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Pandemic Preparedness in Animal Facilities

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Coping ethically with dramatic changes such as those occurring in times of pandemics is a difficult challenge for animal facilities and for researchers using animals for scientific purposes. Managing such situations is impossible without a specific contingency plan. However, because pandemics are rare events, they have not been included in some disaster plans. We present here various ways to manage the broad and rapid changes that may be necessary during a pandemic, focusing on actions for optimizing the conservation of animals while ensuring continuous high standards of animal welfare. The proposed approach is graduated and encompasses research, researchers, animal caretakers, supply chains, and logistics.

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On 31 December 2019, the first suspected cases of an epidemic of viral pneumonia, determined as severe acute respiratory syndrome, of unknown etiology was reported in Wuhan, China.[8] The pathogen is a new virus from the *Coronaviridae* family, SARS-CoV-2,[14] and is responsible for the infectious respiratory disease known as COVID-19.[13] As of the end of April 2020, half of the people on earth were confined at home, resulting in a novel dramatic social and economic crisis that affects all parts of our society, including animal facility activities.

The origin and reservoir for SARS-CoV-2 was probably an animal, and even though SARS-CoV-2 is very close to a virus found in a bat,[3] the species underlying transmission of the virus to humans has not yet been definitively identified. No scientific evidence to date suggests that pets or and livestock contribute to the spread of the SARS-CoV-2 virus, even though some pets have become infected, and some get ill.[6,12] Nonetheless, the virus raises several concerns for most animal facilities in regard to animal-to-human transmission and animal health.

Activities in animal facilities have been and remain highly disturbed by this pandemic, mainly because of personnel unavailability, forced termination of procedures (because researchers and technicians cannot reach the facilities), and potential shipment delays. Plans for continuing critical functions, mainly providing animal care and the breeding of noncommercially available lines, should be implemented according to an animal resource contingency plan. Depending on the country, type of animal facilities (e.g., private, institutional, breeding, commercial) and institutional mandates, such contingency plans might not have been available at the start of the pandemic. Indeed, the current literature mainly describes risks such as power outage, flood, fire, severe storms or earthquakes, which are local and abrupt. For example, Charles River Japan overcame many such disaster situations in their production facility, but only the influenza outbreak of 2008 triggered them to develop a crisis management plan and a business continuity plan.[7] Although rarely adapted to pandemics, basic preparedness concepts and terminology have been described and might be helpful to customize specific plans.[9,10] The challenge is to overcome a nation- or worldwide situation extending over a long period. In the first decade of the 21st century, the multiple warnings of Influenza and SARS virus epidemics sensitized governmental agencies to the need of pandemic readiness planning and guidelines were published.[11] Here we describe the main objectives of such plans, adapted to a worldwide pandemic, from the viewpoint of an academic facility.

The functions of animal facilities cannot easily be stopped due to emergencies such as the COVID-19 pandemic, even though the response may involve stopping all noncritical activities and quarantining workers. If these maintenance stop, the damage that occurs could be catastrophic in the short-, medium-, and long-term. Therefore, a good contingency plan for animal facilities is of utmost importance for maintaining what is required for a swift restart of activities when the situation returns to normal (or near-normal) conditions. Topics to be addressed range from experimental procedures that were ongoing when the quarantine began to conservation of all breeding and unique research models that are kept at the facility. In addition to these activities is the regular engineering maintenance of the facility, which vary depending on the facility's age.

The goal of plan is to prepare realistic and essential measures that can be implemented step-by-step, if and when the situation deteriorates, ensuring the required minimum of animal care and welfare while reducing non-essential activities usually performed at a facility (e.g., genotyping, experimental data collection, starting new experimental procedures, importing or exporting animals).

Pandemic Preparedness Plan

Anticipating a pandemic is the best-case scenario, but this phase might be as short as a few days. Such a situation happened in some French animal facilities, which had only a week implement the contingency plan. Indeed, just the day before the general quarantine started, high-ranking officers of the government claimed that a general quarantine was not a preferred option.[2] Before or at the implementation of the plan, resources necessary to the continuity of activities (such as food, bedding, enrichment stocks, different washing products if needed, and all disinfection and PPE supplies) should already have been accumulated to the level required for normal operations but with a reasonable degree of certainty regarding the likelihood

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of replenishing the stocks in a timely manner. Except in special cases, storing many months-worth of these items is not necessary. Indeed, during pandemics, essential logistics and activities may continue, and panic ordering can result in shortages and the overwhelming of local storage capacity. In some cases, additional storage capability may be required (e.g., outgoing waste that cannot be collected; freezer space for animal cadavers). PPE supplies might be redirected (either voluntarily or by mandate) to emergency units and other medical staff, as occurred in many animal facilities in France and internationally just a few weeks after the start of the Covid-19 pandemic.

In addition, at this stage of preparedness planning, a list of voluntary personnel who are proficient in animal care (i.e., an emergency team) might be drafted. This team would include persons who use the facility on a regular basis for experimental purposes and who are proficient in animal care and facility internal procedures. However, these persons cannot fully replace the animal caretaker team and should provide support only when supervision is available.

Animal Resource Contingency Plan for the Continuity of Critical Functions

The first objective of contingency plan must be personnel safety. The second objective must be animal welfare. The contingency plan's main purpose is to prepare measures and steps to be taken in response to the potentially decreasing number (or proportion) of animal caretakers who may be unable to come to work (e.g., persons calling in sick, caring for children at home because of school closures, supporting others with underlying conditions, self-isolating, encountering public transportation issues). Several levels, which depend on the proportion of staff reporting for work, should be defined (Figure 1).

Some animal depopulation might be done to decrease the workload and avoid critical harm to animal welfare due to the lack of personnel.[5] A plan for how to accomplish this situation can be defined ahead of any pandemic and will allow appropriate decisions to be made. For example, a decrease in staffing may be coupled with adaptation of an activity, such as a modification in the cleaning regime. If the staffing level falls further, then controlled depopulation could occur—for example, reduction of the animal population by 25% if the proportion of available staff remains below 75% for a prolonged period. However, this measure, if taken, should attempt to spare all irreplaceable models and lines. Plans for the order of priority should be made in advance in conjunction with the study or project manager who owns or is responsible for these models or lines, unless the welfare of the animal is compromised (or is likely to be). In some cases, mass depopulation may happen only upon written orders from the highest levels of the governing bodies of the institution governing bodies at which the animals are held. Such decision would not normally be made at the facility level but may happen at the black level of the plan (Figure 1).

All personnel attending the facility should be, in one way or another, authorized and even encouraged to vary the days and shifts on which they work, to decrease the contact between them, providing for their own safety through social distancing. This provision may also be necessary for other practical reasons (e.g., transportation and childcare issues). In the facility, assessment of the working space, air-change regimens, PPE use, and staff movement through an area are should be considered when instructing employees regarding effective social distancing and behavior.

At no point during the pandemic should any of the animal care staff decrease the quality of any actions usually taken to ensure animal care and health. Ancillary activities (e.g., genotyping) may be decreased or stopped, but the quality of care to animals must not be compromised. Indeed, the aim of the plan is to return to normal activities in the future. Moreover, health-related requirements in the context of the pandemic might be enhanced and more stringent in some facilities, if normal operating procedures are insufficient for pathogen containment between staff members. For example, administrative areas should keep all doors open to avoid handling door knobs, and employees should not eat together in the same room and at the same time.

Implementing the Contingency Plan

The first step in implementing a contingency plan is to identify risks due to absence of animal caretakers and to define clearly who would be involved in the emergency response team.[4] These risks may arise from different causes, such as people calling-in sick or self-isolating, those relying solely on public transportation, and parents whose child care situation may mandate their absence. When the contingency plan is formulated, persons in the last 2 categories should be identified and listed.

Figure 1 shows an example plan for an organization that incorporates several levels of contingency, which are driven by animal caretaker availability, starting from a normal staff of 'x' animal caretakers. The proposed situations and actions at each step of the plan are incremental and cumulative. At any given level, the measures taken at the preceding levels remain in effect.

Green level: quasi-normal work (until 15% of staff is absent). At this lowest level of the contingency plan:

- Researchers and technicians who work in the facility regularly are advised regarding the components of the contingency plan and that it has been implemented. Given that the plan has been approved beforehand by the governing bodies of the institution, no further authorization for implementation of the plan is required unless the red level is reached.
- The back-up team, if any, is contacted and further trained for any changes in animal caretaking operations (e.g., cage changing, cage washing, dispensing of food and bedding).
- Essential stocks are checked thoroughly and replenished if needed.
- Quasi-normal functioning may continue for any duration. However, social distancing and increased hygiene must be strictly observed to avoid infection of staff at the facility.
- Staff activity and movement should be adapted to implement social distancing within the facility and animal rooms.
- Enhanced use of PPE and increased hygiene should be observed.
- Lists of animals (or categories of animals) that would be subject to euthanasia at the red level are prepared.
- Additional categorical lists of animals are prepared in consultation with projects managers in view of potential escalation to the black level. Freezing of sperm of embryos might be proposed as well, if feasible, although according to best practices, this should have been done previously.

Yellow level: somewhat decreased operations (until 40% of staff is absent).

At this first escalation in the contingency plan:

- Staff now work in multiple shifts to reduce the risk of in-facility contamination of employees, which would result in simultaneous absences. This accommodation might be implemented by having employees work only every other week or in small groups (2 or 3 persons) during given days, with a re-organization of the work schedule.

CP level	GREEN	YELLOW	ORANGE	RED	BLACK
Proportion of people not attending	<15 %	<40 %	<60%	<75 %	>85%
Animal caretaker workforce	<= X persons	X to Y persons	X to Y persons	X persons	0-X person
Animal facility operations	NORMAL	SOMEHOW LOWERED	LOWERED[§]	HIGHLY LOWERED	CEASE OPERATIONS
Backup team[#]	No	No	Yes	Yes	No[$]
Backup team workforce	0	0	>=X[§]	>=X[§]	=0[$]

Figure 1. Possible components of a contingency plan; [#], predefined list; [§], all people might not attend at the same time; [$], potential step if members of the backup team are unavailable.

- No new experimental procedures may start.
- Routine breeding is stopped.
- The cage-change frequency may be prolonged, especially when cages each contain only a few animals. This accommodation applies only in facilities that use fixed-period cage changes (such as every week, regardless of the housing density) during normal operations.
- Except in special cases (e.g., research on the pandemic pathogen), all import and export of animals ceases.
- Daily monitoring of animals on weekends may be modified and decreased.

Orange level: markedly decreased operations (until 60% of personnel is absent).

At this contingency level:

- For all breeding pairs, new litters are euthanized as soon as detected.
- Experimental procedures may be stopped as decided and prioritized in consultation with the project managers, depending on the availability of additional animals for future use.
- Nonessential animals (e.g., breeding lines that can be recovered from commercial vendors) may be stopped.
- A backup team is formed to reach the minimal number of full-time equivalents. Some persons on this team may work part-time, provided that the required coverage is reached.
- Monitoring of animals on weekends may be further modified and decreased.

Red level: extensively decreased operations (until 75% of staff is absent).

At this final level until general cessation of operation:

- All lines go to minimal maintenance (only young stock is kept for future breeding). New litters are euthanized as soon as detected.
- Animals are monitored on weekends only as possible, according to staff availability (i.e., pandemic-related absences).
- Progressive cessation of ongoing experimental procedures, with project manager involvement; plans are not decided by the facility staff only. Animals are moved to other facilities (when possible) or euthanized.

Black level.

- When over 85% of personnel are absent, further termination of animals would follow the procedure identified when the contingency plan was first developed and implemented.
- Implementing this step will depend on the exact number of regular and back-up staff available to work and on the actual welfare condition state of the animals.
- Mass depopulation might be necessary, but only based on written orders from the highest levels of the governing bodies of the institution housing the animals. This process should be graduated, starting first with lines that are frozen and recoverable and then, according to priority, with single-deletion or genetically modified lines.

Why Is Depopulation of Animals Usually Required?

As reported in the AVMA Guidelines (2019),[1] "… history has shown that the typical research institution will not depopulate as a default in the face of […] unfolding severe situations, but will […] act to recover from any event, including prioritizing the preservation of surviving animal populations. Experience shows that where this approach has failed, the situation will be rapid, of overwhelming scale, and unpredictable with respect to degree of consequence."[1] Although potentially with high monetary and psychologic damage to researchers and animal caretakers, some animal depopulation might be necessary to decrease the workload of animal caretakers. In addition, animal depopulation is needed because the researchers who initiated the experimental procedures are forced to abandon them and the corresponding animals. These animals may often require euthanasia, depending on their status procedures. In any case, the main driver of this depletion is to avoid retaining animals that cannot be given appropriate care. Obviously, with a decrease in the work force available at the facility, necessary tasks, such as cage changing and animal monitoring, become difficult to maintain. The direct consequence may be a decrease in focus, because of a lack of time, on animal welfare. Given that such poor care is ethically unacceptable, the only solution resides in diminishing the number of cages to a level consistent with acceptable animal welfare. Figure 2 illustrates this matter by using

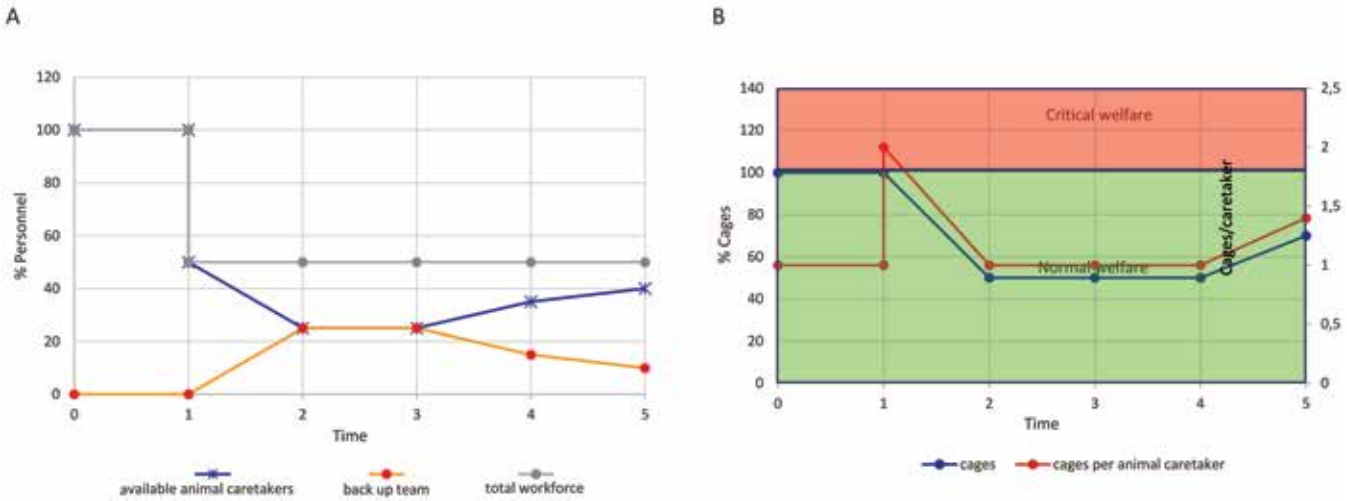

Figure 2. Pandemic-related variations in staffing and possible consequences on animal welfare. (A) Examples of variations in personnel availability during a pandemic with lockdowns. (B) Possible consequences of staff shortage on animal welfare.

theoretical parameters. When personnel availability is at 100% (Figure 2 A, period 1), the cage burden per caretaker (Figure 2 B, orange line) is compatible with normal animal welfare (Figure 2 B, green zone). When the contingency plan is first implemented, a loss of personnel due to team splitting or unavailability (Figure 2, blue line, period 2) results in a dramatic increase in the number of cages per caregiver, potentially reaching a critical level and affecting the animal welfare zone (Figure 2 B, red zone, beginning of period 2). To return to the zone of acceptable animal welfare, 2 solutions are available—depopulation of animals (cage levels, Figure 2 B, blue line) and activation of the back-up team (Figure 2 A, orange line)—to keep a sufficient workforce (Figure 2 A, gray line). Depending on local parameters, all combinations are possible. The best-case scenario is having a back-up team large enough to avoid euthanasia of animals. Nevertheless, this situation arises only if the back-up team is sufficiently large and adequately trained to counter the lack of availability of primary care staff due to the pandemic. During period 3 (Figure 2 A and B), depopulation and/or team backup is sufficient to maintain acceptable animal welfare. However, loss of additional personnel (e.g., due to sickness) and a subsequent critical welfare level might occur. If additional back-up personnel are not available, depopulation again becomes necessary. Conversely, an increase in personnel availability (e.g., due to release from quarantine, personal arrangements) will improve both animal welfare and caretaker workload (Figure 2 A and B, periods 4 and 5). At period 5, a slow increase in animal facility activity might be considered, to smooth the post-pandemic period.

Conclusion

Coping with global disasters such as pandemics in animal facilities is undoubtedly one of the greatest challenges for animal facilities and a grave situation for animals, animal caretakers, and research. Preparedness should be the gold standard for facility managers, but depending on the local context and conditions, widely differing levels of preparedness were present at the onset of COVID-19 pandemic based on review of professional networks. The quarantine of researchers resulted in the cessation of ongoing studies and not starting new ones. However, the subsequent decrease in activity was generally not sufficient to compensate for the lack of availability of trained animal caretakers, resulting in the need for some degree of animal depopulation. This action has high ethical, psychologic, and financial consequences, but based on review of professional networks during the first weeks of general self-isolation, depopulation seemed to be the response adopted most often—first, because many researchers were not available to continue use and management of animals on study, and, second, to avoid critical animal welfare problems due to shortages of animal caretakers.

The contingency plan should include measures for resuming normal activities. Initiating new experiments should be scheduled and prepared for in advance, using the same logic as for the contingency plan but in a reverse order. A prepared progressive restart should be used to prioritize rationally and to communicate in a timely fashion. During the acute phase of a pandemic and during the resumption of normal (or near-normal) operations, weekly communication with every researcher, technician, and engineer regarding the current situation and future plans. This communication will reinforce trust in the efficacy and fairness of the plan and the swift and best possible subsequent resuming of operations.

This unprecedented worldwide population quarantine resulted in a ripple effect in which the decisions made had ramifications in multiple directions. Local recovery from pandemics requires careful planning to protect the safety of staff and animals. A prolonged recovery will affect researchers and subsequently the funders of such research. Furthermore, as recovery starts, external supply chains that service the research communities and the delivery of key goods will be additional considerations. Analysis of responses to the current pandemic will influence how facilities plan for such conditions in the future, and new approaches will be adopted to improve ever-changing business contingency plans.

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