the body. When this is prolonged there is obvious internal organ damage.

Cancer can cause anorexia, weight loss, fatigue, and a weakened immune system. This is medically termed Cancer Cachexia, and is a serious effect of Cancer. Proper diet from the diagnosis and through treatment is very important at increasing the chance for remission.

Another issue that can occur is the deposit of what looks like bone in places where it shouldn't be. Calcium is what we all know goes into making bone, and we all know it can become part of a hard substance. Some tumours cause an effect the production and result in deposits of calcified material in odd places such as the kidney. This can be seen on x-ray, and is medically termed hypocalcaemia. It's one of the most common Paraneoplastic syndromes seen in small animal Cancer.

Hypoglycaemia (low blood sugar) can be a symptom of Insulinoma or a non-islet cell neoplasia. Meaning, it could be pancreatic Cancer, but there are other types of tumours that can generate this effect and further diagnostics are needed to isolate the cause.

The disease Myasthenia Gravis can be acquired through events brought on by the presence of a specific type of tumour. Other such issues like unusual bone growth, strange skin wounds that don't heal or those that heal with hardened layers often go underestimated or unnoticed.

Treatment

Compassionate Care

Compassionate care is the most important goal upon diagnosis. It's a large responsibility, but the weight is not entirely upon you. Step-by-step there is a network built, and it starts with your Veterinary staff and reaches beyond your family and your friends that wish to help.

All options are discussed to develop a team plan. Understanding the disease and the current status of health is important in gauging how future planning will impact the patient. Understanding Stage

and Grade are important for moving forward and even more diagnostics may be necessary or recommended for further assessments. This treatment plan will continuously evolve to provide the best care and best outcome possible.

Working through these decisions isn't immediately indicative of life or death. These moments can be explored, as they can have positive outcomes. And even if palliative care and hospice to euthanasia are steps, then let's make the most of what time is left through support and comfort that can be achieved by a team effort to provide compassionate care.

Support

Pain control and prevention is vital when working through a course of treatment of Cancer. It's the goal of the veterinary staff to seek these supportive measures to help your pet and prevent any secondary sicknesses that can occur as a result of Cancer.

Controlling nausea and preventing it is a main focus in treatment. Its effects can be profound with weight loss and further illness occurring as a result of the nutritional losses. Besides drug treatments many things can be done such as warming foods with aroma and establishing comfortable environments that reduce stress. Preventing these detrimental effects of nausea becomes very important in the overall treatment plan that is developed.

Assessment of overall happiness of your pet (good days versus bad days) should be carefully considered and if a loss of quality of life is noted this should be accounted for and an appropriate response considered.

It is a time when your family needs open communication. Depending on age, almost all should be involved. It's been shown in studies that the fictitious stories of having given Rover to a very nice farm where he'll have all the space in the world to run, apparently isn't helpful in the long run to your child's development.

Pet loss is an unfortunate outcome when the fight against Cancer has been lost. Cancer can be aggressive and strong. These moments of grief are very much understood by your Veterinary team and your family and friends will equally feel the pain in losing this pet that was a part of so many lives. Support exists in all forms to help you work through the grieving process, and it is important that there is open communication. Don't be afraid to ask, and don't be afraid to talk. Your Veterinarian team understand.

Surgery

In many instances surgery is used to allow a diagnosis along with confirming the possible treatment of Cancer. In these cases Grading and Staging are key factors along with an assessment of the local and systemic effects. In some cases, alternative treatments are explored. A decision is made through good communication between Veterinary team and the pet owner/family.

This decision is a goal plan for continuing through with surgery. It's the aim to define why the surgery is occurring. Surgery can be a cure, dramatically reduce size by removal, or palliative surgery to make the animal's quality of life better for what time is left. This plan needs to be established, and talking about options is the best way to come up with a plan.

It's important at this stage of decision and plan making that the surgeon understand the reconstruction, anaesthetics, and pain management.

In surgery the incision path is planned. This is how we refer to the conceptual plan of the surgeon on how to best excise the tumour. Part of this plan is the determination of the Margin, and this is best based on Grading and Staging information previously gathered while deciding the treatment plan.

It's important to weigh-in all the preoperative preparations to consider such as old age, poor nutrition, obesity, low blood oxygen, etc. that many factors exist that need to be carefully considered alongside these other secondary battles that will continue and worsen after surgery if not contended with.

Pain management is a unique plan that starts with your pet at the preoperative stage, extends through surgery and well into recovery. It's a good thing to discuss this with your Veterinary team and discover how to improve your pet's outcome through a proper pain management plan. This should always be combined with postoperative monitoring, fluid therapy, and proper nutrition.

The tissue will need to be sent off to lab to be evaluated to establish the exact margins achieved in treatment. This will occur at surgery, and the tissues removed will be placed into a special container and sent to the lab immediately to achieve the best results on analysis.

Postoperative appearance is something to now consider with a plan of surgery. It's important to discuss this and really visually come to an understanding of what it will look like afterwards. Some surgeries are more dramatic than others, but it's always important to keep seeing the big picture in relation to your pet's health.

Chemotherapy

Of course we all think of those famous scenes in movies and television where we've seen the effects of Chemotherapy on people. Perhaps we've had the unlucky first-hand experience with another experiencing this form of treatment but it should be noted that this is a never ending area of exploration, and as we tend to do with most things, we focus in on the bad and in some cases rare side effects.

Chemotherapy is a treatment modality that is often used to treat certain types of Cancer. Not all Cancer requires a course of Chemotherapy. It's the reason why it's vital to understand the kind of Cancer we're dealing with. This is established by the submission of the sample of tumour, and more importantly the cells inside, to a laboratory to be defined. This definition determines what drugs and combinations of treatment are best to attack the cancerous cells with a goal of remission.

Important factors need to be considered once a Cancer type is discovered. Staging and where in the body is the Cancer is, is very important, as is the patient's overall health. The drugs chosen for the Chemotherapy should have the ability to kill the tumour cells, and it's important to understand the possible side effects that can result in treatment.

Chemotherapy is a form of toxicity, and the pet's health status plays a role on choices and decisions made. As a pet owner, it's very important to understand these things to the best of your ability. This understanding will influence how you make decisions and direct the team of Veterinary professionals to drive forward treatment. The best news about Chemotherapy is that unlike us, our pets actually have a notably better tolerance to Chemotherapy and it can be a very positive part of the treatment of Cancer.

With all sorts of variables afforded in Chemotherapy and the ever emerging areas within it, such as anti-angiogenesis and targeted therapies, it is a process that needs to be planned out. There will be multiple visits involved, and the importance of understanding everything that is going on will aid you in successfully completing this part of the treatment process. Remember your Veterinary team is there to help you, and answer all the questions you have.

Radiation Therapy

Radiation Therapy is very much like that of X-rays that we are familiar with in the imaging part of medicine. But when we use Radiation Therapy to treat Cancer it is a focused form of delivery, purposely confined to the area of treatment as best as possible. The reason behind this is because all cells targeted by radiation will suffer cell death. They will no longer reproduce, and hence tumour growth stops.

In Veterinary medicine this is a relatively new area of growth. Where it has been a successful treatment of Cancer, it is relatively new in its use in Cancer treatment for our pets. Three types of machines exist, Orthovoltage, Radioactive Source, and Particle Accelerators. Each machine has a purpose, but only successful with the proper technicians and oncology professionals. Your

Veterinary team should be able to assist you in understanding if this is an option for the type of Cancer being treated. If they cannot assist you in providing this as a form of treatment, they should be able to refer you to the right facility that can perform these tasks.

Nutrition

All too often we forget that our animals need nutrition. Just any food off the shelf in pet stores isn't a wise way of protecting your pet. Would you eat fast food every day? Quite possibly the brand of food you choose could be the equivalent for your pet.

Nutritional management is an important part of being a pet owner, and it's your task to research and understand what would be the most suitable diet for your pet. Again your Veterinary team will most likely have nutritional experts on hand that can assist you in understanding what you're looking for to meet the needs of your pet.

Nutritional management of the Cancer patient is equally an important role that is necessary to revise and plan. There are very unique changes in the body caused by Cancer, and these changes are in need of nutritional support. Appetite support, prescription diets, palatable foods, and many other options now exist to further the health and vitality of your pet through their battle with Cancer.

Proper food with integral nutrition built-in results in a better quality of life, but in a pet with Cancer it can make for vast improvements. Becoming an educated owner is the first step in understanding the nutritional needs of your pet and what products will be the best to support you in meeting this goal.

Pain Management

As we know Cancer is a prevalent part of disease diagnosis in small animals. Not all Cancer is painful. Different tumour types can present differently and may or may not cause pain.

Many instances of tumour-related pain can be attributed to the location of the tumour in the body. Pain can also be caused by other related problems occurring as a result of therapy, treatment, surgery, and in some cases pain from an unrelated disease that may coincide with the onset of Cancer.

The importance of relieving pain in our pets is as important as ensuring they're free from hunger and thirst. We must make sure they're in comfort with proper temperatures, proper physical well-being, and free of fear and stress. Your pet when free of injury and able to express with normal behaviour is the ideal.

Assessing our pets when they're experiencing pain is a job that requires us to pay special attention and find abnormalities and define where they come from. Behavioural changes are key factors in

assessment of pain that owners can be aware of to better assist the Veterinary team in meeting the needs of your pet allowing them to be comfortable.

Choosing the appropriate therapies necessary are important goals that owner and Veterinary teams need to work through. Feedback and updates are integral in insuring quality of life is kept to a high standard.

The information on this document is brought to you by the specialists at

NOAH

North Dublin Orthopaedic Animal Hospital

NOAH provides an orthopaedic referral service
for injured or ill dogs and cats from the
Republic of Ireland and Northern Ireland