

LOOKING BACK – Celebrating making a difference

Editor's introduction

During the 70-year history of the Institute's Journal our overseas contributors have been an important source of articles. They provide an interesting insight into both the differences and similarities between Animal Technology in different countries and continents and a fascinating reminder of the way things have changed (or in some cases have remained the same). These papers have not been edited and appear in their original style.

Animal Technology at the National Institute for Medical Research: A Century of Innovation

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Based on an IAT/LAVA Congress 2013 Platform Presentation

Reprinted from ATW Volume 13.1 April 2014

Summary

Understanding the past to appreciate the present: A century of animal science and technology at the MRC NIMR.

As the MRC celebrates its centenary year this presentation takes a look back at the history of animal use at the National Institute for Medical Research. The development of key principles, techniques and design that improved animal welfare standards and helped shape the modern animal technology industry, along with the important scientific discoveries made using a range of species will be described.

Particular attention will be paid from the 1940s through to the 1970s, regarded by some as the 'golden age' of Animal Technology and science; this period saw some major advances in caging systems, breeding techniques, laboratory animal nutrition, animal technician training and education, the Laboratory Animals Bureau and animal house design to name just

a few. Insights into these developments and the key people who helped drive forward advances in animal welfare will be presented providing a fascinating account into how life in the 'animal house' has changed over the past 100 years.

Keywords: National Institute for Medical Research, centenary, advances, animal welfare

Introduction

The modern barrier maintained animal facility is controlled with computer monitored environmental conditions and staffed by highly trained technologists caring for animals housed in state of the art caging systems. However, it was not always like this and as part of MRC National Institute for Medical Research Centenary celebrations this presentation recounts a collection of articles, anecdotes and pictures that describe what life was like in the 'Animal House' and how certain technologies and practices evolved.

During the late 1940s the whole of the animal science and technology industry was beginning to rapidly develop and standardisation of feeding, maintenance, colony management, breeding and supply was taking shape.

In response the Medical Research Council (MRC) set up the Laboratory Animals Bureau (LAB) in 1947, later to become the Laboratory Animals Centre (LAC) in 1958. The main function of the LAB was to facilitate the standardisation of the supply of animals for research.

Up until then many laboratory animals were sourced from the commercial pet trade usually with inferior stock which often resorted to poorly funded researchers having to resort to buying large quantities of mice regardless of health and condition – the research industry was being supplied with inferior animals by unscrupulous breeders as the prime stock could be sold as pets for more money. It was therefore essential for Laboratory Animal welfare to take priority, not only to improve the standards of health and welfare for all species but to also supply a good standard animal for research.

Barrier Maintained Animal Facilities

The MRC National Institute for Medical Research (NIMR) has a long history of pioneering the use of barrier maintained animal facilities since it first recognised, in the early 1920s, the importance of keeping research animals at the Rhodes Farm facility free from any chance infection. The initial innovation was the introduction of a 'bathing house' that all researchers and care staff would use to wash in and change into protective rubber clothing before entering the dog compound.



Figure 1. Animal attendant wearing protective rubber clothing, standing at the entrance to the dog compound bathing house.

However, during the post-war years 1945–1950s building materials and labour were prioritised for rebuilding of war damage and new towns and with funds in short supply it was not uncommon for research animals to be housed in wooden sheds where disease spread easily.



Figure 2. A miscellany of huts and sheds that housed many of the animals at NIMR until early 1960s – NIMR Director Sir Peter Medawar referred to this as 'shanty town Mill Hill'.

Sir Peter Medawar made it his priority, when taking directorship of NIMR in 1962, to modernise all the animal units at NIMR, a project that was initiated by Sir Charles Harrington in the early 1960s. Sir Peter Medawar was adamant that strictly controlled purpose built animal facilities was important to help reduce pathogenic burden affecting animal welfare and experimental results.

The sound-proof dog unit was the first of the new units to be completed and was opened in 1966, there being a very good reason why it had to be priority and completely sound proofed!



Figure 3. The new dog facility incorporated kennels, indoor exercise passage, outdoor exercise yard, bathing room and it also boasted a state of the art hospital standard operating theatre.



Figure 4. Bath-time in the new dog facility. Beagles and greyhounds were both housed in the facility – the beagles being mainly used for Diabetes research and the greyhounds, which were ex-racing dogs, used for Osteoporosis research.

Due to an increasing demand, the dogs had been moved from their original wooden hut to a block of kennels on the 3rd floor of the south west wing in the main building where they also had an outside run.

This proved highly entertaining for the local youths, after closing time at the local public house, as they would stand on the road close to the building (at this time there was no perimeter security fencing) barking and whipping the dogs up into a frenzy of noise that was the source of many local complaints. It was therefore considered essential to design the new unit to contain all noise by the use of soundproofing that would absorb the noise while also making it comfortable for staff and dogs.

Apparently after moving the dogs from the main building into the new sound-proof unit the local inebriated youths would still bark but although they got no reaction, several weeks passed before all human barking ceased!

The next priority was to build a modern cat facility as originally the cats were kept in two wooden huts, one for breeding and one for holding.

In 1967 the new modern cat unit was built in the valley which incorporated stud male pens/breeding room and rearing pens as well as offices and staff showers/rest room over two floors. During its highest period of activity, the new cat units were producing over 1750 cats per year – approximately half of these would be for internal use and the rest would be made available commercially to other research institutions.

The demand for a good quality research cat was increasing not only at NIMR by the Physiology



Figure 5-6. Pictures of the old units – the cats were kept in racks of cages for stock and littering down but there was also a rotation system in place allowing the cats out for exercise.



Figures 7-8: The new NIMR cat facility circa 1969.

department which required 500 per year over 3 kilos in weight but also across the whole research industry and the Laboratory Animals Centre wished to take the MRC and the rest of the research industry out of the infamous cat market as many cats were being supplied by unscrupulous dealers with animals rife in parasites that was causing a national concern.

There was a substantial economic cost to running the cat unit but Doug Short MBE, FIAT, the original Chief Animal Technician at NIMR, insisted it solved the greater ethical problem of where and how to source quality cats and also provide them with the best possible welfare.

Specific Pathogen Free (SPF) Unit

Construction of the SPF unit started in 1969 and was completed, commissioned and ready for occupation in December 1972. The original stock animals were Caesarean-rederived germ-free rats and mice that were maintained in pressure isolators in the Gnotobiotics unit and later contaminated with suitable identified gut flora. Rabbits and Guinea pigs were introduced a few years later.

By late 1973 the SPF unit was producing over 10,000 mice and 2,500 rats per month and supplying nearly all the institutes' rodent requirements. The efficiency of the unit is reflected by the fact that the death rate among the 50,000 mice and 8000 rats housed was less than 0.1% compared to over 25% in the stocks previously housed in conventional units – the elimination of infantile diarrhoea in mice being the major contributory factor.

It is interesting to note that when the NIMR director Sir Peter Medawar first proposed the building of the SPF unit in the 1960s he faced opposition from certain elements of the scientific community for proposing that in the future all major biological research institutes re-establish their animal colonies on a 'specific pathogen free' basis and that the use of pure inbred strains and first generation (F1) hybrids would be the research models of choice.

It is well known that many within the scientific community still believed that the use of these animals was in some way unnatural or artificial and would give misleading results and not be representative of the characteristics of mammalian life.

A quote by Sir Peter Medawar sums up his foresight into what is today regarded as standard: *"The provision of SPF [specific pathogen-free] animals is not to be thought of as a great romantic adventure in the world of biological research, but as something that will in a few years' time be as commonplace as the provision of inbred strains is today"*.

Automation and feeding the rabbits

Another popular research animal at NIMR during the 1960–1980s was the rabbit which were to be given a new home in the soon to be developed SPF unit. However the original rabbitry is still very interesting for two reasons:

The first was the development of a new pelleted rabbit diet in 1959 – the previous rabbit diet was known as Diet18¹ which was developed by H.M. Bruce and A.S. Parkes in 1945 and was very successful. However some of the ingredients of Diet18, in particular linseed cake meal and bone meal, were prone to becoming rancid if stored for any length of time. The number of rabbits being used was increasing rapidly and it was impractical to order the amounts of the diet needed as fresh regular orders and if ordered in bulk it went rancid before it could be used.

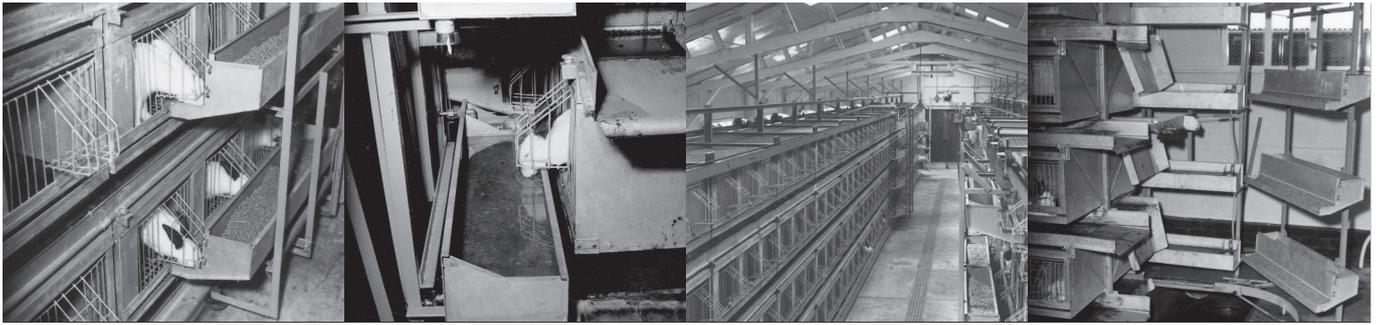
This problem was also being reported elsewhere in the industry with animals becoming lethargic and out-of-condition when fed Diet18 that had been kept in storage. As a solution for this problem Doug Short and Len Gammage (NIMR Senior Animal Technician) developed a new pelleted diet with a high protein content (with human food grade ingredients) less prone to deterioration and with the help of a nutritionist the new diet was trialled successfully with animals quickly improving condition and breeding performance improving.

The new diet was supplemented with hay for rabbits and could also be used for Guinea pigs when supplemented with hay and green-stuffs. This new diet was to become known as SG1 (after Short and Gammage) and was eventually made available commercially and the formula used in the industry for over 2 decades.

The only problem with the SG1 diet was that the animals found it so palatable ordinary stock animals became fat as they would not stop eating it when fed via a conventional hopper system and it was thought that feeding little and often was too time consuming for the technicians.

After a visit to a local poultry farm where he saw a chicken battery with an automatic feeding system, Doug Short, being the visionary that he was, decided that the way forward in the animal house was automation. Thanks to the help of the NIMR engineering department, an automatic chicken battery was converted into a fully automated feeding and watering system for the rabbit facility.

In this converted chicken battery the food hopper would go around a track on the outside of the rabbit cages (672 cages in total) and stop for short intervals at each cage, this would then be followed a few minutes later



Figures 9-12. Automated rabbit feeding, watering and cleaning system.

by the water trough on the same track and re-filled from the mains water supply after triggering a valve.

Not being content with just automated feeding and watering, Doug Shorts' modifications also incorporated fully automated cleaning – the rabbit cages having a grid bottom floor that allowed urine and faeces to drop through onto a plate glass shelves that were bonded together to run the length of the rack and a squeegee was attached to the hoppers that pushed the rabbit excreta along the glass shelf and emptied it into a drain where it was flushed into the sewers.

This system had no adverse effect on the animals breeding or temperament and the rabbits could not gorge themselves on the food constantly. It also reduced labour considerably and odours.

Rodent cage design and standardisation of animal feeds at MRC NIMR

When the Small Animals Department at Rhodes Farm, Mill Hill, was built in the early 1920s the rats and mice were kept in wooden boxes, made by an on-site carpenter. These original wooden boxes had no food hopper or water bottle holder as the animals were fed a diet of wet mash only – dried, cubed feed was not yet being commercially available.

Some mice were also kept in large glass bowls (similar to goldfish bowls) which was standard practice in the industry.

Until the years following World War 2 (WW2) – mice and rats were fed this diet of wet mash which would be made by the animal care staff, incorporating pretty much anything they could get their hands on from local food suppliers and the works' canteen kitchen waste, supplemented where possible with dried milk and egg products and margarine – there was no provision for water bottles and the mash would be changed daily

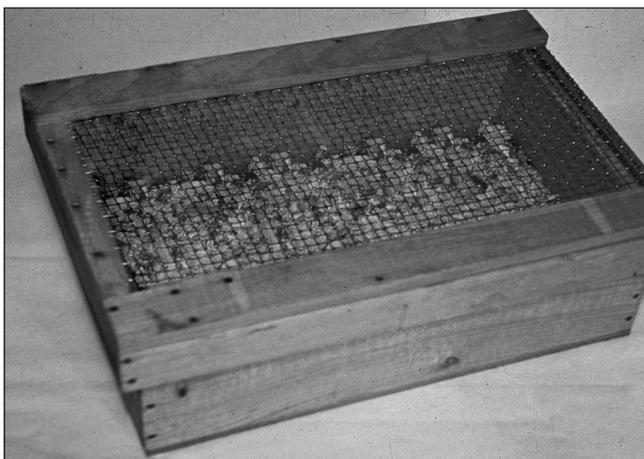
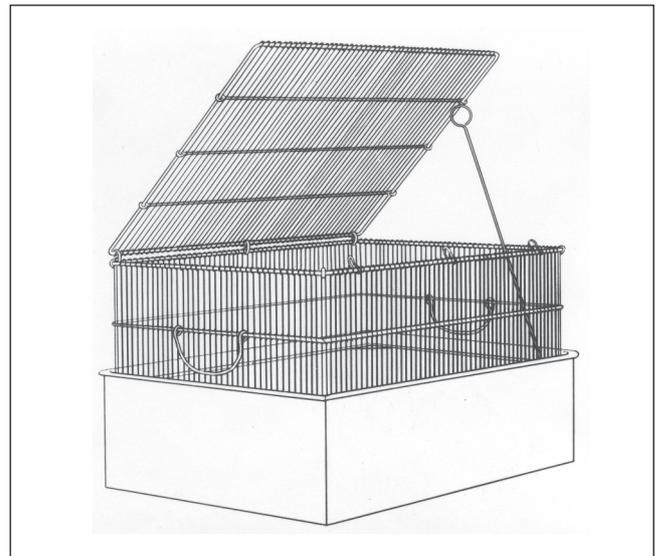
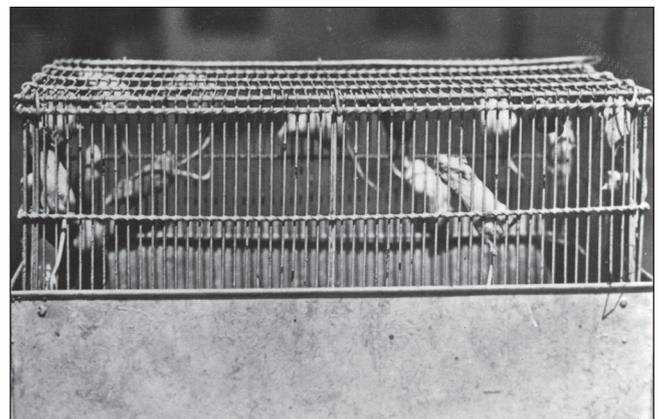


Figure 13. Replica of an early wooden mouse cage.



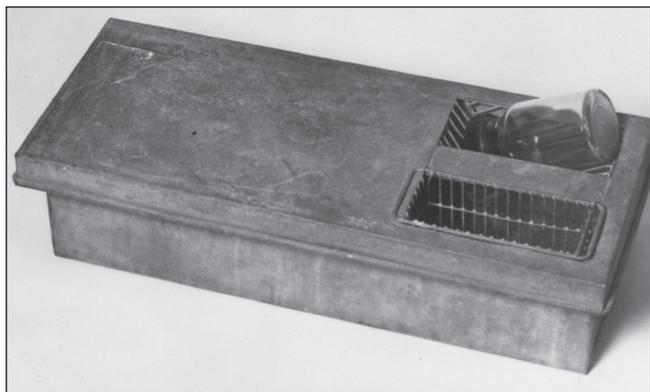
Figures 14-15. The first NIMR metal cages.

and fed in rations to lactating mums first, followed by pregnant breeders and young weaners with the stock animals being fed what was left. However post WW2 the necessity to change because of food shortages and lack of manpower – changing the soiled wet mash daily was seen as both time consuming and wasteful. The wet mash also soiled the animals' cages and bedding so was far from ideal from a welfare perspective.

The wooden rodent boxes had limited life as the animals were quite adept at gnawing their way out, so new metal caging was designed and implemented and by 1930 both the Hampstead laboratories and Rhodes Farm small animals department were now using metal rodent cages as standard. These cages were still made on site as cages made commercially were still not readily available, food and water hoppers were not incorporated into the design as the animals were still being fed the diet of wet mash.

However, by 1945 Sir Alan Parkes and Hilda Bruce had started working on standardisation of the animal feeds by developing compound diets in a cubed and pelleted form that would be suitable for all standard small laboratory animals. In 1949 and after nearly five years of research at NIMR, a diet called 41B went into commercial production as the first complete un-supplemented dried rodent diet for mice and rats – and was used in the same formula industry wide for over 3 decades.

The new standard dried and cubed rodent diets now meant provision of separate water was a necessity as was an easier method of feeding the diet. As metal was becoming easier to source post WW2 cages were being made out of zinc – the original zinc boxes just had a perforated lid which made for a very cold and damp environment in the winter for the animals. These boxes were adapted for inclusion of a small diet hopper and water bottle holder. The first water bottles used were actually ink bottles with a small rubber bung and spout. This also caused the problem during the winter months of the water bottles freezing as the animals were kept in huts with little or no environmental control/heating.



This led to a purpose built rodent box designed in the late 1940s by NIMR Animal Technicians and then Senior Technician, Doug Short with a bottle and food hopper. These cages were still made on site as required and were seen as a revelation, in terms of animal welfare, as the animals could be checked regularly without removing lids and fed/watered daily with a minimum of fuss and no wet mash to soil the cages.

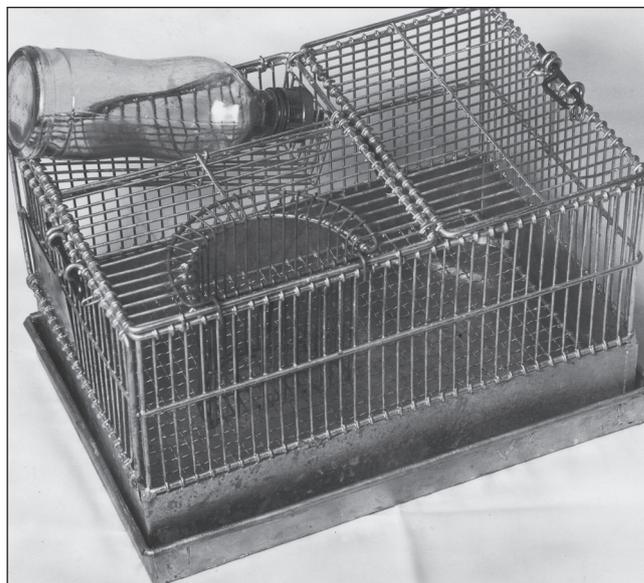


Figure 16. A 'modern' style rodent cage circa 1950s.

Standardisation of animal supply and training

The MRC had been breeding and supplying other research institutes for some time but were unable to meet demand so they set up a system of regulation and an accreditation scheme for commercial breeders to the research industry. This accreditation scheme was developed at NIMR and based on the knowledge, expertise and experience of the animal care team and senior researchers Sir Alan Parkes and Hilda Bruce.

The accreditation scheme was initiated for regulating laboratory animal supply nationally. Commercial breeders were invited to apply for accreditation and most breeders of repute did so.

The accreditation scheme demanded strict regulations such as

- stock must be raised primarily for research use
- breeding stock must be self-contained
- strict standards of hygiene should be implemented
- annual inspections will be carried out

The Laboratory Animals' Centre published the Mouse Newsletter (until the mid-1970s) detailing all mouse strains available to the researcher and also maintained 15 of the commonest laboratory mouse strains at NIMR which it supplied to institutes and commercial

breeders with a nucleus of stock together with instructions on how to breed using the 'traffic light system' in order to maintain genetic integrity.

**SERVICES OFFERED BY THE
LABORATORY ANIMALS BUREAU
(MEDICAL RESEARCH COUNCIL)**

In 1945 a committee appointed by a number of scientific societies prepared a memorandum on the supply of experimental animals. As a result of this, the Laboratory Animals Bureau was set up in 1947 to act as a clearing house for information about the production, supply, maintenance and use of laboratory animals. The information it has collected is offered to all those who work with the use of animals; in particular the Bureau provides the following services:

SUPPLIES OF ANIMALS.
The Bureau does not itself supply animals, but those who notify the Bureau of their requirements of any species will be given the names of suitable suppliers (a convenient *Registration Card* is obtainable from the Bureau for this purpose).

1. Guinea Pigs, Mice and Rabbits (Accredited Stocks).
In order to exercise some control over the quality of commercial stocks, which form a high proportion of the total supplies of these species, a system of accreditation has recently been introduced. To become accredited, a breeder must:—

- Raise stock predominantly, if not entirely, for laboratory use.
- Maintain a closed colony, subject to a period of quarantine if, for any reason, it is necessary to introduce outside stock.
- Supply to the laboratory direct and not from or through any agent or dealer.
- Observe standards in the management of his stock which are consistent with the production of free-class stock, with particular emphasis on the prevention and control of infection.

In return are offered facilities for laboratory investigations and technical advice, favourable scales of rationed foodstuffs and other advantages. A register of accredited breeders is available on request.

Breeders may justifiably look to users for co-operation in the working of the Accreditation Scheme, and the following points deserve particular mention:—

- Whenever demand is reasonably steady, or predictable, contracts or orders in advance should be placed. An unexpected demand, especially if heavy, can often only be met by "buying in"—a practice which is not legitimate for the accredited breeder. Even if the acceptance of regular supplies leads to occasional supplies, it will usually be found to be economical over a period in view of the better quality to be expected.
- Reports on the quality of animals obtained, whether favourable or adverse, are the chief means by which the Bureau can keep a check on accredited stocks (and for that matter other supplies). Users are asked to send such reports to the Bureau whenever occasion demands—they will be treated as confidential.
- Many breeders are in a small way of business, and prompt payment of accounts is a matter of great importance to them. For the same reason, immediate return of travelling boxes (where reasonable) should be the rule.

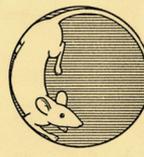
2. Monkeys.
Arrangements exist for obtaining certain species of monkeys from West Africa at prices generally below that of Indian monkeys. The common ones are the baboon (*Papio* spp.) and the green monkey (*Cercopithecus* spp.), but others can be had. Requirements should be notified to the Bureau as long as possible in advance. It is not intended to import these monkeys during the winter months.

3. Dogs and Cats.
The supply of these animals is constantly difficult and the prices asked by dealers are often higher than many laboratories consider reasonable. The Bureau is able to obtain supplies from time to time; enquiries for these should state the price which the laboratory is prepared to pay.

4. All other vertebrates.
The Bureau is able to put users in touch with sources of supply of other vertebrates, both native and exotic, and including non-accredited guinea pigs, mice and

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MOUSE NEWS LETTER



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The LAB initiated annual conferences for exchanges of information for animal technicians and scientists on all aspects of laboratory animal care and welfare; but there was also a spontaneous movement amongst animal technicians nationwide that resulted in the formation of a new technical organisation, The Animal Technicians Association (ATA) at the 1950 LAB conference – this new organisation with Sir Alan Parkes as its first president would put the provision of training for animal technicians as a priority and put an end to the belief which had prevailed for too long that the work of the animal technician was an unskilled occupation.

"FEEDING AND BREEDING OF LABORATORY ANIMALS."

A list of papers from the President's (Dr A.T.A.) Laboratory, to date, on this subject. References are to the *Journal of Hygiene*:

No.	Species:	Title of this particular paper.	Author(s)	Year.	Reference J. Hyg; Camb. pp.
I	Rat & Mouse.	Cubes & cube containers.	PARKES, A.S.	1946	44, 491-500
II	Rabbit.	Growth & maintenance without fresh green food	BRUCE, H.M. and PARKES, A.S.	1946	44, 501-07
III	Guinea pig.	(General)	BRUCE, H.M. and PARKES, A.S.	1947	45, 70-87
IV	Rabbit.	Breeding of, without fresh green food.	BRUCE, H.M.	1947	45, 169-172
V	(General)	Record-Cards for the Analysis of Breeding Performance.	BRUCE, H.M. and PARKES, A.S.	1947	45, 327-32
VI	Mouse.	Breeding of,	BRUCE, H.M.	1947	45, 420-30
VII	Mouse.	Breeding of: (Testing of diets, etc.)	BRUCE, H.M. and EMMENS, C.	1948	46, 434-7
VIII	Guinea pig.	Breeding of,	BRUCE, H.M. and PARKES, A.S.	1948	46, 434-7
IX	Mouse & Rat.	Complete Cubed Diets.	BRUCE, H.M. and PARKES, A.S.	1949	47, 202-8
X	Monkey	A Compound diet for,	SHORT, D.J. and PARKES, A.S.	1949	47, 209-12

Abstracts from the Scientific Literature.

LABORATORY ANIMALS. Feeding and Breeding of,

The following brief abstracts of the two latest papers in this now classic series, will be of lively interest to members.

(IX) A Complete Cubed Diet for Mice and Rats. by H.M. Bruce and A.S. Parkes. (*J. Hyg., Camb.*, 1949 (June), 47, No. 2, pp. 202-08)., with 5 tables, 5 figures and 12 references.

The authors describe carefully controlled experiments dealing with the intensive reproductive behaviours and rapid growth-rates of mice and rats. An important side-issue was the finding that resistance to *Salmonella* infection is poor with oats-containing dietaries, better with other cereals and good with wheat. Comparative detailed analysis of four diets are given, and cubed diet "41", unsupplemented is recommended as being the standard diet for all mice and rats maintained at the National Institute for Medical Research.

(X) Monkeys. A Compound Diet for, by D.J. Short and A.S. Parkes. (*J. Hyg., Camb.*, 1949 (June), 47, No. 2, pp. 209-12).,

Dr. Parkes, assisted by the Chief Technician in charge of the Medical Research Council Laboratories (now at Mill Hill), presents the results of experiments upon a (limited) number of rhesus and mangabey monkeys. Growth, pregnancy and lactational performances, were compared and statistically analysed, for several dietaries. It is concluded that cubed diet "41" (as described also in paper IX), supplemented only by green food and water, is nutritionally adequate, psychologically acceptable, and cheap enough to be recommended as a standard maintenance diet for experimental laboratory monkeys.

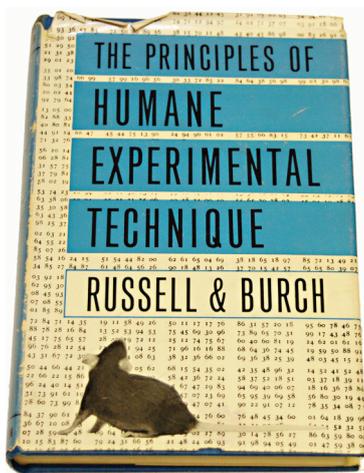
Figure 17. List of papers printed in the 1st Journal of the Animal Technicians Association by the President Dr A.S. Parkes FRS.

Although Sir Alan Parkes and Hilda Bruce set the foundations for the standardisation of the Animal Technology industry with their work on diets and breeding, NIMR animal technicians led by Doug Short and the Animal Technicians Association (ATA) (later to become the IAT – Institute of Animal Technology)

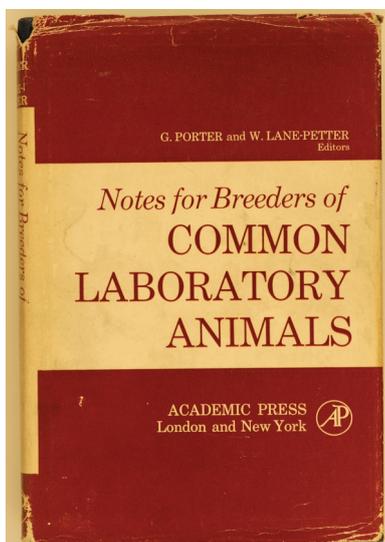
spearheaded the development of modern standards and pioneered many advances that would not only improve standards at NIMR but also help establish the standard for the whole industry

The late 1950s and early 1960s also saw the publication of many important books following the formation of the LAB and ATA as there became an ever increasing demand for the sharing of knowledge:

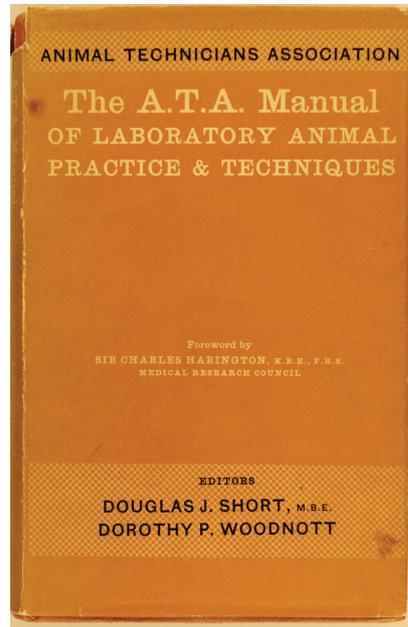
1959 – publication of Russell & Burch book ‘The Principles of Humane Experimental Technique’ which introduced the concept of the 3Rs (Replacement, Refinement and Reduction) and they credit the MRC’s LAB for carrying out the 1st systematic survey of animal use in the UK and the work carried out by the ATA for improving the efficiency of animal technicians and encouraging communication.



1961 – Following the ‘3Rs’ book the MRC’s LAC published the 1st practical guide for commercial breeders and those involved in their care – the MRC/LAC accreditation scheme developed at NIMR formed the nucleus for this book.



1962 – Publication of the first concise textbook of Laboratory Animal Technology based on the ATA education syllabus with 24 chapters covering everything from animal handling to the law, all but 6 were written by NIMR or LAC people.



So the Animal Technology industry was by now a modern forward thinking profession with the skilled animal technician regarded as an important asset to biological research and a quote by Dr. Lane-Petter, director of LAC in 1962 sums up the advances perfectly:

The status of animal technicians has, during the past fifteen years, undergone a major revolution. During this period the very title, animal technician, was coined. These people are technicians in the sense that they practise techniques that have to be acquired by considerable training. Their work is an essential part of the biological team

Conclusions

Animal Technologists and care staff across the whole Biomedical industry have been responsible for some ground-breaking advances in laboratory animal science and welfare in the last few decades. This is just a small snapshot of advances and innovations made in the past 100 years at MRC NIMR that have contributed towards improved laboratory animal welfare across the whole industry – advances and innovations driven forward largely by animal care staff working alongside researchers and veterinarians. Undoubtedly a similar story could be told for many establishments across the country.

References

- Bruce, H.M.** and **Parkes, A.S.** (1946). Feeding and breeding of laboratory animals: growth and maintenance of rabbits without fresh green food. *Journal of Hygiene, Cambridge, Vol.44 pp. 501-507*