Chapter 1
Biotherapy – An Introduction

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'Biotherapy' is as old as the hills, in that man has learnt, over the millennia, mostly by trial and error, what the natural world around him has to offer, to alleviate or enhance his condition. By interacting with things, working with them, eating them, or rubbing them on, certain effects will follow, sometimes with dramatic results, including of course, death. As scientists, we divide the natural living world, somewhat arbitrarily, into the plant and animal kingdoms, but these have a massively 'fuzzy' interface. The biological world is diverse, complex, sophisticated and mysterious, changing inexorably over time, so that, whatever we might study or utilise, it is the end result of literally millions, even billions, of years of natural 'research and development'. The 'Bio'- epithet thus is open to a wide range of connotations. A glance at the World Wide Web confirms this diversity of use.

When the International Biotherapy Society (IBS) was founded, at our first conference in May 1996, we defined 'Biotherapy' as 'the use of living organisms in human medicine'. The focus then was primarily on 'Maggot Therapy', 'Hirudothotherapy' and 'Apitherapy'. The emphasis was on utilising the natural abilities, aptitudes and responses of certain organisms, in an environment determined by the practitioner. We were particularly concerned to learn how such organisms would respond to a variety of clinical situations, such as maggots in chronic wounds, and leeches on congested flaps in plastic surgery. Our ideal was to manage the organisms themselves so that they would remain 'happy and hungry', and thereby function optimally, throughout the treatment period, recognising the fact that the environment itself, to which we were subjecting them, might be, or might become, hostile to their wellbeing.

A clinically successful outcome is thus the result of specifically chosen organisms, appropriately prepared for clinical use, introduced to a patient at an opportune time by practitioners who understand the inherent biology of these organisms,

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M. Grassberger et al. (eds.), *Biotherapy - History, Principles and Practice: A Practical Guide to the Diagnosis and Treatment of Disease using Living Organisms*,
DOI 10.1007/978-94-007-6585-6_1, © Springer Science+Business Media Dordrecht 2013

and can manage the clinical environment to obtain optimal behaviour. This is challenging, and demanding, and is for many practitioners an entirely new concept, but the clinical results can be dramatic and magnificent.

Modern scientific endeavour is essentially reductionist, whereby objects and phenomena are studied at ever increasing depths of detail. Thus, there are now literally hundreds of known elementary sub-atomic particles, with concepts such as 'String Theory' now well established, albeit yet to be 'captured' and 'looked at'. However, the more that is discovered the more there seems to be open for future discoveries. We may know a lot about 'mass' and 'energy', but 'dark matter' and 'dark energy' still comprise 95 % of all that's there! We may have cracked the human genome, but 'non-coding' or 'Junk DNA' is still 98 %!

By complete contrast with all this, and perhaps aimed at the other end of the spectrum of human enquiry and activity, 'biotherapy' is 'holistic'. The term 'holistic' is yet another with a wide scatter of applications. We use it here to define our aim to engage with naturally occurring phenomena and *healthy intact* organisms, in all their diversity and complexity, introducing them into the clinical arena, with the goal of fully *integrating* biotherapy into modern medicine.

Biotherapy is expanding. Our website (www.biotherapysociety.org) now addresses:

Maggot Therapy: The use of the larvae of the blowfly *Lucilia sericata* as agents of cleansing or débridement, and enhancement of healing of open wounds.

Hirudotherapy: The application of leeches for extraction of blood from congested or inflamed tissues, in a wide range of pathologies.

Apitherapy: The introduction of bee venom, by live bees or by injection, for a wide range of chronic ailments. Bee products such as propolis, honey and Royal Jelly are also efficacious, each in its own spectrum of conditions.

Ichthyotherapy: The use of certain species of small fresh-water fish as scavenging agents for dermatological conditions such as psoriasis.

Helminth Therapy: The use of certain nematode worms as agents for the stimulation of host immunological responses appropriate to the alleviation of certain inflammatory auto-immune bowel diseases such as Crohn's Disease and Ulcerative Colitis. There is the potential use of the schistosomiasis parasite in the prevention of Type 1 insulin-dependant diabetes.

Phagetherapy: The therapeutic use of bacteriophages to treat pathogenic bacterial infections (especially those that do not respond to conventional antibiotics) in human as well as in veterinary medicine.

Animal-assisted therapy: This type of therapy involves higher animals (mainly dogs and other pet animals) for people with physical, psychological, cognitive, social, and behavioural problems. The special term Equine-assisted therapy is applied when a horse is part of the treatment team.

Biodiagnostics: The training of selected dogs to recognise life-threatening medical conditions, such as cancer and diabetic crises, at an early stage, allowing for successful management of the condition by conventional means.

All these aspects of our Society's activities are explained and described in more detail in the appropriate chapters of this book.

Engaging in this way with all these organisms, each with their own particular biology, raises the cogent and attractive question as to whether the active agents, enzymes, cytokines, immuno-stimulants and the rest, that these organisms produce, might be identified and processed by laboratory techniques, to provide us with an enhanced pharmacopoeia. A great deal of study of active agents produced or processed by bees and leeches, has been undertaken. The exo-enzymes secreted by maggots are under active investigation. The volatiles given off by patients suffering from various pathological states, such as cancer and diabetes, are also under scrutiny. 'Sniffer machines' are being developed to recognise specific 'marker' molecules at low concentrations. This must ideally be in collaboration with dogs being trained to identify the chosen 'markers', and the resulting intrinsic specificity fed into the machine programming.

Going down the route towards a 'magical new aspirin' at face value. runs counter to our philosophy of working with intact bio-complexity. A living organism is anything but a tablet. A maggot in a chronic wound will seek out those parts of the wound which provide it with optimal feeding, move relentlessly in the wound in this quest, engage in very efficient group-feeding with other maggots in the wound, produce heat to speed up the wound healing, use oxygen from the air as against from the wound bed, induce the production of cytokines to enhance production of host wound repair cells, produce exo-enzymes appropriate to the type of tissue (skin, fat, muscle) undergoing decomposition, free bacteria from their biofilm, engulf and digest them, thereby increasing its body weight (re-cycling organic waste) 50–80 fold, in 3 days!

There is an aspect of 'biotherapy' not listed above, but which is of fundamental importance to much of modern bio-research and development, and that is the bacterium. Numerous laboratory procedures depend on harnessing selected species of bacteria, and using their natural biology to produce quantities of a given desired product. Their DNA can be altered or added to, to give them further specific laboratory uses. If used in this way to create products of pharmaceutical value, this is a form of biotherapy. But it does not have the *bedside hands-on* aspect that is intrinsic to our other bio-therapeutic protocols.

We mentioned above that biological (natural?) 'research and development' has been active for 'millions of years'. This perforce takes us back to the very first bacterium, with zero antecedents, and enough integrity to withstand a hostile environment perhaps as formidable as that surrounding fumaroles in the deep oceans of today, where certain bacteria are still very much 'at home'. This first bacterium also had to reproduce within hours in order to survive and multiply. From a very early stage, clusters of a mono-culture of these bacteria would then have developed 'quorum sensing' and produced biofilm, with its powerful protective and exclusive attributes. Then such colonies of bacteria would have learnt how to interact with other colonies, themselves protected by their biofilm, and thereby the first multi-cellular organism, of a sort, would have evolved. This phenomenon we now name as a *microbiome*. But, microbiomes interact with other species, for good or ill, and in many ways are controlled by 'host' species, such as insects, that can for instance

preserve in an enclosed sac a mono-culture of organisms to provide them with vitamins.

We have lived for decades with the concept that all microbes are bad for us, and demand ever more powerful *Antibiotics*. We, by contrast, should be looking for new '*Probiotic*' mechanisms, that we can harness, and use in the whole arena of '*Biotic*' control (see for example the chapter on phagetherapy in this volume). We do not necessarily need to know the details of how these mechanisms work, any more than for instance we understand how a dog recognises cancer in a human being, or another dog.

But, we need to have the humility to recognise that nature's answers to the challenges of life, as against our mechanistic modern industrial endeavours, out-class us in most aspects of life. In addition, we need to realise that such mechanisms are ubiquitous, and could be harnessed, using our bio-therapeutic principles central to this adventure, to the enhancement of the well-being of our fellow human beings, the prevention and management of disease, and the nurturing of the environment we all live in.

In summary, biotherapy is challenging and demanding, but it is efficacious, relatively safe, low tech, low cost, and eco-friendly, while properly conducted, it is tremendously rewarding.